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Bu dergi daha önceden *İnönü Üniversitesi Tıp Fakültesi Dergisi* **ismiyle yayınlanan derginin devamıdır.**
This journal was formerly published as ***Journal of Inonu University Medical Faculty*** and is the continuation of it.

AMAÇ ve KAPSAM

Turgut Özal Tıp Merkezi Dergisi (ISSN: 1300-1744) İnönü Üniversitesi Tıp Fakültesi'nin bilimsel içerikli resmi yayın organıdır. Mart, Haziran, Eylül ve Aralık aylarında olmak üzere dört sayı yayınlanmaktadır. Turgut Özal Tıp Merkezi Dergisi'nin hedefi tıp alanında yapılan, bilimsel açıdan nitelikli ve literatüre yeni bir katkı sunacak olan klinik ve deneysel araştırma yazılarını yayınlamaktır. Bölgesel sıklık ve özellik gösteren hastalıklarla ilgili yapılan çalışmalara değerlendirme ve basım aşamasında öncelik verilir. Bunun yayında, derginin hedef kitlesinde yer alan hekimler ve sağlık profesyonellerin eğitimine ve pratiğine katkı yapacak ve yazarlarla okuyucular arasındaki bilimsel iletişimi ve bilgi birikimini artıracak olan derleme yazıları, olgu sunumları, editöryal yorumlar, editöre mektuplar derginin kapsamına girmektedir.

Derginin yayın dili Türkçe ve İngilizce'dir. Dergiye gönderilen makaleler bağımsız hakemler tarafından çift kör hakemlik değerlendirme sistemine göre değerlendirilmektedir. Dergiye makale yazımı ile ilgili kurallar dergimizin web sitesinde (www.totmdergisi.org) ve yayınlanmış sayılarında mevcuttur.

Çevreyi ve doğayı koruma sorumluluğu çerçevesinde, derginin basılı nüshası sınırlı sayıda üretilmekte ve baskı asitsiz kâğıda yapılmaktadır. Ancak dergide yayınlanan tüm yazıların özet, tam metin ve diğer tüm dergi içeriklerine www.totmdergisi.org adresinden ücretsiz olarak ulaşılabilmektedir ve yazılar indirilebilmektedir.

Derginin mali giderleri İnönü Üniversitesi Tıp Fakültesi tarafından karşılanmaktadır. Dergiye gelir sağlamak amacıyla, bilimsel çerçevenin ve etik kuralların dışına çıkmayan ticari duyuru ve ilanlar dergide basılabilir. Dergiye ilan vermek için Editör ofisine başvurulmalıdır.

Baskı İzinleri: Baskı izinleri için başvurular dergi editör ofisine başvurulmalıdır.

İndekslenme: Türk Tıp Veri Tabanı, Türkiye Atıf Dizini, Index Copernicus, Directory of Open Access Journals, Türk Medline, EBSCO, Google Scholar, Akademik Dizin, Dergi Park

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Bu dergi daha önce ***İnönü Üniversitesi Tıp Fakültesi Dergisi*** ismiyle yayınlanan derginin devamıdır.

AIMS and SCOPE

Journal of Turgut Ozal Medical Center (ISSN: 1300-1744) is the scientific official journal of the Inonu University School of Medicine. It is published quarterly March, June, September and December. The essential aim of the Journal of Turgut Ozal Medical Center is to publish scientifically high quality clinical and experimental research articles on fields of medicine which can contribute to the literature data. Manuscripts on regionally frequent and specific diseases will be prioritized during evaluation and publication stages. In addition, review articles, case reports, editorials, letters to the editors and manuscripts on publication ethics and medical history, which can contribute to the education and practices of physicians and health sector professionals within the scope of the journal's target audience and which can increase the level of scientific communication between the authors and readers, are included in the scope of the journal.

The journal publishes articles in both Turkish and English languages. All articles are evaluated through a double-blind review process by independent and unbiased reviewers. Information on preparing and submitting manuscripts for publication and information on article evaluation process are available in Instructions for Authors page both online at www.jtomc.org and in printed issues of the journal.

In order to protect the environment, the journal is printed in limited numbers on acid-free paper. Full content of all manuscripts published by the Journal of Turgut Ozal Medical Center is available and can be downloaded at www.jtomc.org free of charge.

Financial expenses of the journal are covered by the Inonu University School of Medicine. In addition, in order to generate revenue for the journal, commercial announcements and advertisements which are within the scientific scope and ethic guidelines may be published in the journal. For advertisement arrangements the editorial office of the journal should be contacted.

Publishing Permissions: Applications for publishing permissions should be sent to the Editorial Office.

Indexing and Abstracting: Türk Tıp Veri Tabanı, Türkiye Citation Index, Index Copernicus, Directory of Open Access Journals, Türk Medline, EBSCO, Google Scholar, Akademik Dizin, Dergi Park

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YAZARLARA BİLGİ

GENEL BİLGİLER

Turgut Özal Tıp Merkezi Dergisi, tıp bilimlerinde yapılan orijinal araştırmaları, olgu sunumlarını, editöryal yorumları, editöre mektup ve derlemeleri yayınlar. Derginin resmi dili Türkçe ve İngilizcedir. Dergide yayınlanmak üzere gönderilen yazılar, araştırma ve yayın etiğine uygun olmalıdır.

Dergiye gönderilen yazıların daha önce yayınlanmamış veya bir başka dergiye yayın için teslim edilmemiş olması gerekir. Eğer makalede daha önce yayınlanmış alıntı yazı, tablo, resim vs. varsa makale yazarı yayın hakkı sahibi ve yazarlarından yazılı izin almak ve bunu makalede belirtmek zorundadır. Dergiye gönderilen makale biçimsel esaslara uygun ise, editör ve en az iki danışmanın incelemesinden geçip, gerek görüldüğü takdirde istenen değişiklikler yazarlarca yapıldıktan sonra yayınlanır. Tüm yazarların gönderilen makalede akademik-bilimsel olarak doğrudan katkısı olmalıdır. Kongre veya sempozyumlarda sunulan bildirilerin, bu etkinliklere ait kitapta tümüyle yayınlanmamış olması ve bu durumun bir dipnot ile belirtilmesi gerekir.

Makale Başvuruları: Dergiye gönderilecek yazılar dergimizin www.totmdergisi.org veya www.jtomc.org adresinde bulunan online makale gönderme sisteminden yapılır. Online başvuru dışında gönderilecek yazılar değerlendirmeye alınamayacaktır.

Yayın Hakkı: Yayınlanmak üzere kabul edilen yazıların her türlü yayın hakkı dergiyi yayınlayan kuruma aittir. Yazılardaki düşünce ve öneriler ve maddi hatalar tümüyle yazarların sorumluluğundadır. Makale yazarlarına yazıları karşılığında ücret ödenmez. Yazıları yayına kabul edilen yazarlar www.totmdergisi.org adresindeki "Yayın Hakkı Devir Formunu" makaleleri basılmadan önce dergi ofisine göndermek zorundadır.

YAZI ÇEŞİTLERİ

Dergiye yayınlanmak üzere gönderilecek yazılar şu şekildedir.

1. Orijinal Makale: Prospektif ve retrospektif her türlü klinik ve deneysel araştırmalar yayınlanabilmektedir. Yazarlar makalenin gereç ve yöntemler bölümünde kurumlarının etik kurullarından onay ve çalışmaya katılmış insanlardan "bilgilendirilmiş olur" aldıklarını belirtmek zorundadır. Çalışmada deney hayvanı kullanılmış ise yazarlar, makalenin gereç ve yöntemler bölümünde "Guide for the Care and Use of Laboratory Animals" prensiplerine uyduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır.

Orijinal Makale Özeti: Türkçe ve İngilizce, 200-250 kelime arasında, amaç, gereç ve yöntemler, bulgular ve sonuç bölümlerinden oluşan yapılandırılmış özet gereklidir.

Orijinal Makalenin Yapısı: Giriş, Gereç ve Yöntemler, Bulgular, Tartışma, Sonuç, Teşekkür ve Kaynaklar bölümünden oluşur.

2. Derlemeler: Yalnızca yazılan derleme konusunun uzmanı ve konuyla ilgili çalışmaları olan yazarların derlemeleri ve davetli derlemeler kabul edilmektedir.

Derlemelerin Özeti: 200-250 kelime arasında, yapılandırılmamış, Türkçe ve İngilizce özet

Derlemelerin Yapısı: Konu ile ilgili başlıklar ve kaynaklar.

3. Olgu Sunumu: Nadir görülen ve tanı ve tedavide farklılık gösteren makalelerdir. Yeterli miktarda görsellerle desteklenmelidir. Olgu sunumlarında hastanın kimliğinin ortaya çıkmasına bakılmaksızın hastalardan "bilgilendirilmiş olur" alınmalıdır. "Bilgilendirilmiş Olur Formu" na www.totmdergisi.org adresinden ulaşılabilir.

Olgu Sunumu Özeti: 100-150 kelime arasında, yapılandırılmamış, Türkçe ve İngilizce

Olgu Sunumunun Yapısı: Giriş, Olgu Sunumu, Tartışma ve Kaynaklar bölümlerinden oluşmalıdır.

4. Editöryal: Dergi editörü ve editöryal kurul üyelerinin değerlendirme yazılarıdır. Özet ve anahtar kelimeler gerekmez.

5. Editöre Mektup: Son bir yıl içinde dergimizde yayınlanan makaleler ile ilgili veya bağımsız konularla ilgili okuyucuların değişik görüş, tecrübe ve sorularını içeren en fazla 1000 kelimelik yazılardır. Mektuba cevap editör veya makalenin yazarları tarafından yine dergide yayınlanarak verilir

Editöre Mektubun Yapısı: Başlık ve özet bölümleri yoktur. Kaynak sayısı en fazla 10 tanedir. Hangi makaleye ithaf olunduğu belirtilmelidir.

YAZIM KURALLARI

Dergimize gönderilecek yazılar Microsoft Word programında iki satır aralıklı yazılmalı, kenarlarda en az 3 cm boşluk bırakılmalıdır. Gönderilen yazılarda bölümler şu şekilde sıralanmalıdır: Türkçe ve İngilizce özet, anahtar kelimeler, ana metin, teşekkür, kaynaklar, tabloların her biri ve şekil alt yazıları. ilk sayfadan itibaren alt veya üst köşede sayfa numarası olmalıdır. Türkçe makalelerde Türk Dil Kurumunun Türkçe sözlüğü veya www.tdk.org.tr adresi esas alınmalıdır

Kısaltmalar: Kelimenin ilk geçtiği yerde parantez içinde verilir ve tüm metin boyunca o kısaltma kullanılır. Özet bölümünde kısaltma ve kaynak numarası kullanılmaz.

Anahtar Kelimeler: En az 3 adet, Türkçe ve İngilizce yazılmalıdır. Kelimeler birbirinden noktalı virgül (;) ile ayrılmalıdır. Türkçe anahtar kelimelerde Türkiye Bilim Terimleri'ndeki (bkz: http://www.bilimterimleri.com) terimler, İngilizce anahtar kelimelerinde MESH (Medical Subject Headings, www.nlm.nih.gov/mesh) terimleri esas alınmalıdır.

Teşekkür: Eğer çıkar çatışması, finansal destek, bağış ve diğer bütün editöryal (istatistik, dil) ve/veya teknik yardım varsa metnin sonunda sunulmalıdır.

Kaynaklar: Kaynaklar makalede geliş sırasına göre yazılmalı ve cümle sonunda bir boşluk bırakılıp noktadan önce parantez içinde yazılmalıdır. Kaynaklar listesi makalenin bitimi sonrası iki satır aralığı boşluk bırakarak makalede geçiş sırasına göre numaralandırılmak suretiyle yazılmalıdır. Kaynak yazımında, yazar sayısı 6 ve üzerinde ise ilk 6 yazar yazılıp sonrası için İngilizce kaynaklar için "et al." Türkçe kaynaklar için "ve ark."ifadesi kullanılmalıdır. Metinde geçtikleri sıraya göre kaynak sayısının editöre mektuplar için 10, olgu sunumları 15, araştırma makaleleri ve derlemeler için 50 ile sınırlı kalmasına özen gösterilmelidir. Kaynaklarda dergi adlarının kısaltılmış yazımları için "List of Journals Indexed in IndexMedicus" esas alınmalıdır (bkz: http://www.icmje.org). Makale, kitap, internet sayfası, kongre sunusu, gazete haberi, CD/DVD, Kabul edilmiş

ancak basılmamış makaleler, Online yayınlanmış makaleler, tezler kaynak olarak gösterilebilir.
Kaynakların yazımı için örnekler:

Makale: Yazarlarının soyadları, isimlerinin baş harfleri, makale ismi, dergi ismi, yıl, cilt, sayı ve sayfa numarası belirtilmelidir. Örn: Short FL, Blower TR, Salmond GPC. A promiscuous antitoxin of bacteriophage T4 ensures successful viral replication. Mol Microbiol 2012;83(4):665-8.

Kitap: Kitap için yazarların soyadları ve isimlerinin baş harfleri, bölüm başlığı, editörlerin isimleri, kitap ismi, kaçıncı baskı olduğu, şehir, yayınevi, yıl ve sayfalar belirtilmelidir.

İngilizce editörlü kitap: Underwood LE, Van Wyk JJ. Normal and aberrant growth. In: Wilson JD, Foster DW, eds. Williams' Textbook of Endocrinology. 1st editon. Philadelphia: WB Saunders; 1992. p. 1079-138.

İngilizce editörsüz kitap: DiMaio WJ, DiMaio D. Time of death. In: Forensic Pathology. 2nd edition. CRC Press, London, 2001;21-42.

Türkçe editörlü kitap: Tür A. Acil Hava Yolu Kontrolü ve Endotrakeal Entübasyon. Şahinoğlu AH, editör. Yoğun Bakım Sorunları ve Tedavileri. 2. Baskı. Ankara: Türkiye Klinikleri; 2003. p.145-210.

Türkçe editörsüz kitap: Polat O. Aydınlatılmış onam. İçinde: Tıbbi Uygulama Hataları. 1.baskı. Seçkin Yayıncılık, Ankara, 2005;91-112.

İnternetten Kaynak Gösterme: Beware: Toy Noise may be too loud for kids. http://hearingaiddocs.wordpress.com/tag/loud-toys access date (erişim tarihi) 22.04.2013

Kongre Sunumu: Brandes U, Wagner D. A Bayesian paradigm for dynamic graph layout. 11th International Symposium on Graph Drawing, 12-15 November 2003. New York, USA, 236-47.

Gazeteden Kaynak Gösterme: Susan S. How to prevent breast cancer. Australian 23 October 2003.

CD-DVD Kaynak Gösterme: The Oxford English Dictionary [CD-ROM]. 2nd ed. New York: Oxford University Press; 1992.

Kabul edilmiş basılmamış makale: Kaya A, Aktas EO. Perception differences between in violence against child. Med-Science. Accepted article: October 25, 2013. Published Online: Nov 19, 2013.

Tezi Kaynak Gösterme: Karakoc Y. Biological effect of direct electrical current in essential (idiopathic) hyperhidrosis. Ph.D. thesis, Istanbul University, Istanbul, 1996.

Şekil, Resim, Tablo ve Grafikler: Şekil, resim tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmelidir. Şekil, resim, tablo ve grafiklerin açıklamaları makale sonuna eklenmelidir. Şekil, resim ve fotoğraflar ayrı birer .jpg veya .gif dosyası olarak (pixel boyutu yaklaşık 500×400, 8 cm eninde ve 300 çözünürlükte taranarak) sisteme yüklenmelidir. Kullanılan kısaltmalar şekil, resim, tablo ve grafiklerin altındaki açıklamada belirtilmelidir. Daha önce basılmış şekil, resim, tablo ve grafik kullanılmış ise yazılı izin alınmalıdır ve bu izin açıklama olarak resim, tablo ve grafik açıklamasında belirtilmelidir. Resimler ve fotoğraflar renkli, ayrıntıları görülecek kadar kontrast ve net olmalıdır.

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INFORMATION FOR AUTHORS

GENERAL INFORMATION

Journal of Turgut Ozal Medical Center welcomes original articles, case reports, editorials, and letters to the editor and review articles on basic and clinical medical sciences. The official languages of the journal are Turkish and English. All manuscripts which will be published in the journal must be in accordance with research and publication ethics.

Manuscripts are received with the explicit understanding that they have not been published in whole or part elsewhere, that they are not under simultaneous consideration by any other publication. Direct quotations, tables, or illustrations that have appeared in copyrighted material must be accompanied by written permission for their use from the copyright owner and authors. All articles are subject to revie by the editors and referees. Acceptance for publication is based on significance, and originality of the material submitted. If the article is accepted for publication, it may be subject to editorial revisions to aid clarity and understanding without changing the data presented. All authors should contribute to the submitted article directly either academically or scientifically. Presentations at congresses or symposia are accepted only if they are not published in whole in congress or symposium booklets or proceedings. Authors are expected to acknowledge the event at which they presented their work as a footnote.

Manuscript submission: All manuscripts should be submitted through the online system of the journal at www.totmdergisi.org or www.jtomc.org. Articles submitted in other formats will not be considered.

Copyright statement: The journal owns the copyright of all published articles. Statements and opinions expressed in the published material herein are those of the authors. Manuscript writers are not paid by any means for their manuscript. All manuscripts published must be accompanied by the "Copyright Transfer Form" that is available on the journal web site.

CATEGORIES of MANUSCRIPTS

Journal of Turgut Ozal Medical Center publishes the following types of articles:

1. Original Articles: Original prospective or retrospective studies of basic or clinical researches in areas relevant to medicine.

Abstract of an Original Article: Turkish and English, 200-250 words, the structured abstract should contain the following sections: objective, material and methods, results, conclusion. Editorial office will provide abstracts in Turkish for non-native Turkish speakers.

Structure of an Original Article: Introduction, Materials and Methods, Results, Discussion, Acknowledgements, References sections must be included.

2. Review Articles: The authors may be invited to write or should be experts in the proposed subject of review article.

Abstract of a Review Article: Turkish and English, 200-250 words, without structural divisions. Editorial office will provide abstracts in Turkish for non-native Turkish speakers.

Structure of a Review Article: Titles or related topics and references.

3. Case Reports: Brief descriptions of a previously undocumented disease process, a unique unreported manifestation or treatment of a known disease process, or unique unreported complications of treatment regimens. Case reports should include an adequate number of images and figures. Case reports should be accompanied by "Informed Consent" whether the identity of the patients is disclosed or not. The "Informed Consent Form" is available at www.inonutipdergisi.com

Abstract of Case Reports: Turkish and English, 100-150 words, without structural divisions. Editorial office will provide abstracts in Turkish for non-native Turkish speakers.

Structure of Case Reports: Introduction, Case Report, Discussion, References.

4. Editorial: Special articles are written by editor or editorial board members. Abstract is not required for editorials.

5 Letter to the Editor: These are letters which include different views, experiments and questions of the readers about the manuscript that were published in this journal in the recent year and should not be more than 1000 words. The answer to the letter is given by the editor or the corresponding author of the manuscript and is published in the journal.

Structure of Letter to the Editor: There is no title or abstract. The number of references should not exceed 10. Submitted letters should include a note indicating the attribution to an article published in a journal.

PREPARING the MANUSCRIPT

Manuscripts should be typed double-spaced with margins of 3 cm. Articles should be set out as follows: cover letter, title page, abstract and key words, main text, acknowledgment, references, tables and illustrations. Table and illustration pages should also include the heading or legend, and be numbered below or above the page.

Abbreviations: Abbreviations should be defined in parenthesis where the full word is mentioned. For commonly accepted abbreviations and usages, please refer to "Scientific Style and Format" (The CBE for Manual for Authors Editors and Publishers, 6th ed. New York: Cambridge University Press, 1994). Abbreviations should not be used in Abstract sections.

Keywords: They should be at least three keywords both in Turkish and English. The words should be separated by a semicolon (;). Key words should be in line with "Medical Subject Headings" (MESH) (please see www.nlm.nih.gov/mesh).

Acknowledgements: Conflicts of interest, financial support information, grants and all other editorial and/or technical assistance should be presented at the end of the text.

References: References in the text should be numbered in parenthesis and listed serially according to the order of appearance on a separate page, double-spaced, at the end of the paper in numerical order. All authors

should be listed if six or fewer, otherwise list the first six and add the et al. References should be limited to 10 for letter to the editor, 15 for case reports, 50 for clinical/experimental reports and review articles. Journal abbreviations should conform to the style used in the Cumulated Index Medicus (please see www.icmje.org). Journal articles, books, web pages, conference presentations, newspapers, audio-visual sources like CDs and DVDs, articles pending for publication, theses and dissertations can be used as references.

Reference Format for Journal Articles: Authors' initials, names and surnames, article titles, journal titles, date, volume,number and pagination must be indicated. E.g.:
Short FL, Blower TR, Salmond GPC. A promiscuous antitoxin of bacteriophage T4 ensures successful viral replication. Mol Microbiol 2012;83(4):665-8.

Reference Format for Books: Initial's of author's names and surnames, chapter title, editor's name, book title, city, publisher, date and pages must be indicated.

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References to articles pending for publication: Kaya A, Aktas EO. Perception differences between in violence against child. Med-Science. Accepted article: October 25, 2013. Published Online: Nov 19, 2013.

References to theses and dissertations: Karakoc Y. Biological effect of direct electrical current in essential (idiopathic) hyperhidrosis. Ph.D. dissertation, Istanbul University, Istanbul, 1996.

Figures, Pictures, Tables and Graphics: All figures, pictures, tables and graphics should be cited at the end of the relevant sentence. Explanations about figures, pictures, tables and graphics must be placed at the end of the article. Figures, pictures/photographs must be submitted to the system as separate .jpg or .gif files (approximately 500×400 pixels, 8 cm in width and scanned in 300 resolution. All abbreviations must be explained at the bottom of each figure, picture, table and graphic. For figures, pictures, tables and graphics, relevant permissions need to be provided and indicated during submission. Pictures and photographs must be in color, clear and with appropriate contrast showing details adequately.

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Evaluating Anxiety and Stress Coping Skills and Related Variables of Mothers with Mentally Retarded Children

Zihinsel Engelli Çocuğu Olan Annelerin Anksiyete ve Stresle Başa Çıkma Becerileri ve İlişkili Değişkenlerin Belirlenmesi

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Abstract

Aim: Our aim is to compare the socio-demographic characteristics of mothers with mentally disabled children with those without, and to evaluate anxiety levels and ability of these mothers to cope with stress.

Materials and Method: Our study is designed as a cross-sectional descriptive study. We included the mothers of 110 children with mental disabilities as the study group, and mothers of 117 children in a primary school without any mental disabilities as the control group. Socio-demographic data of all the mothers participating in the study were recorded and Beck Anxiety Inventory and The Ways of Coping Scale were applied.

Results: The mean age of the study group was 31.2±3.45 years in the study group and 28.62±2.25 years in the control group; there was no statistical difference between the groups (p=0.215). Monthly household income was statistically significantly lower in the study group (p=0.005). The average Beck Anxiety Inventory score of the mothers with mentally disabled children was 29.88±12.68, and that of the control group was 28.76±16.86; there was no statistically significant difference between the groups (p=0.578). The average Ways of Coping Scale score of the mothers of mentally disabled children was 70.83±13.49 and average score of the control group was 73.64±16.20; there was no statistically significant difference (p=0.158). However, the average scores of mothers with mentally handicapped children of the three subscales of Ways of Coping Scale, including Submissive Approach, Seeking for Social Support and Optimistic Approach, were significantly higher than the control group (p: 0.001, 0.001, 0.005, respectively).

Conclusion: We suggest that mothers of mentally disables children should be followed up closely and supplied with psychosocial support, and rehabilitation services; even, measures to improve their economic situation should be taken.

Keywords: Disabled Children; Anxiety; Psychological Status.

Özet

Amaç: Çalışmamızda zihinsel engelli çocuğu olan ve olmayan annelerin sosyodemografik özelliklerini ve zihinsel engelli çocuğu olan annelerin, kontrol grubundaki annelere göre anksiyete düzeylerini belirleyebilmek ve stresle başa çıkma becerilerini değerlendirebilmek amaçlanmıştır.

Gereç ve Yöntem: Çalışmamız kesitsel tanımlayıcı bir çalışma olarak planlanmıştır. Şubat 2015 tarihinde Malatya Rehberlik ve Araştırma merkezine müracaat eden sadece zihinsel engeli olan ilköğretim çağındaki 110 çocuğun anneleri ile kontrol grubu olarak bir ilköğretim okulunda herhangi bir zihinsel engeli olmayan 117 çocuğun anneleri alınmıştır. Çalışmaya katılan tüm annelere Sosyodemografik Veri Formu, Beck Anksiyete Ölçeği, Stresle Başa Çıkma Tarzları Ölçeği uygulanmıştır.

Bulgular: Çalışmaya katılan annelerin yaş ortalaması zihinsel engelli çocuğu olanlarda 31.2±3.45 yıl, kontrol grubunda 28.62±2.25 yıl olup istatistiksel olarak benzer idi (p=0.215). Hane halkının aylık geliri zihinsel engelli çocuğu olan annelerde kontrol grubuna göre istatistiksel olarak anlamlı derecede daha düşük idi (p=0.005). Beck Anksiyete Ölçeği puanı zihinsel engelli çocuğu olan annelerde 29.88±12.68, kontrol grubunda 28.76±16.86 olup her iki grup arasında istatistiksel olarak anlamlı bir fark yoktu (p=0.578). Stresle Başa Çıkma Tarzları Ölçeği puanı zihinsel engelli çocuğu olan annelerde 70.83±13.49, kontrol grubunda 73.64±16.20 idi (p=0.158). Ancak Stresle Başa Çıkma Tarzları Ölçeğinin alt ölçeklerinden olan Çaresiz Yaklaşım, Boyun Eğici Yaklaşım, Sosyal Destek Arama gruplarında zihinsel engelli çocuğu olan annelerde kontrol grubuna göre anlamlı düzeyde daha yüksekti (p sırasıyla 0.001, 0.001, 0.005).

Sonuç: Zihinsel engelli çocuğu olan annelerin psikososyal açıdan daha çok desteklenmesi ve yakından takip edilmesi hatta ekonomik durumlarının iyileştirilmeye çalışılması ve kendilerine de rehabilitasyon hizmetleri verilmesi sağlanmalıdır.

Anahtar Kelimer: Engelli Çocuklar; Anksiyete; Ruhsal Durum.

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INTRODUCTION

Contributing to the creation of family structure and the need to love among family members, child is an important and indispensable element of family life (1). Even the slightest inclination that they might have a handicapped baby brings about a complex psychology among individuals in family. Learning that a child has a disability is quite a traumatic situation for family members regardless of the degree and kind (mental or physical) of disability (2).

Disability is defined as the inadequacy to play the roles set by age, sex, and socio-cultural differences due to inabilities (3). In 2009, calculations estimated that 10% of the world's population was disabled, and out of the 650 million people with disabilities, an estimated 200 million would be children (4). In Turkey, this number is reported to be 12,3% in the total population (5).

Many studies on families with mentally or physically handicapped children show that family members are much more stressed with much higher anxiety levels compared to families with non-handicapped children (6). It is also known that somatic complaints, depression, and psychological problems such as anxiety disorders are more common in mothers with disabled children than mothers with non-handicapped children (7). However, factors that affect the stress these family members experience and defense mechanisms they use against stress are not clear.

In our study, we aim to evaluate sociodemographic characteristics of families with mentally disabled children and of families without disabled children, the pregnancy of mothers with mentally disabled children, determine the anxiety levels of these mothers, and evaluate their ability to cope with stress.

MATERIALS and METHODS

Our study is designed as a cross-sectional descriptive study. Our study includes the mothers of 110 elementary school children with mental disabilities who consulted to Malatya Yesilyurt Guidance and Research Centre (GRC) of the Ministry of Education in February 2015 and, as the control group, the mothers of 117 children without any mental issues from a nearby elementary school.

We started our research after obtaining the approval of the Inonu University, Faculty of Medicine, Clinical Research Ethics Committee.

The questionnaire was based on sociodemographic data form, Beck Anxiety Inventory (BAI), and The Ways of Coping Scale (WOCS). The sociodemographic data form we prepared contained questions concerning the age and profession of the mothers, whether they were conceived willingly, their pregnancy period, the age and sex of the disabled their children, and monthly income of the family members. BAI is a scale developed by Beck et al. in 1988. It is used to determine prevalence of anxiety symptoms and level of anxiety in times of stress; the validity and reliability of the scale for Turkey was carried out by Ulusoy et al. in 1998 by (8, 9). Divided into two as emotion-based and problem-based and developed by Folkman and Lazarus in 1988, WOCS is a scale measuring coping with stress and cognitive and behavioural efforts individuals develop to cope with stimuli from the environment in times of stress (10). The validity and reliability of this scale for Turkey was conducted by Sahin and Durak in 1995 (11). Sahin and Durak have prepared the 30-question scale in five subgroups: Desperate Approach (DA), Submissive Approach (SBA), Search for Social Support (SSS), Safe Approach (SFA), and Optimistic Approach (OA) (12). Before the survey, mothers were informed that filling in the questionnaire was totally voluntary and that they did not need to specify their names. Then, we had face to face interviews and enabled them to ask questions at any time they wished.

The obtained data were evaluated with SPSS ver. 17 and the level of significance was accepted as p 0,005. For the statistical analysis, basic parameters were summarised as mean, standard deviation, and percentages. To compare the numerical data, we used Student t test; for the comparison of nominal parameters, we used the chi-square test.

RESULTS

The average age of mothers with mentally disabled children was 31,2±3,45 years; this was 28,62±2,25 in the control group and there was no statistically significant difference (p=0,215). Comparing the occupations of the participants, we found out that many of the mothers with healthy children worked for the state institutions, which was statistically significantly (p=0,012), despite the majority of the mothers in both groups were housewives. The monthly household income was significantly lower in the patient group (p=0,003). Some of the socio-demographic data of the participants are given in Table 1.

Table 1. Socio-demographic data of the paticipants.

	Patient	Control	p
Sex of the disabled child			
Female	57	60	0.116
Male	53	57	
Mother's occupation			
Housewife	87	86	
Position at a state institution	8	18	
Worker	3	4	0.012
Private sector	5	9	
Other	7	0	
Monthly household income			
Below 1000 Turkish lira	66	46	
1001-2000 Turkish lira			
2001-3000 Turkish lira	26	47	
3001-4000 Turkish lira	13	11	0.003
Above 4001 Turkish lira	4	3	
	1	10	

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Comparing the average BAI and WOCS values of the mothers who participated in the study, the mean BAI value of mothers with mentally disabled children was 29,88±12,68; this was 28,76±16,86 in the control group; there was no statistically significant difference between the groups (p=0,578). The comparison of the WOCS mean values of the groups showed that the WOCS score of the families with mentally handicapped children was 70,83±13,49; this score was 73,64±16,20 in the control group, with no statistically significant difference (p=0,158).

Evaluating WOCS sub-scale scores in both groups, we found out that mothers with handicapped children had statistically higher scores in DA, SBA, and SSS (p:0,001; 0,001; and 0,005, respectively); there was no statistically significant difference in terms of SFA and OA (Table 2).

Table 2. The distrubition of mean scores according to WOCS.

	Mean±SD		
	Patient	Control	P
Desperate Appraoch (DA)	16.56± 4.19	17.77± 3.52	0.001
Submissive Approach (SBA)	16.90± 4.40	15.04± 3.75	0.001
Search for Social Support (SSS)	9.71± 2.52	8.83± 2.17	0.005
Safe Approach (SFA)	14.41± 4.08	14.76± 4.43	0.532
Optimistic Approach (OA)	11.22± 2.62	11.15± 2.99	0.837

DISCUSSIONS

In our study evaluating the WOCS and BAI scores of mothers with mentally handicapped children and those of the mothers in the control group, we observed that WOCSS and BAI scores of mothers were similar but mothers with handicapped children had considerably higher scores from the WOCS subgroups of SBA, SSS, and OA than the mothers in the control group.

Having mentally retarded children is quite traumatic for family members. Especially because it is a lifelong experience and family members know that disabled children cannot sustain life in their absence, productivity of family members declines as the frequency of anxiety increases. Many studies show that mothers with children who have mental disabilities have high levels of anxiety compared to mothers of healthy children (13, 14). Studies in the literature point that, regardless of the disability type and degree of their children, mothers with mentally retarded children have intense expectations about their children and, accordingly, have higher anxiety levels than mothers with healthy children (15-17). In our study, in line with these studies, we have observed higher levels of anxiety in mothers with mentally handicapped children compared to the mothers in the control group and these levels were statistically significant. These results indicate that mothers in the patient group have moved on from denial and projection periods, which are among the initial responses upon receiving the news that their children will be disabled, into the acceptance period.

Studies show that as the amount of social support to mothers of children with mental disabilities increases, their access to this support gets easier, which helps them to use their skills to cope with stress more easily (18). In our study, although mothers with mentally handicapped children had higher SSS scores than the control group, this difference was not statistically significant. This can be because of the fact that mothers in the patient group were selected from those who had applied to GRC probably seeking support. This case should be investigated with further community-based studies comparing mothers with motives to seek for support and those without such motives.

Damrosch et al. have stated that diagnosis of mental disability for children is the most feared diagnosis for parents and that it is a very serious source of stress. They have also related that, in case of such a situation, there are many families who think that giving in is the only option to cope with this unresolvable problem (19). Similarly, our study has shown that mothers with mentally handicapped children often use SBA, SSS, and OA methods. This can be a sign of the possibility that, having survived the anxiety period, mothers with mentally retarded children have now moved into submissive and fatalistic period during which they are more inclined to look for social support. Yildirim et al. have showed that the average DA and SBA scores, two sub-scales of WOCS, of mothers with mentally disabled children decrease in line with the level of education while average SFA scores increase significantly. According to this picture, as parents' self-confidence increases, negative emotions tend to diminish. Women with chronic diseases and mothers with disabled children should not be left on their own; they should receive rehabilitation services to teach them how to deal with these problems (18, 20). To provide this awareness, psycho-educative sessions must be organised and their skills should be increased through individual and group therapies.

It is clear that strength of families with disabled children and factors affecting these endurance skills are more frequently investigated in recent years. Raising a disabled child requires additional responsibility and skills and parents who achieve these skills become stronger; yet, parents need time to establish such skills (21). Heiman believes that this strength associated with talking to family, friends, and professionals about this situation, having a positive bond within family, continuous therapy and psychological support family members receive. Heiman relates that 93.5% of the parents with mentally handicapped children who were enrolled in his study receive help from special education centres and psychological support consultants. Again, his study shows that these participants were stronger, more sturdy and realistic, and, acting in this way, they

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believed that their children would also have a more optimistic view in the future (22). In our study, we observed that mothers of mentally disabled children make use of SBA, SSS, and OA methods the most. This can be interpreted as their search for social support in a fatalistic mood at the end of which they become more resistant and stronger.

Studies in the literature show that mothers of mentally handicapped children share a lower level of income compared to those without mentally disabled children (14, 23). Our study confirms that mothers with mentally disabled children have a lower income than those without such disabled children.

It is observed in the literature that, along with social support awareness levels, stress and anxiety levels of mothers with mentally disabled children increase as the income level of families decreases (14). Our study has shown that income level of mothers with mentally handicapped children is statistically significantly low. However, we could not detect any significant results in the correlation analysis concerning the relationship between monthly income and anxiety levels. We believe that there is need for further studies with wider participation to investigate the relation between income and stress and anxiety levels.

Studies on the professions of mothers who have children with mental retardation show that majority of these mothers are housewives. These studies also reveal that these mothers, due to cultural expectancies, believe that they should spend more time with their children and, thus, even quit their jobs if they have any (24, 25). In our study, 91.2% of mothers were housewives similar to the literature.

The small number of samples, selecting mothers who had already consulted to GRC, and attempting to evaluate the mental state of these mothers through scales can be counted among the limitations of our study.

To sum up, mothers with mentally disabled children who enrolled in our study had higher scores in SBA, SSS, and DA, three sub-groups of WOCS. This can interpreted as a sign of the condition that, having survived the denial and projecting periods upon hearing the news that they will have disabled children, mothers have moved into acceptance period during which they show submissive stance. This requires that these families need more psycho-social support and their mental conditions should be followed more closely. At the same, their economic conditions should be improved and mothers, like their children, should be provided with rehabilitation services.

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Our Initial Experiences and Outcomes of Pediatric Kidney Transplantations

Çocuk Hastalara Yaptığımız Böbrek Nakilleri ile İlgili İlk Deneyimlerimiz ve Sonuçlarımız

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Abstract

Objectives: Kidney transplantation is the best treatment method associated with improved quality of life and better survival for both adult and pediatric patients with end stage renal disease. We have performed a total of 117 kidney transplantations from living or deceased donors between November 2010 and May 2014. Thirteen of these were pediatric kidney transplantations. Here, we present our initial experiences and outcomes of these pediatric kidney transplantations.

Materials and Methods: One of the pediatric recipients who underwent en bloc and dual-kidney transplantation from a deceased donor was excluded from this study. This recipient was a 40-month-old patient whose donor was an eleven-month-infant. Her allograft kidneys were explanted because of vascular thrombosis on the first postoperative day. We collected and retrospectively analyzed the data of the other twelve pediatric transplantation recipients and their donors. Seven of these kidney transplantations were from deceased donors and five from living donors. All recipients and the five living donors underwent a thorough examination and their clinical history was studied with in detail.

Results: Deceased to living donor ratio was 7:5, respectively. The mean follow up period was 31.8 (1-42) months from living donors group and 16.8 (2-28) months from deceased donors group, respectively. Graft survival was 100% during this period. No kidney was lost from rejection, technical causes, infection or recurrent diseases. The living donors are also still alive without any problems.

Conclusion: For pediatric end stage renal disease patients, kidney transplantation should be done from deceased or living donors as soon as possible.

Keywords: Pediatric; Kidney; Transplantation.

Öz

Amaç: Hem çocuk hem de erişkin böbrek yetmezliği hastaları için en iyi tedavi seçeneği yaşam süresini ve kalitesini de artıran böbrek naklidir. Kasım 2010 ile Mayıs 2014 tarihleri arasında toplam 117 hastaya böbrek nakli yaptık bunların 13'ü çocuk hastalardı. Çocuk hastalara yaptığımız böbrek nakilleri ile ilgili ilk deneyimlerimizi ve sonuçlarımızı burada sunmayı amaçladık.

Materyal ve Metot: En bloc ve dual böbrek nakli yaptığımız bir olgumuz bu çalışmanın dışında bırakıldı. Geriye kalan 12 hasta ve donörlerinin kayıtları geriye doğru toplanarak incelendi.

Bulgular: Hastalarımızın 7'sine kadavradan, 5'ine canlı donörlerinden nakil yaptık. Canlı donörden nakil yaptığımız alıcıların ortalama takip süreleri 31.8 ay(dağılım; 1-42 ay), kadaverik donörden nakil yaptığımız alıcıların ise16.8 aydı (dağılım; 2-28 ay).

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Sonuç: Çocuk yaş grubundaki kronik böbrek yetmezliği olan hastlara kadaverik ya da canlı donörden olabildikçe erken böbrek nakili yapılmalıdır. Çocuklara; hem kadavradan hemde canlıdan nakiller nakil merkezi yeni kurulmuş olsada güvenli bir şekilde yapılabilinir.

Anahtar Kelimeler: Çocuk; Böbrek; Nakil.

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INTRODUCTION

Kidney transplantation (KT) is the most effective treatment method associated with improved quality of life and better survival since it enables satisfactory physical, social and psychological rehabilitation for pediatric patients with end stage renal disease (PPESRD) (1-5). We have performed a total of 117 kidney transplantations form living or deceased donors between November 2010 and May 2014. Thirteen of these operations were pediatric kidney transplantations. The aim of this study is to share our initial experiences and outcomes of these pediatric kidney transplantations.

MATERIALS and METHODS

We performed thirteen pediatric KTs between November 2010 and May 2014. One pediatric recipient had en bloc and dual-kidney transplantation from a deceased donor and, thus, was excluded from this study. This recipient was a 40-month-old infant with an eleven-month-donor. Her allograft kidneys were explanted because of vascular thrombosis on the first postoperative day. We collected and retrospectively analyzed the data of the remaining twelve pediatric transplantation recipients and their donors. Seven of these kidney transplantations were from deceased donors and five from living donors. All recipients and the five living donors underwent detailed examination as we also accuretely collected data about their clinical history. All living donors were evaluated according to the criteria of Amsterdam Forum (6). Human Leukocyte Antigen (HLA) typing and tissue cross match between donors and their recipients were also carried just before transplantation.

We used routine methylprednisolone (MP) and induction immunosuppressive drugs just before surgery. We used prophylactic antibiotic and low molecular weight heparin in all patients. Bladders of recipients were lavaged with gentamycine plus serum physiologic.

There are only two transplant surgeons in our kidney transplant team. Because of this reason, we started off with donor nephrectomy procedure from living donor transplantations. After completing dissections, we gave a break to donor nephrectomies. Then, we prepared implantation areas, which was mainly extraperiotenal area in right or left iliac fossas in the recipients. After completing this procedure, we gave a break to recipient operations. Then, we turned to the donor nephrectomies again. After the donor nephrectomies, we immediately started implantation procedures in the recipients.

Six left and six right kidneys were transplanted. Ten kidneys were placed in the right iliac fossa of the recipients. The other two kidneys were placed in the left iliac fossa of the recipients who underwent native nephroureterectomy. Renal vessels were anastomosed to external iliac vessels in ten recipients. Renal vessels were anastomosed to common iliac vessels in the other two recipients. Ureteroneocystostomy (UNC) was performed extravesically, using Lich-Gregoir technique over a double J (DJ) stent in all cases (7). The urethra was prepared by removing redundant urethral length, preserving adequate distal blood supply, and spatulating posterior by at least 10 millimeters. We used 6/0 or 7/0 polydioxanone surgical (PDS) suture for anastomosis. The detrusor muscle was closed exteriorly to create an antireflux mechanism by one-by-one 3/0 absorbable sutures. The recipients and the five living donors were followed up in our transplant clinic during hospitalization. Fluid replacement was given according to urine output at postoperative first night and balance was ensured at about + 500 (fluid input more than urine + drainage fluid). Oral fluid intake was ensured within the postoperative 6-8 hours. Intravenous fluid replacement was decreased on the postoperative first day and was generally stopped on the second day.

Complete blood count, profile of coagulation and routine biochemistry tests including renal function tests were performed at the postoperative first night and daily during patients' stay at the hospital. Immunosuppressive drug level was controlled and regulated on postoperative second day and then daily during this period. Transplanted kidney wasn't imaged routinely in the postoperative hospitalization period. All patients were followed by the Pediatric Nephrology outpatient clinic after discharge. As two of these patients turned 18, they started to be followed up by the Nephrology outpatient clinic.

RESULTS

We performed seven KTs from deceased donors and five from living donors. Male to female ratio was 9:3 in the recipients and 4:8 in the donors, respectively. The mean age of living donors and their recipients were 42.8 (33-50) and 11.6 (4-17) years, respectively. The mean age of deceased donors and their recipients were 15.5 (4-46) and 12.7 (9-17) years, respectively. All transplantations from living donors were performed to their related recipients. Three of these living donors were recipients' fathers, one was recipient's mother and one was recipient's grandmother. In the deceased donor group, the recipients and their donors were not related.

The relationship between the recipients and donors with regards to mismatched HLAs is presented in Table 1. All patients and their donors had compatible blood groups. Demographic traits of donors and their recipients and also the causes of end stage renal disease (ESRD) in patients are shown in Table 1.

The mean warm ischemic time was 91.4 (67-110) seconds and the mean totally ischemic time was 88.4 (55-108) minutes in the living donors group. The mean cold/totally ischemic time was 1284.8 (850-1628) minutes in the deceased donors group. The mean time of discharge from hospital was postoperative 5.8 (5-7) days in the living donors group and 8.1 (5-13) days in the deceased donors group, respectively. The mean follow up times were 31.8 (1-42) months in the living donor

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group and 16.8 (2-28) months in the deceased donors group, respectively (Table 1).

Left kidney donor nephrectomy was preferred as much as possible for the living donors. If there were vascular problems or a condition in favor of the donor, we preferred right kidney nephrectomy. The left donor nephrectomy to right donor nephrectomy ratio was 4:1 in the living donor transplantations. The left kidney to right kidney ratio was 2:5 in the deceased donor transplantations (Table 1).

Right iliac fossa was usually preferred for implantation in the recipients. If there was a vascular problem, surgical necessity such as native nephrectomy, we preferred left iliac fossa. Ten kidneys were placed in the right iliac fossa of the recipients. The other two kidneys were placed in the left iliac fossa of the recipients who underwent native nephroureterectomy (Table 1).

Table 1. Demographic traits of recipients and donors.

Number of Patient/ Follow up period (months)	Age and Gender	Donor (Living or Deceased)	Side of Transplanted Kidney/ Implantation area	Age and Relation of Donors to the Recipients	HLA MM	Cause of ESRD	Renal Replacement Options and duration
1/ 42	4, M	Living	Left/ Right	Grandmother, 50	2 MM	Idiopathic	Preemptive
2/ 40	17, M	Living	Left/ Left	Father, 43	3 MM	VUR	PD, 9 months
3/ 40	10, M	Living	Right/ Left	Father, 33	2 MM	Renal Tubular Acidosis	Preemptive
4/ 36	13, M	Living	Left/ Right	Father, 47	3 MM	VUR	PD, 5 years
5/ 28	17, M	Deceased	Right/ Right	Unrelated, 5	5 MM	MPGN (Type 2)	HD+PD, 2 years
6/ 26	9, F	Deceased	Left/ Right	Unrelated, 4	4 MM	Idiopathic	PD, 2 years
7/ 25	16, F	Deceased	Right/ Right	Unrelated, 46	4 MM	VUR	HD+PD, 3 years
8/ 22	13, F	Deceased	Right/ Right	Unrelated, 5	5 MM	Neurogenic bladder	PD+HD, 7 years
9/ 11	9, M	Deceased	Right/ Right	Unrelated, 9	4 MM	Idiopathic	PD, 1.5 years
10/ 4	14, M	Deceased	Right/ Right	Unrelated, 27	4 MM	VUR	HD+PD, 1 year
11/ 2	11, M	Deceased	Left/ Right	Unrelated, 13	5 MM	Idiopathic	HD+PD, 9.5 years
12/ 1	14, M	Living	Left/ Right	Mother, 41	3 MM	Idiopathic	HD, 2 years

M; Male, **F;** Female, **HLA;** Human Leukocyte Antigen, **MM;** Mismatch, **ESRD;** End Stage Renal Disease, **VUR;** Vesicoureteral Reflux, **MPGN;** Membranoproliferative Glomerulonephritis, **PD;** Peritoneal Dialysis, **HD;** Hemodialysis.

Renal vessels were anastomosed to external iliac vessels in ten recipients. Renal vessels were anastomosed to common iliac vessels in the other two recipients. Nine patients' arteries were anastomosed in end-to-side fashion, using a continuous 6/0 polypropylene suture. One patient's artery was anastomosed in end-to-side fashion, using a continuous 7/0 polypropylene suture. In the other two recipients, we anastomosed one face of the renal artery with continuous 6/0 polypropylene suture and the other face of the renal artery with one by one 7/0 polypropylene suture technique. We performed artery anastomosis with donor aortic patch from all deceased donor kidney transplantations except for one patient. Except one patient, having two renal arteries, all other patients' kidneys had one renal artery. Two renal arteries were anastomosed with common aortic patch of the deceased donor's abdominal aorta wall.

We used induction immunosuppressive drugs as corticosteroids, Anti Tymosit Globulin (ATG) in ten patients, and Basiliximab in two patients. Tacrolimus, mycophenolate mofetil (MMF), and corticosteroid were given to recipients as postoperative immunosuppressive drugs.
We performed two native nephroureterectomies due to potential recurrent urologic infection. One of these patients had incurable vesicoureteral reflux (VUR), and the other had incurable vesicoureteral stenosis. The causes of renal failures were idiopathic in 5 patients, VUR in 4 patients, renal tubular acidosis in 1 patient, Membranoproliferative Glomerulonephritis (MPGN) in 1 patient and neurogenic bladder in 1 patient. The causes of renal failures are also shown in Table 1.

One patient suffered from ureteral stenosis two months after the transplantation. For this patient, we inserted a percutaneous nephrostomy catheter though balloon dilatation couldn't be achieved. He was treated with surgical intervention.

BK virus nephropathy occurred in only one recipient. The patient's creatinine level is higher than 2 mg/dl; fortunately, the graft function is now stable. After the BK virus infection, he suffered from VUR with the transplanted kidney. He was treated with endoscopic surgical intervention at the Department of Urology. A tephlon was injected into the submucosal area of UNC. This patient is our only patient whose creatinine level is still higher than 2 mg/dl. There were two Cytomegalovirus (CMV) cases associated with acute rejection episode in two recipients. Both of them were treated with high dose MP and parenteral ganciclovir.

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One of these patient's creatinine level is still higher than 1.5 mg/dl; fortunately, the graft function is currently stable. Our ten patients' creatinine levels are lower than 1.5 mg/dl currently. The recipients' creatinine levels in discharge time and currently are shown in graphic 1.

The graft survival rate was 100% during this period (Figure 1). No kidney was lost due to rejection, technical causes, infection or recurrent diseases.

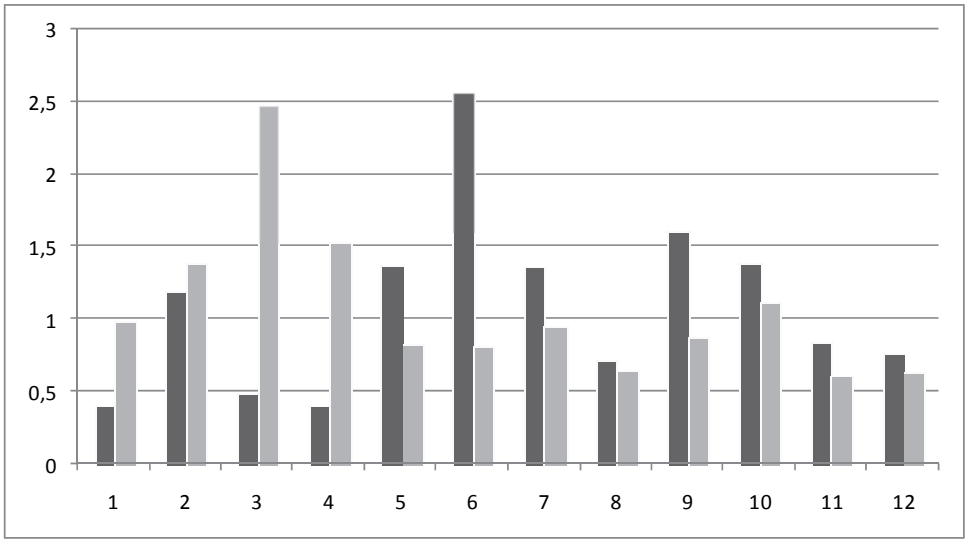

Figure 1. Recipients' current creatinine levels (light columns) and their creatinine levels at the time of discharge (dark columns). The living donors are alive and in good health without any problems.

DISCUSSIONS

KT improves quality of life and better survival as it also enables satisfactory physical, social, potential normalization growth and psychological rehabilitation for PPESRD (1-5). It reduces rate of mortality seen with dialysis (4). It liberates PPESRD patients from dialysis while it is also more cost-effective than dialysis. This treatment option has been performed less in the past, but its popularity is increasing worldwide day by day (4).

We used triple (Tacrolimus, corticosteroid and MMF) immunosuppressive drugs as they are used worldwide (1, 8, 9). Non-compliance of immunosuppressive is high among pediatric recipients (2). We didn't encounter non-compliance or use of discontinuation of immunosuppressive drugs.

Infections are an important cause of post-transplant mortality and morbidity in pediatric kidney transplant recipients (PKTR) in developing countries (1). Also, according to Garcia et al' study, infection is the main cause of death of PKTRs (5). We encountered three important viral infections. Two of these were CMV infections and one was BK virus infections. The CMV infections triggered acute rejection in these patients. Both of them were treated by high dose MP and parenteral ganciclovir. The BK virus infection occurred due to the BK virus associated with nephropathy in the allograft kidney. Treatment of BK virus nephropathy since the most common cause of renal failure in patients has been reported to be congenital lesions (14). We advised our patients to visit Pediatric Nephrologists in later periods for a check-up for potential kidney diseases.

consists of reduction of immunosuppression (10, 11). We reduced amounts of immunosuppressive drugs in our patient. Two of these three patients' creatinine levels are higher than 1.5 mg/dl to this day. All our PKTRs live their lives with stable graft functions.

According to Fraser et al' study, indications for native nephrectomy prior to renal transplantation have included the following causes: chronic renal parenchymal infection with high grade VUR, hydronephrosis or calculi, glomerulopathy with heavy proteinuria, uncontrollable hypertension, symptoms arising from large polycystic kidneys, acquired renal cystic disease, and malignancy (12). We performed two native nephroureterectomies with concerns of possible recurrent urologic infection. One of these had incurable VUR, and the other had incurable vesicoureteral stenosis.

According to Singh et al' study, vascular thrombosis remains a major cause of graft failure, accounting for 12.2% of failed index transplants and 19.2% of repeat transplants (13). We encountered vascular thrombosis in one patient who underwent en bloc and dual kidney transplantation from a deceased donor and thus was excluded from this study. We didn't encounter any vascular complications in our 12 patients, who were transplanted a single kidney.

The most causes of renal failure were idiopathic in 5 patients in our series. This is different from the literature

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The small number of patients and short follow up period were the limitations of our study.

In conclusion, the best treatment option for PPESRD is KT. However, it is necessary to increase awareness and educate patients and their relatives for KT. KT for PPESRD should be performed as soon as possible either from deceased or living donors.

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Decompressive Surgery for Malignant Middle Cerebral Artery Infarctions

Malign Orta Serebral Arter İnfarktında Dekompresif Cerrahi

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Abstract

Aim: The aim of the study is to evaluate patients who underwent decompressive surgery followed by malignant MCA infarction diagnosis in our center and compare and discuss our results with the current literature.

Materials and Methods: This is a retrospective evaluation of thirty-one malignant middle serebral artery infarction patients who underwent decompressive surgery and were admitted to the Inonu University Turgut Ozal Medical Center, Neurology Clinic Stroke Unit between January 2013 and May 2015.

Results: All patients underwent decompression + duraplasty procedures. The survival rate of the patients who underwent surgery and were followed for at least six months was 29%. The mean age of 18 women and 13 men patients was 65.5 years. The survival rate was 50% in patients under ≤65.

Conclusion: The mortality rate was higher than expected compared with the literature because of the wide range of indications. We observed that multiple risk factors for cerebrovascular diseases and age (above 65) resulted in a statistically significant increase in postoperative mortality. The decompressive surgery in eligible patients may reduce mortality and may provide partial functional well-being.

Keywords: Stroke; Malignant MCA İnfarction; Decompressive Surgery.

Öz

Amaç: Merkezimizde malign Orta serebral arter tıkanıklığı ile takip edilirken dekompresif cerrahi uygulanmış olan hastaları değerlendirmek ve sonuçlarını güncel literatür bilgileriyle karşılaştırarak tartışmak.

Gereç ve Yöntem: Ocak 2013-Mayıs 2015 tarihleri arasında İnönü Üniversitesi Turgut Özal Tıp Merkezi Nöroloji kliniğini inme ünitesinde malign Orta serebral arter tanısı almış ve dekompresif cerrahi yapılmış 31 hasta retrospektif olarak değerlendirilmiştir.

Bulgular: Hastaların tamamına dekompresyon+duraplasi cerrahi prosedürü uygulandı. 18 kadın, 13 erkek hastanın yaş ortalaması 65,5'ti. Cerrahi uygulanan hastaların en az altı aylık izlem sonunda sağ kalım oranı %29 olarak bulundu. Yaş ≤65 alındığında sağ kalım %50 oranında gözlendi.

Sonuç: Mortalite oranı literatür ile karşılaştırıldığında beklenenden yüksek olmakla beraber bu durumun cerrahi için hasta seçiminde kriterlerin daha geniş aralıkta tutulmasından kaynaklandığı düşünülmektedir. İnme için risk faktörü sayısının birden fazla olması ve cerrahiye alınan hastaların yaşının >65 olmasının cerrahi sonrası mortaliteyi istatiksel olarak anlamlı bir şekilde arttırdığı görülmüştür. Uygun hastalarda yapılan dekompresif cerrahi mortaliteyi azaltırken, fonksiyonel anlamda kısmi iyilik hali sağlayabilir.

Anahtar Kelimeler: İnme; Malign OSA Tıkanıklığı; Dekompresif Cerrahi.

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GİRİŞ

İnme, merkezi sinir sisteminde iskemi ya da kanamaya bağlı olarak ortaya çıkan nörolojik defisit şeklinde tanımlanır. Nörolojik acil bir durumdur. İnme hemen bütün ülkelerde morbiditenin ve uzun süreli sakatlığın en önemli nedeni olup endüstrileşmiş ülkelerde, kardiyovasküler hastalıklar ve kanserden sonra üçüncü en sık ölüm nedenidir (1,2). 2010 Dünya sağlık örgütü verilerine göre her yıl dünyada 15 milyon yeni inme vakası görülmekte olup bunların üçte biri ölümle sonlanmakta, üçte birinde ise kalıcı sakatlıklar oluşmaktadır (3). İnmelerin büyük çoğunluğu iskemik inme olup (%80), diğerleri intraserebral hemoraji (%15) ve subaraknoid kanamadır (%5) (4). Ülkemizde de ulusal düzeyde tüm yaş gruplarında görülen ilk 10 ölüm nedeni arasında serebrovaküler hastalıklar %15 ile ikinci sırada yer almaktadır.

İnmedeki yüksek mortalite ve morbiditenin önemli sebeplerinden biri enfarkt veya hemoraji alanın etrafındaki yaygın ödem sonucu gelişen kafa içi basınç artışına bağlı herniasyondur. İskemi alanı ne kadar geniş olursa, intrakranial hacim sabit olduğundan ödemli dokunun şişmesi daha fazla olacak ve kafa içi basıncında artma meydana gelecektir. Bu durum normal beyin parankimini etkileyerek beyin kan dolaşımını ve dolayısıyla da perfüzyon basıncını bozacaktır (5). Malign orta serebral arter (OSA) enfarktları, lober ve kortikal hematomlar unkal ve transtentorial herniasyona yol açarken, serebellar enfarkt, serebellar ve beyin sapı hematomları ise transforaminal tonsiller herniasyona yol açabilirler (6). Malign OSA infarktı terimini ilk olarak Hacke ve ark. kullanmış olup, ilk 48 saat içinde gelişen büyük enfarkt alanının, artan beyin ödemi ve kitle etkisi ile genellikle ilk hafta içinde, agresif medikal tedaviye rağmen transtentorial herniasyon ve ölüme yol açması ile sonuçlanabilen orta serebral arter tıkanıklıklarını tanımlamak için kullanılmıştır (7). Tüm akut iskemik inmelerin %10 kadarını oluşturur. Malign OSA infarktında OSA sulama alanında BT'de en az %50 hipodansite ve 2/3'ünden fazlasında perfüzyon defekti vardır (8). Malign OSA enfarktları etkin medikal tedaviye rağmen %80'lere varabilen yüksek mortalite oranına sahiptir (9).

Dekompresif cerrahi ilk olarak 1901 yılında Kocher tarafından postravmatik beyin ödemi için, 1905 yılında ise Cushing tarafından beyin tümörlü bir vakada kafa içi basıncı azaltmak için yapılmıştır (10,11). Günümüzde en sık uygulanan şekliyle (Kraniektomi+duraplasti) 1981 yılında Rengachery tarafından gerçekleştirilmiştir (12,13). Amaç cerrahi dekompresif kraniyektomi ile ilave hacim alanı sağlamak ve enfarkt- ödem-enfarkt kısır döngüsünü kırmaktadır. Cerrahinin komplikasyonları; yara enfeksiyonu, higroma, beyin omurilik sıvı kaçağı, hidrosefali ve paradoksal herniasyon olarak sayılabilir (14). Buradaki önemli sorunlardan biri hangi hastaların dekompresif cerrahiden fayda görecekleri ve zamanlamadır. İnme olayının başında bu sorunun cevabını vermek oldukça güç olmakla beraber bu işlemin geri dönüşümsüz olayların gelişmesinden önce uygulanması akılcıdır. Böylece normal dokunun ve penumbranın kompresyonu önlenerek enfarktın sınırlandırılması mümkün olacaktır (15). Bir başka ifadeyle geniş enfarktlı ve büyük hematomlu hastalarda, medikal tedaviye rağmen kitle etkisinde artış devam etmekteyse dekompresif cerrahi yaşam kurtarıcı bir tedavi seçeneği olabilir (16,17).

Bu yazıda, merkezimizde akut inme olgularından malign OSA infarktı olan ve dekompresif cerrahi uygulanan hastalar retrospektif olarak değerlendirilmiş olup, operasyon sonrası izlem süreleri, sağ kalım oranları, dizabilite skorları ve sağ kalım oranlarını etkileyen risk faktörleri mevcut literatür bilgileriyle karşılaştırılmıştır.

GEREÇ VE YÖNTEM

Değerlendirmeye Ocak 2013-Mayıs 2015 tarihleri arasında İnönü Üniversitesi Turgut Özal Tıp Merkezi Nöroloji kliniği inme ünitesinde inme tanısı almış hastalardan malign OSA enfarktı olan 18 kadın, 13 erkek toplam 31 hasta alındı. Değerlendirmeye alınan hastaların ayrıntılı anamnezleri, özgeçmişleri, nörolojik muayeneleri kaydedildi. Enfarkt alanı BT ve MRG tetkikleri ile belirlendi. Olgular klinik ve radyolojik olarak takip edilerek herniasyon riski açısından Nöroşirurji Anabilim dalı ile konsulte edildi. Medikal tedaviye rağmen beyin ödemi ve doku şiftinde artış gösteren hastalar herniasyon gelişimini önlemek amacıyla Nöroşirurji tarafından dekompresif cerrahiye alındı. Cerrahiye alınma kriterleri etkili medikal tedaviye rağmen bilinçte gerileme ve beyin herniasyon klinik bulgularının ortaya çıkması, yaşam beklentisinin 3 yıldan az olmaması, tedaviyi bozacak başka ciddi bir hastalığın olmaması, inme öncesi modifiye Rankin Skalası (mRS) skorunun≥2 olmaması, Glaskow Koma Skalasında (GKS) ≥2 azalma olması, bilateral ışığa yanıtsız dilate pupil olmaması, ışık refleksinin alınıyor olması ve gebelik olmaması olarak belirlendi. Cerrahi uygulanan hastaların inme sonrası cerrahiye kadar geçen süreleri, risk faktörleri, geliş ve çıkış GKS, mortalite oranları, dizabilite skorları ve cerrahi sonrası yaşam süreleri kaydedildi. Fonksiyonel bağımlılık ve iyileşmeleri değerlendirmek için mRS kullanıldı (Tablo 1).

Tablo 1. Modifiye Rankin Skalası

0	Hiç semptom yok
1	Belirgin sakatlık yok, semptomlara rağmen hasta günlük aktivitelerini ve görevlerini yerine getirebiliyor
2	Hafif sakatlık; geçmişte yaptığı bütün olağan görev ve aktiviteleri yapamıyor ama yardım olmaksızın kendi işlerini yapabiliyor
3	Orta derecede sakatlık; kendi işlerini görmek için kısmen yardıma ihtiyacı var, ama kendi başına yardımsız yürüyebiliyor
4	Ağır sakatlık; yardımsız yürüyemiyor ve yardımsız bedensel ihtiyaçlarını karşılayamıyor
5	Çok ağır sakatlık; yatağa bağımlı, inkontinans ve devamlı bakıma ve dikkate muhtaç
6	Ölüm

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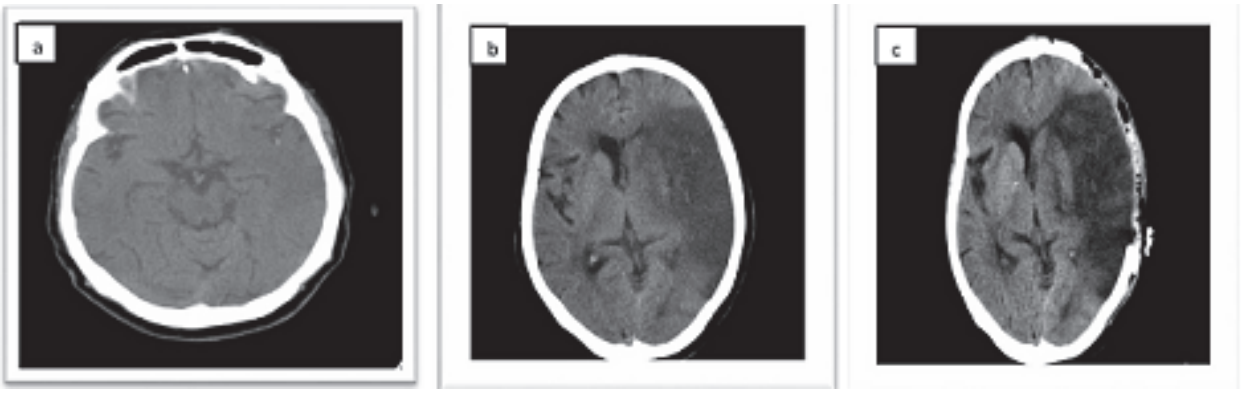
Çalışmanın istatistikleri SPSS ver 20.0 (Statistical Package for the Social Sciences) istatistik programı kullanılarak yapıldı. Sürekli değişkenlerin dağılım paternleri Kolmogrov-Smirnov testi ile ölçüldü. İki grubun ortalamaları student t- testi ile karşılaştırıldı. Non-parametrik verilerin karşılaştırılmasında Fisher exact chi-square testi kullanıldı. Veriler, ortalama ve standart sapmalar (SS) olarak verildi. İstatistiksel anlamlılık seviyesip<0.05 olarak kabul edildi.

BULGULAR

1-13 gün içinde etkili anti-ödem tedaviye rağmen klinik kötüleşme gösteren ve dekompresif cerrahiye alınan 18 kadın, 13 erkek olmak üzere toplam 31 malign OSA enfarktlı hasta değerlendirildi. Malign OSA kriteri olarak; BT ve MRG'da OSA sulama alanının en az %50'sinde hipodansite olması alındı (8). Yaşları 31-81 (ortalama 65.5) arasında değişen hastaların tamamına kraniektomi+duraplasti cerrahi prosedürü uygulandı (Resim 1).

Cerrahi sonrası 9 (%29) hasta yaşarken (izlem süresi en az 180 gün), 22 (%71) hasta kaybedildi. Sağ kalımla cinsiyet arasında anlamlı farklılık yoktu (erkek sağ kalım %30.8, kadın sağ kalım %27.8). Yaşayan hastaların yaş ortalaması 62,6 iken, kaybedilenlerin 66,7 olarak gözlendi. Etyolojide hastaların %61,3'ü kardiyoembolik inme iken, %38,7'si aterotrombotik inme olarak saptandı. Ölen hastaların cerrahi sonrası ortalama yaşam süreleri 12,8 gündü. Bu hastaların 12'si kardiyak nedenlerden, 3'ü enfeksiyon nedeniyle, 7 hasta ise herniasyon nedeniyle ölmüştü. Cerrahiye alınan hastaların cerrahi öncesi ortalama GKS'ları 8.45, ortalama mRS ise 4.26 idi. Yaşayan hastaların mRS'na bakıldığında operasyon öncesi ortalama değer 4 iken, ölenlerin ise 4,36 olarak saptandı. Yaşayan hastaların cerrahi öncesi ortalama GKS'sı 9,22 iken ölenlerin 8,14 olarak bulundu. Hastaların inme sonrası cerrahiye kadar geçen ortalama süresi 3,16 gündü. Hastaların %22,6'sında hemorajik transformasyon gelişti (Tablo 2).



Resim 1. Aksiyal non-kontrast BT incelemesi. **a**-Geliş BT incelemesi. **b**-1. günde sol OSA sulama alanında ortaya çıkan enfarkt, sol lateral ventrikülde ödeme sekonder silinme. **c**-Dekompresif cerrahi sonrası hastada operasyon öncesine göre herniasyon bulgularının belirginleşmediği görülüyor.

Tablo 2. Dekompresif cerrahi uygulanan hastaların özellikleri

	Yaşayan(N=9)	Ex(N=22)	p
Yaş, yıl	62,6 ±7,21	66,7 ±13,18	0,282
Erkek, n(%)	4(%44,4)	9(%40,9)	0,583
Hemorajik transformasyon, n(%)	3(%9,7)	4(%12,9)	0,319
Ortalama GKS	9,22	8,14	0,222
Ortalama mRS	4	4,36	0,074
Risk faktörleri, n(%)			
Hipertansiyon	4(%44,4)	14(%63,6)	0,279
Diyabet	1(%11,1)	6(%27,3)	0,320
Sigara	2(%22,2)	1(%4,5)	0,195
Koroner arter hastalığı	2(%22,2)	10(%45,5)	0,215
Atrial fibrilasyon	0(%0,0)	3(%13,6)	0,343
Hiperlipidemi	1(%3,2)	3(%13,6)	0,298

Cerrahi zamanı, GKS, ve mRS değerleri, etyoloji, yaş ve hemorajik transformasyon parametrelerinin sağ kalımla istatistiksel olarak anlamlı olmadığı görüldü. Risk faktörleri olarak hipertansiyon, diyabet, koroner arter hastalığı, hiperlipidemi, aritmi ve sigara değerlendirmeye alındı. Teker teker risk faktörlerinin sağ kalım ile

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istatistiksel olarak anlamlı olmadığı fakat risk faktörü sayısının sağ kalımla istatiksel olarak anlamlı olduğu görüldü (risk faktörü sayısı yok veya bir ise sağ kalım %25,8, üzerindeyse %3,2. p:0,031) (Tablo3). Yaşayan hastaların izleminde mRS değerinde ortalama 1 puan azalma gözlendi.

Tablo 3. Risk faktörü sayısının mortalite ile ilişkisi

Risk sayısı	Yaşayan(n) (%)	Ex (n) (%)	P değeri
≤1	8 (%25,8)	10 (32,39)	0,031
>1	1 (%3,2)	12 (38,7)	
Toplam	9 (%29)	22 (%71)	

TARTIŞMA

Malign OSA infarktlarında kan basıncı kontrolu, antiödem tedavi gibi konvansiyonel medikal tedaviler zaman zaman intrakranial basıncı azaltmakta etkisiz kalabilmektedir. Bu durumda artmış kafa içi basıncı serebral kan akımını ve beyin oksijenasyonunu bozar. Bu kısır döngüyü kırarak penumbra dokusunu kurtarmak için, geriye dönüşsüz hasar oluşmadan, dekompresif cerrahi uygulanarak ödemli beyin dokusuna genişleyecek alan sağlamak gerekir.

Dekompresif cerrahinin sağ kalım ve fonksiyonel iyileşme üzerine etkileri son yıllarda yapılan bazı çalışmalarda, eski çalışmaların aksine olumlu sonuçlar göstermiştir (18).

Malign OSA enfarktlarında dekompresif cerrahi ile ilgili yapılan, 32 hastanın randomize edildiği DESTINY çalışmasında bir ayın sonundaki mortalite oranı dekompresyon yapılan grupta %12, cerrahi uygulanmayan grupta %53 saptanmıştır (19). 64 hastanın randomize edildiği HAMLET çalışmasında ise ondördüncü günde mortalite oranı dekompresyon yapılanlarda %16, yapılmayanlarda %56 bulunmuştur (20). 38 hastanın randomize edildiği DECIMAL çalışmasında mortalite oranı bir ayın sonunda dekompresyon yapılanlarda %16, yapılmayanlarda %33 saptanmıştır (21). Bizim çalışmamızda ise malign OSA enfarktı olan dekompresif cerrahi uygulanan hastaların mortalite oranı bir ayın sonunda %71 gibi yüksek bir değerdeydi. Çalışmamızda malign OSA infarktlı hastalardan dekompresif cerrahiye alınmış olanlar değerlendirilmiş olup malign OSA tıkanıklığı olup medikal tedavi ile takip edilen hastalar çalışmaya dahil edilmemiştir. Bu durum çalışmamızdaki en önemli sınırlayıcı faktördür. Mortalite oranlarında diğer çalışmalardan bu farklılık ve mortalitenin neredeyse malign OSA tıkanıklığı olan ve medikal tedavi verilen hastalardaki mortalite oranlarına yaklaşık olması cerrahiye alınan hastaların seçimiyle ilgili görünmektedir.

Hastaların akut enfarkt sonrası cerrahiye alınma zamanı DESTINY çalışmasında 36 saat, HAMLET çalışmasında 24-96 saat, DECIMAL çalışmasında 48 saat ile sınırlandırılırken sunulan çalışmada değerlendirilen hastaların akut enfarkt sonrası cerrahiye alınma zamanı 1-13 gün (ortalama 3,16 gün) gibi geniş bir aralıktaydı (22). Cerrahinin zamanlamasıyla ilgili yapılan çeşitli çalışmalarda mortalite açısından erken (0-23 saat) ve geç (24-48 saat) cerrahi arasında istatiksel olarak anlamlı sonuçlar bulunmamasına rağmen güncel çalışmalarda erken cerrahide komplikasyonların daha düşük oranda olduğu gösterilmiştir (22,23). Bunun aksine bir başka çalışmada ise erken dönem cerrahinin mortaliteyi azalttığı, geç dönem cerrahide ise mortalitenin azalmadığı fakat dizabilite açısından farklılık göstermedikleri gösterilmiştir (24). Sonuç olarak erken cerrahinin mortalite üzerine ya direkt etkisi olduğu ya da komplikasyonlar üzerinden dolaylı etkisinin olduğunu söylemek yanlış olmaz. Erken cerrahi için hasta seçiminde enfarkt alanının %50'den fazla olması durumlarında 6. saatteki difüzyon MR görüntülemesinde enfarkt volümü>82 ml ve 14. saatteki enfarkt volümü>145 ml ise herniasyon açısından oldukça yüksek risk belirtmekle beraber masif ödem gelişeceği ile ilgili tahmin yeteneğimiz yanılmaz olmadığından gereksiz cerrahi açısından dikkatli olunmalıdır (22). Çalışmamızdaki mortalitenin yüksek değeri retrospektif olarak çalışmaya alınan hastalarda cerrahiye alınma zamanının geniş bir aralıkta olması ile ilgili olabilir.

Diğer hasta seçim kriterlerine bakılacak olursa HAMLET çalışmasında yaşın 18-60 aralığında olması, National Institutes of Health stroke scale (NIHSS) skorunun sağ hemisfer lezyonlarında 16'dan, sol hemisfer lezyonlarında 21'den büyük olması, yaşam beklentisinin 3 yıldan fazla olması ve tedaviyi etkileyecek diğer ciddi hastalıkların olmaması sayılabilir (20). DECIMAL çalışmasında yaşın 18-55 aralığında olması, NIHSS skorunun 16'dan büyük olması, sekonder hemorajik transformasyonun olmaması, yaşam beklentisinin 3 yıldan az olmaması ve tedaviyi bozacak ciddi başka bir hastalığın olmaması sayılabilir (21). DESTINY çalışmasında ise yaşın 18-60 arasında olması, NIHSS skorunun non-dominant hemisferde >18, dominant hemisferde >20 olması, inme öncesi mRS ≥2 olmaması, GKS<6 olmaması, hemorajik transformasyon olmaması, yaşam beklentisinin 3 yıldan az olmaması, başka bir ciddi hastalığının olmaması ve başka bir eşlik eden beyin lezyonu olmaması olarak belirlenmiştir (19). Çalışmamızda yaş sınırlaması yoktu (31-81 yaş, ortalama 65,5). Literatürde daha genç malign OSA enfarktlı hastalarda cerrahinin mortalite açısından daha iyi sonuçlar verdiği bildirilmiştir (22). Sunulan çalışmada değerlendirilen hastaların yaşı ≤65 olarak alınırsa 14 hastanın 7 (%50,0)'si yaşarken 7(%50,0) hasta ex olmuştur. Bir başka ifade ile sağ kalım, cerrahiye alınan hastaların yaşı ≤65 olduğunda %29'dan %50,0'ye çıkmaktadır (Tablo 4).

Ayrıca hastalarımızda sekonder hemorajik transformasyon olması ve NIHSS skoru çalışmaya alınma kriteri değildi. Çalışmamızdaki yüksek mortalite oranının nedeni hasta seçiminde çalışmaya alınma kriterlerinin geniş bir aralıkta olması olabilir.

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Tablo 4. Yaş ile mortalite arasındaki ilişki

Yaş	Yaşayan (N) (%)	Ex (N) (%)	Toplam (N)	P değeri
≤65	7 (%50,0)	7 (%50)	14	
>65	2 (%11,8)	15 (%88,2)	17	0,026

Mortalite oranları DESTINY çalışmasında bir ay, HAMLET çalışmasında ondört gün ve DECIMAL çalışmasında ise bir aylık izlem sonuçlarına göre verilmiştir. Çalışmamızda ise mortalite en az 180 günlük izlem süresi sonunda değerlendirildi. Bu durum daha kısa izlem süreleri olan diğer çalışmalara göre çalışmamızdaki yüksek mortalite nedenlerinden biri olabilir. Daha uzun izlem sürelerinde mortalite oranlarının ne olduğu hasta sayısı artırılarak değerlendirilmelidir.

İnme için yaş, cinsiyet, ırk gibi değiştirilemeyen risk faktörlerinin yanında hipertansiyon, diyabet, hiperlipidemi, sigara, asemptomatik karotis stenozu ve orak hücreli anemi gibi değiştirilebilen risk faktörleri sayılabilir. Suyama K ve ark. yaptığı çalışmada malign OSA infaktlarında dekompresif cerrahi sonrası mortalite ile atrial fibrilasyonun ilişkili olduğu gösterilmiştir (25). Hemisferik inmelerde uygulanan dekompresif cerrahi için prognostik faktörleri inceleyen bir başka çalışmada ise hipertansiyonun cerrahi sonrası kötü sonlanım için bağımsız bir risk faktörü olduğu saptanmıştır (26). Sunulan çalışmada dekompresif cerrahiye alınan hastaların risk faktörü sayısının mortalite ile ilişkili olduğunu gördük. Hipertansiyon, koroner arter hastalığı, diyabet, sigara, hiperlipidemi ve aritmiyi içeren risk faktörü sayısı birden çok olduğunda sağ kalımın istatiksel olarak anlamlı bir şekilde azaldığı görüldü. Bu durum dekompresif cerrahi için hasta seçiminde göz önünde bulundurulmalıdır.

Malign OSA infaktlarında yapılan dekompresif cerrahinin mortaliteyi azalttığı yapılan birçok çalışmada yukarıda bahsedildiği gibi gösterilmiştir (19, 20, 21). Fakat bu çalışmaların ve diğer birçok çalışmanın bir diğer ve belki de daha önemli amaçları cerrahi sonrası fonksiyonel iyilik halinin değerlendirilmesidir. Yaşam kalitesi ve bağımsız yaşam cerrahinin etkili bir tedavi seçeneği olup olmadığını belirlemede önemlidir. Fonksiyonel açıdan bakıldığında bu üç Avrupa çalışmasında da, cerrahi sonrası iyi fonksiyonel sonuç için mRS≤3 alındığında anlamlı iyilik saptanamamış olup ancak mRS≤4 alındığında anlamlı fonksiyonel iyilik hali saptanmıştır (22). Çalışmamızda yaşayan hastaların takibinde operasyon öncesi ortalama mRS 4 iken, operasyon sonrası bu değer ortalaması 3'e inmişti. Böylece malign OSA infarktlı hastalara uygulanan cerrahi tedavinin özellikle ≤65 yaş, erken cerrahi zamanı ve inme için bilinen risk faktörü sayısı ≤1 olduğunda mortaliteyi azalttığı fakat fonksiyonel anlamda hastaların kendi ihtiyaçlarını görebilmelerine yetecek düzeyde iyileşme sağlamadığı söylenebilir.

SONUÇ

Malign OSA enfarktlarında medikal tedaviye rağmen kötüleşen hastalarda yapılacak cerrahi mortaliteyi azaltmakta ve kısmende olsa fonksiyonel iyilik sağlamaktadır. Sunulan çalışmadaki mortalite oranları literatür ile karşılaştırıldığında beklenen düzeyde olmamakla beraber bu sonucun hasta seçiminde kullanılan kriterlerin geniş tutulmasına bağlı olduğu düşünüldü. Çalışmamızda özellikle ≤65 yaş ve serebrovasküler hastalıklar için bilinen risk faktörü sayısının≤1 olması düşük mortalite açısından istatiksel olarak anlamlı bulunmuştur. Bir başka ifade ile malign OSA enfarktı olan ve dekompresif cerrahi yapılması planlanan hastaların yaşı≤65 ve hipertansiyon, diyabet gibi bilinen vasküler risk faktörü sayısı birden fazla değilse cerrahi sonrası sağ kalımın daha yüksek oranlarda olacağı söylenebilir. Cerrahi sonrası fonksiyonel iyilik hali ise daha az yüz güldürücü olmakla beraber kısmende olsa düzelme sağlamaktadır. Çalışmamızda da istatiksel olarak anlamlı olmasada mRS değerinde cerrahi sonrası yaşayan hastalarda 1 puanlık fark vardı. Sonuç olarak malign OSA enfarktlı hastalarda, etkin medikal tedaviye rağmen beyin ödemindeki artış engellenemiyorsa, uygun kriterlerle seçilecek hastalarda dekompresif cerrahi iyi bir tedavi seçeneği olabilir. Bu konuda hasta sayısı artırılarak ve daha seçici davranılarak hangi hastaların cerrahiden fayda görebileceklerini belirleyecek daha fazla sayıda çalışmaya ihtiyaç vardır.

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The Effects of Serum Neurotensin-C Levels on Insulin Resistance in Polycystic Ovary Patients

Polikistik Over Tanısı Alan Hastalarda İnsülin Rezistansı Üzerine Serum Neurotensin-C Düzeylerinin Etkisi

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Abstract

Aim: Neurotensin has a role in the onset of diabetes mellitus. In this study, we aim to compare serum neurotensin levels between obese and non-obese patients with PCOS.

Materials and Methods: Patients were divided into four groups. We measured and calculated the following parametres: age, BMI, biochemical and hormonal profiles, and serum neurotensin levels. The results were compared within the groups. As statistical methods, we used the chi-square test and the Mann-Whitney-U test.

Results: We found certain differences between the PCOS patients and control groups. Mean values of age, FGS, and LH levels were higher than those of the control groups. LH levels were higher in the non-obese PCOS patients than the non-obese control group patients. Weight, BMI, LDL, and triglycride levels were also higher in the obese PCOS patients than the non-obese PCOS patients. HOMA-IR values were found to be highest in the obese PCOS patients. There was no significant difference between the groups in terms of NT. Evaluating the results, we observed that NT levels were similar in the non-obese PCOS patients (NT:0,67±0,709) and obese control group patients (NT:0,66±1,47). Similarly, NT levels were quite similar in the obese PCOS patients (NT: 0,43±0,362) and non-obese control patients (NT:0,47 ±0,406).

Conclusion: It was determined that lipid profile and HOMA-IR values are higher in patients with PCOS. Also, in non-obese PCOS patients and obese control group, the lipid profile, HOMA-IR values, fasting glucose and fasting insulin levels are determined to be significantly higher than the values of the non-obese control group. However, no significant difference was found in NT values between the patient groups.

Keyword: Polycystic Over Syndrome; Diabetes Mellitus; Neurotensin-C.

Öz

Amaç: Bu çalışmada polikistik over sendromu tanısı olan obez ve non-obez hastalarda diyabetes mellitus insidansını belirleyen serum nörotensin düzeyinin kontrol gruplarıyla karşılaştırılması amaçlanmıştır.

Gereç ve yöntemler: Hastalar 4 gruba ayrıldı. Bu hastaların yaş, VKİ, biyokimyasal ve hormonal profilleri ile NT düzeyleri karşılaştırıldı. İstatistiksel yöntem olarak Ki-Kare testi, Mann-Whitney U testi kullanıldı.

Bulgular: PKOS olan hastalar ile PKOS olmayan hastalarda yaş, FGS, FSH, LH değerleri arasında istatiksel olarak anlamlı farklılık tespit edildi. PKOS hastaların yaş ortalaması, FGS ve LH değerleri PKOS olmayan hastalardan daha yüksek tespit edildi. Non-obez PKOS hastalar ile non-obez kontrol grubundaki hastalar arasındaki karşılaştırmada LH, PKOS hastalarında daha yüksek olarak tespit edilmiştir. Obez PKOS hastalarında kilo, VKİ, LDL ve trigliserid non-obez PKOS hastalarına oranla daha yüksek olarak bulunmuştur. HOMA-IR değerinin ise obez PKOS hasta grubunda en yüksek olduğu tespit edilmiştir. Nörotensinin (NT) gruplar arasındaki dağılımına bakıldığında non-obez PKOS hasta grubunun (NT:0,67±0,709) obez kontrol grubuyla (NT:0,66±1,47) hemen hemen yakın değerlere sahip olduğu gösterilmiştir. Obez PKOS hastalar (NT: 0,43±0,362) ile non-obez kontrol grubunda (NT:0,47 ±0,406) NT düzeyi birbirine oldukça yakın olarak tespit edilmiştir.

Sonuçlar: PKOS tanısı alan hastalarda lipid profilinin ve HOMA-IR değerinin daha yüksek olduğu tespit edildi. Obezitesi olmayan PKOS ve obez kontrol hastalarında benzer şekilde lipid profilinin, HOMA-IR değerinin, açlık glukoz ve açlık insülin değerlerini obez olmayan kontrol grubundan anlamlı olarak yüksek olduğu tespit edilmiştir. Ancak nörotensin düzeyi açısından hasta grupları arasında anlamlı bir fark tespit edilemedi.

Anahtar Kelimeler: Polikistik Over Sendromu; Diyabetes Mellitus; Neurotensin-C.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common reproductive endocrine disorder seen in women of reproductive age. Although the overall frequency varies according to different diagnostic criteria, its incidence is around 6-8% in childbearing age (1). It was first defined by Stein and Leventhal in 1935 within an amenorrhea, hirsutism, and obesity triad. Although significant improvements have been recorded in the intervening 70 years in terms of PCOS, there are still ongoing debates as to the pathogenesis and diagnosis of the syndrome (2). Insulin resistance plays an important role in its etiopathogenesis; yet, hyperinsulinemia together with insulin resistance leads to abnormalities and changing gonadotropin responses in the metabolism of androgens in the ovaries. These hormonal changes, bring about clinical symptoms such as menstrual disorders, anovulation, and hyperandrogenism (3).

Combination of deterioration in glucose tolerance and type 2 diabetes mellitus is frequently seen in PCOS patients. PCOS is recognized as an independent risk factor for the development of type 2 diabetes mellitus; therefore, all PCOS patients are recommended to undergo screening for diabetes mellitus. In this patient group, too, insulin resistance is known to play a major role in the development of this condition (4).

Primarily released from the central nervous system and gastrointestinal tract, neurotensin is a peptide consisting of 13 amino-acid types. Neurotensin secretion is stimulated by food intake at the periphery while this also regulates gastric motility and the pancreas and bile secretion. At low levels of glucose, neurotensin is observed to increase insulin and glucagon secretion. Studies have shown that patients with high levels of neurotensin have a lower risk of diabetes in the long term (5).

MATERIALS and METHODS

We included 42 women volunteers in the study who met the Rotterdam PCOS diagnosis criteria. The volunteers were selected from women of reproductive age (16-38 years) presenting at the Gynecology and Obstetrics Clinic at Inonu University, School of Medicine, Turgut Ozal Medical Centre. The control group consisted of healthy women. A total of 84 patients - the 42 volunteers who met the Rotterdam PCOS criteria and 42 PCOS-free volunteers - were divided into 4 different groups. Sample size was determined by power analysis. Patients with a body mass index (BMI) of over 30 were evaluated in the obese group. The first group contained PCOS patients with BMI less than thirty (non-obese PCOS); the second group comprised of PCOS patients with BMI of over thirty (obese PCOS); the third group were non-PCOS patients BMI over thirty (obese control group); and the fourth group consisted non-PCOS patients with BMI under thirty (non-obese control group).

From each individual involved in the study, we obtained antecubital venous blood samples in the early follicular phase (on the 2nd-5th days of the regular or progesterone-induced menstruation) after 12-hour fasting. These samples were put in anticoagulant-free tubes. The serums of the samples were separated after 5-minute centrifugation at 4000 rpm. Until they were examined, the samples were stored in eppendorf tubes at 20° C.The samples were evaluated after they were cooled down to room temperature. While evaluating the results obtained in this study, we used average, standard deviation, rating, and frequency values for the descriptive statistics of the data. In the analysis of quantitative data, we used the Mann-Whitney U test.

For the qualitative data analysis, we made use of the chi-square test; in cases when the conditions were not met for the chi-square, we preferred Fisher's exact test. We used SPSS 17.0 software for the analysis and p value <0.05 was considered to be statistically significant.

RESULTS

We calculated the demographic and anthropometric averages of the groups. Statistically, we primarily conducted general comparisons between the groups. We determined the statistically significant differences and compared the groups once again within one another (Table 1). We found out that there was no significant differences between the groups in terms of age and height. However, BMI values varied between groups. The average BMI results for the groups were as follows: Group 1: 20.4; Group 2: 31.8; Group 3: 32.9; and Group 4: 22.3.

Table 1. Anthropometric data of the patients. **BMI:** Body mass index; **FGS:** Ferriman Galleway Score

Parameters	Group1 (n:21)	Group2 (n:21)	Group3 (n:21)	Group4 (n:21)	*P value*
Age	22,9±4,5	25±6,6	31,9±5,5	27,8±7,4	*0,0001*
Height	164,04±5,7	160,8±5,6	160,4±6,1	162,2±6,9	*0,119*
Weight	56±5,7	81,4±4,5	84,2±10,5	59,5±9,4	*0,0001*
BMI	20,4±2,08	31,8±1,8	32,9±4,04	22,3±2,5	*0,0002*
FGS	19,7±10,3	21,04±11,08	0,90±4,14	1,19±5,4	*0,0001*

First, the groups were compared in terms of hirsutism and oligomenorrhea, two factors that could not be measured in quantity. There were significant differences between non-PCOS groups (group 3-4) and PCOS groups (groups 1-2) in terms hirsutism and oligomenorrhea. The differences concerning hormonal

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and biochemical parameters between the groups are summarised in Table 2. There were also significant differences between the groups as far as LH, SHBG, triglycerides, LDL cholesterol, fasting glucose, fasting insulin, and HOMA-IR values were concerned. Evaluating the neurotensin distribution between the groups, we observed that non-obese PCOS patient group (NT: 0.67 ± 0.709) had similar values with the obese control group (NT: 0.66 ± 1.47).

Table 2. Serum biochemstry and hormonal data of the patients. **FSH:** Follicle stimulating hormone; **LH:** Luteal hormone; **E2:** Estradiol; **tTestesteron:** Total Testosterone; **fTestosterone:** Free Testesteron; **DHEAS:** Dehydroepiandrosterone Sulphate; **SHBG:** Sex hormone-binding globulin; **LDL:** Low density lipoprotein; **HDL:** High density lipoprotein; **HOMA-IR:** Homeostasis model assessment–IR (fasting glucose (mg/dL) x fasting insulin (pmol/L) / 405).

Parametres	Group1 (n:21) M± SD	Group2 (n:21) M± SD	Group3 (n:21) M± SD	Group4 (n:21) M± SD	*P value*
FSH	4,7±1,3	4,9±0,94	6,6±2,3	6,1±2,7	*0,019*
LH	5,7±2,3	7,2±8,05	3,1±1,3	3,5±1,6	*0,0001*
E2	63,5±32,2	69,4±61,1	58,01±14,2	46,9±16,3	*0,143*
tTestesteron	33,3±16,8	43,8±23,7	29,8±16	28,6±13,8	*0,020*
fTestesteron	1,4±0,42	1,9±0,79	1,5±0,61	1,4±1,03	0,013
DHEAS	212,8±130,3	200,3±90,1	166,4±63,9	171,7±88,6	*0,78*
SHBG	58,8±38,8	49,9±51,2	27,6±15,01	56,1±43,1	*0,008*
Triglyceride	85,4±43,8	140±55,6	132,2±57,9	117,7±93,5	*0,003*
Cholesterol	152,2±30,5	182,1±41,5	178,1±40,5	176,6±35,9	*0,28*
LDL	88,04±23,3	115,09±31,9	142,04±132,4	115,6±34,9	*0,003*
HDL	49,1±6,3	45,5±9,1	41,6±7,7	46,1±8,6	*0,024*
Fasting glucose	86,6±7,6	89,9±7,04	100,8±26,5	77,4±6,2	*0,0001*
Fasting insuline	12,2±8,1	22,6±14,6	25,6±23,05	9,71±4,07	*0,0001*
HOMA-IR	2,5±1,5	4,9±3,4	7,4±7,8	1,74±0,76	*0,0001*
Neurotensin	0,67±0,7	0,43±0,36	0,66±1,4	0,47±0,4	*0,555*

The NT levels were found to be quite close to each other in the obese PCOS patients (NT: 0.43 ± 0.362) and non-obese PCOS-free patients (NT: 0.47 ± 0.406). Considering these differences between PCOS and non-PCOS groups, we observed that healthy patients had higher neurotensin levels (0.56 ± 1.07) while this was not statistically significant.

DISCUSSIONS

Polycystic ovary syndrome is the most common ovulatory dysfunction. While its overall clinical perspective is very wide, it often accompanies hyperandrogenism, ovulatory dysfunction, and polycystic ovaries with an incidence rate of 6-8%. PCOS is a systemic pathology ranging from reproductive function weakness to cardiovascular diseases and cancer in the long-term (1, 6). Indeed, researchers have been curious for many years to understand how an ovary-induced pathology can have systemic impacts to this extent and focused on insulin resistance for an answer (3). Developing insulin resistance affects blood lipid levels, increases central obesity as well as the incidence of cardiovascular diseases. In return, increasing obesity worsens insulin resistance and has negative affects on glucose tolerance by increasing fasting glucose values (7). As far as the insulin-receptor interaction is concerned, the relationship between this pathology, which is thought to be caused by post-receptor intracellular signal transmission, and hyperandrogenism was first defined by Burghen et al. Since then, there have been other studies focusing on the relationship between these two (8). It is inevitable as well as, time and again, reported that PCOS patients would naturally have high fasting glucose, fasting insulin, and HOMA-IR values due to their insulin resistance. Gerard et al.'s study on 131 patients has shown that patients in the obese PCOS group had higher fasting glucose levels than the patients in the non-obese PCOS (9). Likewise, Li X et al.'s study conducted on 192 PCOS patients has reported that fasting insulin and fasting glucose levels were higher in the obese PCOS patients compared to non-obese PCOS group patients (10). Amisi et al.'s study on 104 patients has similarly shown that PCOS patients had higher HOMA-IR values than the patients in the control group (11). In our study, too, PCOS patients who had BMI>30 and were diagnosed with obesity had significantly higher fasting glucose, fasting insulin, and HOMA-IR values than non-obese PCOS patients.

Although how insulin resistance develops is known, its cause still remains a mystery to this day. There is a great number of studies trying to unveil this mystery. In these studies, focusing on serum neurotensin levels has become more popular in recent years. Pancreatic beta cells contain neurotensin receptors. It is through these receptors that insulin secretion takes place due to increased intracellular calcium. Besides, it is an insulin-sensitive regulator that plays key role in transporting glucose to muscle and fat tissues (12). Because of its effect on pancreatic, muscular, and fat tissues, neurotensin is considered as a mediator preventing the development of diabetes. There are several animal studies describing the relationship between neurotensin and blood glucose as well as lipid concentration. Boules et al.'s study on rodents has shown that small rodents, which were given analogous neurotensin, gain less weight than the control group. It was also determined that rodents receiving analogous neurotensin experience weight reduction due to decrease in food intake. It was

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shown that neurotensin increases blood glucose levels and corticosterone in some rodents (13). Sahu et al.'s on rats has shown that intracerebral and intraperitoneal administration of neurotensin antiserum blocks the effect of leptin while Kim et al.'s study has reported that rats that lack neurotensin do not show the effects of leptin (14, 15). Considering the results of these studies, we can conclude that leptin, which affects the feeling of satiety and nutrition habits in humans, creates this impact in some relation to neurotensin, that neurotensin mediates in the leptin effect, and that low serum neurotensin levels are in an indirect relationship with weight gain and obesity. In our study, the serum neurotensin levels of obese patient group were lower than the non-obese patients; yet, this relationship was not statistically significant.

Trying to explain the effect of neurotensin through leptin is inadequate; yet, extensive studies in recent years have shown that it has relationship with different mediators as well. Leinninger et al.'s study has shown that leptin, which affects neurotensin-mediated neurons, controls the release of orexin (16). Tsuneki et al.'s study on rats has revealed that orexin receptor agonists inhibit insulin resistance and that patients with low orexin levels also have greater insulin resistance (17). Yılmaz et al.'s research on PCOS patients has shown that PCOS patients have lower orexin levels (3).

CONCLUSION

The pathology of the patients diagnosed with PCOS is based on insulin resistance. Despite numerous pathophysiological mechanisms behind the development of insulin resistance, causes of this resistance have not been set out clearly yet. Even though neurotensin is a mediator that has received much interest in recent years, it is often studied on animals in relation to the development of diabetes mellitus and weight balance.

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Evaluation of Metallo Beta Lactamase E test Results from Different Brands of Mueller Hinton Agar Plates

MBL E Test Araştırmasında 5 Farklı Marka Müller-Hinton Agar Besiyerlerinden Elde Edilen Sonuçların Değerlendirilmesi

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Abstract

Aim: MBL E test for MBL screening in carbapenem resistant Pseudomonas aeruginosa isolates is recommended as a fast and reliable phenotypic screening test. However, as it has been put forward by some reserachers, because of variations in antibiotic susceptibility tests or MBL E test with different brands of Müeller- Hinton Agar (MHA) media, the possibility that carbapenem MIK values and MBL E test results can, therefore, be influenced by these media. To this end, we aim to determine the most suitable MHA media to be used in search for MBL E test in routine microbiology laboratories by employing five different brands of MHA media.

Materials and Methods: 29 carbapenem resistant *Pseudomonas aeruginosa* strains isolated from hospitalised patients have been used in this study. *P.aeruginosa* isolates were identified by conventional methods. Imipenem and meropenem E test were used for verification of carbapenem resistance. MBL E test was used for detecting MBL production by five different brands of Mueller Hinton agar plates and the results of these tests were compared with polymerase chain reaction (PCR) results.

Results: IMP, VIM, GIM, SIM and SPM type genes were found to be negative with polymerase chain reaction for 29 isolates that were resistant to carbapenem. One isolate with BBL brand MHA, two isolates with Oxoid brand MHA, 19 isolates with Himedia brand MHA, 21 isolates with Merck brand MHA, and 27 isolates with Plasmatec brand MHA gave positive results.

Conclusion: The present results indicate that use of BBL or Oxoid brand MHA media, especially in laboratories without any fascilities for molecular diagnosis, can be more reliable compared to other brands.

Keywords: MBL E Test; Pseudomonas Aeruginosa; Metallo Beta-Lactamase.

Öz

Amaç: Karbapenem dirençli *Pseudomonas aeruginosa* izolatlarında MBL taraması için MBL E test; hızlı ve güvenilir fenotipik test olarak önerilmektedir. Ancak antibiyotik duyarlılık testlerinde MBL E testinde kullanılan farklı marka Müeller- Hinton Agar (MHA) besiyerlerinde karbapenem MİK değerleri ve MBL E test sonuçlarının etkilenebileceğini gösteren çalışmalar mevcuttur. Bu nedenle çalışmamızda 5 farklı marka MHA besiyeri kullanarak, rutin mikrobiyoloji laboratuarlarında MBL E test araştırılmasında kullanılabilecek en uygun marka MHA besiyerini belirlemeyi amaçladık.

Gereçler ve Yöntemler: Çalışmada yatan hastalardan izole edilen, karbapenemlere dirençli 29 *Pseudomonas aeruginosa* izolatları konvansiyonel yöntemler ile tanımlanmıştır. Karbapenem direncini doğrulamak için imipenem ve meropenem E test (AB BIODISK, Solna, İsveç) kullanılmıştır. MBL üretimini belirlemek için MBL E test (AB BIODISK, Solna, İsveç) beş farklı marka (Oxoid, BBL, Merck, Himedia, Plasmatec) Müller Hinton agar (MHA) besiyerinde test edilmiş ve elde edilen sonuçlar Polimeraz Zincir Reaksiyonu sonuçları ile karşılaştırılmıştır.

Bulgular: Karbapenemlere dirençli 29 izolatta Polimeraz Zincir Reaksiyonu ile IMP, VIM, GIM, SIM ve SPM tipi metallo beta-laktamaz geni saptanmamıştır. MBL E test ile BBL marka MHA besiyerinde bir izolat (1/29), Oxoid marka MHA besiyerinde iki izolat (2/29), Himedia marka MHA besiyerinde 19 izolat (19/29) Merck marka MHA besiyerinde 21 izolat (21/29), Plasmatec marka MHA besiyerinde 27 izolat (27/29) pozitif sonuç vermiştir.

Sonuç: Moleküler tanı yapma olanağı olmayan laboratuvarlarda MBL E test araştırmalarında BBL ve Oxoid marka besiyerlerinin, diğer besiyerlerine oranla daha güvenilir bir şekilde kullanılabileceği sonucuna varılmıştır.

Anahtar Kelimeler: MBL E Test; Pseudomonas Aeruginos; Metallo Beta-Laktamaz.

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GİRİŞ

P.aeruginosa birçok antimikrobiyal ilaca doğal olarak dirençli bir mikroorganizmadır. Kromozomal ve plazmid kaynaklı beta-laktamazların üretimi, hedef ve porin proteinlerindeki değişiklik sonucu dış membran geçirgenliğinin azalması, efluks pompa sistemi ile antimikrobiyal ilacın dışarı atılması başlıca direnç mekanizmalarıdır. Genişlemiş spektrumlu beta-laktamazlar (GSBL), AmpC tipi beta-laktamazlar, imipenem (IMP) ve/veya meropenemi hidrolize edebilen karbapenemaz enzimlerine sahiptirler. Karbapenemaz enzimleri içerisinde klinik yönden en önemlileri metallo-beta-laktamaz (MBL) enzimleridir. Aztreonam hariç tüm beta-laktam antibiyotikleri hidrolize edebilen MBL enzimlerini kodlayan genler plazmid ve integronlarda lokalize olabilmekte, bu durum direncin diğer bakterilere aktarılmasını mümkün kılmaktadır. *P. aeruginosa*'da IMP, VIM, SPM, GIM ve SIM tipi MBL'lar tanımlanmış olup; VIM-2 şu an dünyada en yaygın olan MBL enzimidir (1-3). Türkiye'de yapılmış çalışmalarda *bla*VIM-2, *bla*VIM-5 ve *bla*IMP-1,OXA-48 tipi MBL genleri taşıyan *P. aeruginosa* izolatları bildirilmiştir. Ülkemiz için bunlar arasında en önemlisi ve yaygını OXA-48 olmakla birlikte, son yıllarda artan oranlarda NDM-1 ve KPC-2 enzimleri de bildirilmiştir. Karbapenemazların hızla yayılması tedavi ve enfeksiyon kontrolü açısından ciddi sorun oluşturmaktadır (4-6). Karbapenem dirençli *P. aeruginosa* izolatlarında MBL taraması için MBL E test; hızlı ve güvenilir bir fenotipik tarama testi olarak önerilmektedir (7,8). Ancak yaptığımız literatür taramasında gerek antibiyotik duyarlılık testlerinde, gerekse MBL E testinde farklı marka Müeller- Hinton Agar (MHA) besiyerlerinin test sonucunu etkilediğini gösteren çalışmalar mevcuttur (8-10). Bu nedenle çalışmamızda 5 farklı MHA besiyeri kullanarak, MBL E test araştırılmasında kullanılabilecek en uygun besiyerini belirlemeyi amaçladık.

GEREÇ VE YÖNTEMLER

Çalışmada yatarak tedavi gören hastaların laboratuarımıza gönderilen klinik örneklerinden izole edilen, karbapenemlere dirençli 29 *P. aeruginosa* izolatı çalışma kapsamına alınmıştır. Her hastadan tek bir örnek çalışılmıştır. Gram negatif, aerop, nonfermentatif, hareketli, oksidaz pozitif, karekteristik trimetilamin kokusuna sahip, Mueller-Hinton agar (OXOID, Hampshire, İngiltere) besiyerinde mavi-yeşil pigment yapan suşlar *P.aeruginosa* olarak değerlendirilmiştir (1,3).

Antibiyotik duyarlılık testleri Clinical and Laboratory Standards Institute(CLSI) önerilerine göre ve Kirby-Bauer disk difüzyon yöntemi ile yapılmıştır (11). Karbapenem direnci, imipenem ve meropenem E test (AB BIODISK, Solna, İsveç) ile doğrulanmıştır. MBL üretiminde fenotipik tarama testi olarak MBL E test (IP/IPI E test: AB BIODISK, Solna, İsveç) kullanılmıştır. Her bir izolat için, beş farklı marka MHA besiyeri kullanılmış ve MBL E testleri eş zamanlı olarak çalışılmıştır. Bu amaçla Oxoid(OXOID LTD.Basingstroke,hampshire,England; Lot no :654362), BBL(Becton Dickinson and Company,France; Lot no:7015175), Merck(Darmstadt, Germany; Lot no :VL219337 046), Himedia(Himedia Laboratory Put.LTD.,Mumbai, India; Lot no:0000079622) ve Plasmatec(Plasmatec Laboratory Product LTD, UK; Lot no: 106100/308) marka MHA besiyerleri kullanılmıştır.

MBL-E test için, bir gecelik inkübasyon sonunda imipenem ve/veya meropeneme dirençli veya orta derecede duyarlı olan *P. aeruginosa* izolatlarından, 0.5 McFarland bulanıklığında süspansiyon hazırlanarak MHA plaklarına ekilmiştir. MBL E test şeritleri plaklara yerleştirilmiş, 35°C'deki etüvde 18 saatlik inkübasyon sonrasında IMP için bulunan MİK değeri, IMP+EDTA için bulunan MİK değerine oranlanmıştır. Üretici firmanın önerilerine göre ≥3 dilüsyonluk (≥8 kat) fark saptanan izolatlar MBL pozitif olarak değerlendirilmiştir (7,8).

Metallo beta-laktamaz üretimine neden olan IMP, VIM, GIM, SIM ve SPM genleri daha önce tanımlandığı şekilde, multipleks PZR yöntemiyle araştırılmıştır (13). Bu amaçla; 18-24 saatlik kültürden elde edilen örneklerden DNA izolasyonu, QIAmp DNA mini kit(QIAGEN, Hilden, German) kullanılarak yapılmıştır. Amplifikasyon için mastermiks(QIAGEN, Hilden, German)kiti kullanılmıştır. 95°C'de 15 dk denatürayonu takiben 40 siklus; 94°C'de 30 sn, 55°C'de 90 sn, 72°C'de 90 sn olarak uygulanmıştır. Son uzama için 72°C'de 10 dk bekletilmiş, amplikasyon ürünleri %2'lik agaroz jelde elektroforeze tabi tutularak UV transilluminator altında görüntülenmiştir. Elde edilen verilerin istatistiksel analizi SPSS 17.0(SPSS Incorporated, Chicago) programında Ki-kare testi($p<0.05$: anlamlı) kullanılarak yapılmıştır. Antibiyotik duyarlılık testleri, MBL E test ve multipleks PZR yönteminde kontrol suşları olarak *P. aeruginosa* ATCC 27853, *bla*VIM pozitif *P. aeruginosa, OXA-48 Klebsiella pneumoniae ve NDM-1Klebsiella pneumoniae* kullanılmıştır.

BULGULAR

İzolatların %72'si yoğun bakım ünitelerindeki hastalardan izole edilmiştir. İzolatların elde edildikleri örneklere göre dağılımı sıklık sırasına göre; trakeal aspirat (10/29), idrar(6/29), yara (4/29), kan (3/29), dren (3/29), balgam (2/29) ve katater (1/29) şeklindeydi. En sık neden oldukları enfeksiyonlar sırası ile; pnömoni (%41), cerrahi alan enfeksiyonu (%24), idrar yolu enfeksiyonu (%21) ve sepsis (%10) olarak saptandı. İzole edilen 29 *P. aeruginosa* örneğinde disk difüzyon yöntemi ile karbapenem direnci belirlendi ve bu direnç imipenem ve meropenem E test ile doğrulandı. İmipenem E test ile izolatların 15'i dirençli (MİK≥ 16 µg/ml), 13'ü orta derecede duyarlı (MİK: 8-12 µg/ml) olarak bulundu. İmipeneme duyarlı (MİK: 4 µg/ml) olan bir izolatın meropeneme dirençli (MİK: 16 µg/ml) olduğu belirlendi (Tablo 1). Karbapenemlere dirençli 29 izolatta multipleks PZR ile IMP, VIM, GIM, SIM ve SPM tipi MBL geni saptanamadı. Bu izolatlara beş farklı marka MHA besiyerlerinde MBL-E testi yapıldı. MBL E test ile BBL marka MHA besiyerinde bir izolat (1/29), Oxoid marka MHA besiyerinde iki izolat (2/29), Merck marka MHA besiyerinde 21 izolat (21/29), Plasmatec marka MHA besiyerinde 27 izolat (27/29), Himedia marka MHA besiyerinde 19 izolat (19/29) 'ın MBL pozitif olduğu belirlendi.

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Tablo 1. 29 P. aeruginosa izolatının imipenem ve meropenem duyarlılığı*

		Meropenem		Toplam
		Duyarlı	Dirençli*	
İmipenem	Duyarlı	-	1	1
	Dirençli*	10	18	28
	Toplam	10	19	29

*İmipenem ve/veya meropeneme orta derecede duyarlı olan izolatlar tabloda dirençli olarak gösterilmiştir.

BBL marka ve Oxoid marka MHA besiyerlerinde elde edilen MBL E test sonuçları ile PZR sonuçları arasındaki istatistiksel farkın anlamlı olmadığı (p >0,05; *Fisher'in Ki-kare testi*), ancak Merck, Plasmatec ve Himedia marka MHA besiyerlerinden elde edilen MBL E test sonuçları arasında istatistiksel olarak farkın anlamlı olduğu saptanmıştır (p<0,001; *continuity correction*), (Tablo 2)

Tablo 2. PZR ile MBL negatif 29 P. aeruginosa izolatında, standart suş ve MBL pozitif suşlarda 5 farklı marka besiyerinden elde edilen MBL E test sonuçları

İzolat No	Oxoid	BBL	Merck	Plasmatec	Himedia
1	negatif	negatif	negatif	pozitif	pozitif
2	negatif	negatif	negatif	pozitif	pozitif
3	negatif	negatif	pozitif	pozitif	pozitif
4	negatif	negatif	pozitif	pozitif	pozitif
5	negatif	negatif	pozitif	pozitif	negatif
6	negatif	negatif	negatif	pozitif	pozitif
7	negatif	negatif	negatif	pozitif	negatif
8	negatif	negatif	pozitif	pozitif	negatif
9	negatif	negatif	pozitif	pozitif	pozitif
10	pozitif	negatif	pozitif	pozitif	pozitif
11	negatif	negatif	pozitif	pozitif	pozitif
12	negatif	negatif	pozitif	pozitif	pozitif
13	negatif	negatif	pozitif	pozitif	pozitif
14	pozitif	negatif	pozitif	pozitif	pozitif
15	negatif	negatif	pozitif	pozitif	negatif
16	negatif	negatif	pozitif	pozitif	pozitif
17	negatif	negatif	negatif	pozitif	pozitif
18	negatif	negatif	pozitif	pozitif	pozitif
19	negatif	negatif	pozitif	pozitif	pozitif
20	negatif	negatif	negatif	pozitif	pozitif
21	negatif	negatif	pozitif	pozitif	negatif
22	negatif	negatif	pozitif	pozitif	negatif
23	negatif	pozitif	pozitif	pozitif	pozitif
24	negatif	negatif	negatif	negatif	negatif
25	negatif	negatif	negatif	pozitif	negatif
26	negatif	negatif	pozitif	pozitif	pozitif
27	negatif	negatif	pozitif	pozitif	negatif
28	negatif	negatif	pozitif	negatif	negatif
29	negatif	negatif	pozitif	pozitif	pozitif
P.aeruginosa ATCC 27853	negatif	negatif	negatif	negatif	negatif
blaVIM pozitif P. aeruginosa	pozitif	pozitif	pozitif	pozitif	pozitif
OXA 48 K.pneumoniae	pozitif	pozitif	pozitif	pozitif	pozitif
NDM-1 K.pneumoniae	pozitif	pozitif	pozitif	pozitif	pozitif

TARTIŞMA

P.aeruginosa enfeksiyonlarının tedavisinde yoğun olarak kullanılması nedeniyle son yıllarda karbapenemlere karşı direnç artmaktadır. *P.aeruginosa*'da düşük düzey karbapenem direnci OprD porin proteini kaybı, aktif efluks pompa sistemleri ve IBL salgılayan dereprese mutantların oluşumu, OXA tipi karbapenemaz enzimleri gibi birkaç faktörün bir arada bulunmasıyla mümkündür. Ambler moleküler sınıf B grubu MBL enzimleri ise yüksek düzeyde karbapenem direncinden sorumludur ve klinik yönden en önemli karbapenemazlardır. *P.aeruginosa*'da tanımlanmış olan MBL'ların üretimi genellikle karbapenemlerin yanı sıra diğer beta-laktam antibiyotiklere de direnç gelişimine neden olmaktadır (1,2,13).

Özellikle epidemiyolojik çalışmalar açısından önemli olan MBL pozitif suşların saptanması için rutin laboratuvarlarda kullanılabilecek hızlı, güvenilir ve maliyet etkin fenotipik tarama testlerine ihtiyaç vardır. Klinik mikrobiyoloji laboratuvarlarında Modifiye Hodge testi, IMP-EDTA kombine disk testi, IMP-EDTA çift disk sinerji testi ve MBL E test MBL saptanmasında kullanılan basit tarama testleridir. Gerek çalışma kolaylığı, gerek sayısal sonuç vermeleri ve yorumlama kolaylığı nedeniyle MBL E testin kullanıldığı çok sayıda çalışma mevcuttur. Bu çalışmalarda *P.aeruginosa* izolatları için MBL E test duyarlılık ve özgüllük oranları sırasıyla % 75-100 ve % 86-100 olarak bildirilmiştir (7,12-17).

Çalışmamızda imipeneme ve/veya meropeneme dirençli 29 izolatın hiçbirinde PZR ile MBL geni saptanamamıştır. MBL E test ile pozitif saptadığımız örneklerde MBL

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geninin negatif olması, muhtemelen OprD porin protein kaybı sonucu karbapenem direncinin ortaya çıkmış olabileceği şeklinde yorumlanabilir. Meropenem ve diğer beta-laktam antibiyotiklerin farklı kanallardan dış membranı geçebilmesi de azalmış duyarlılığı açıklar niteliktedir. Yine karbapenemler dahil çoklu ilaç direncine sahip izolatlarda OprD porin protein kaybıyla birlikte efluks pompa sistemlerinin ve OXA tipi karbapenemaz enzimlerinin dirençten sorumlu olabileceği söylenebilir (18-20).

MBL E test için çalışma prospektüsünde, testin mutlaka MHA besiyerinde çalışılması önerilmekte ve farklı marka MHA besiyerlerinin çinko oranları farklı olabileceğinden, karbapenem MİK değerlerinin ve MBL E test sonuçlarının markalara göre değişebileceği belirtilmektedir. Tutarlı sonuçlar için tercihen BD marka MHA(Bio Science, USA) besiyeri önerilmektedir (MBL E test package insert, AB BIODISK, Solna, Sweeden). MHA besiyerindeki iyon konsantrasyonlarının antibiyotik duyarlılık testleri ve MBL E test yöntemi üzerindeki etkilerini inceleyen ve bu amaçla farklı marka besiyerlerinin bir arada kullanıldığı çalışmalar mevcuttur (8-10). Mazarrasa ve arkadaşları (9) E-test yöntemi ile Tigesiklin MİC değerlerini üç farklı marka Mueller-Hinton Agar besiyerinde incelemişler. Merck marka besiyerinde hem standart suşların hem de klinik örneklerin MİC değerlerini Oxoid ve Difco marka besiyerlerine göre yüksek bulmuşlardır. Merck MHA'ın diğer iki markaya göre daha yüksek manganez içerdiğini tespit etmişlerdir. Aynı çalışmada Difco ve Merck marka MHA besiyerlerinin çinko içeriği Oxoid marka MHA besiyerine göre 2-2,5 kat yüksek bulunmuştur. Araştırılan diğer iyon konsantrasyonları (Fe, Ca, Mg, Ni, Cd, Pb) üç farklı marka besiyeri için benzer bulunmuştur. Torrico ve ark.(10) enterik bakterilerde tigesiklin duyarlığını farklı marka MHA besiyerlerinde ve agar dilüsyon, broth mikrodilüsyon ve E-test yöntemleri ile araştırmışlardır. En yüksek MIC değerini Oxoid marka ile,en düşük inhibisyon zonu değerini Oxoid ve bioMereux besiyerinde saptarken, E-test ile en düşük MIC değerini Difco ve Merck marka besiyerinde saptadıklarını bildirmişlerdir. Walsh ve arkadaşları (8) yaptıkları çalışmada farklı marka MHA(Accumedia, BDMS, Oxoid, Difco ve Remel) plaklarındaki MBL E test sonuçlarını irdelemiş ve Difco hariç diğer marka MHA plaklarındaki sonuçların kabul edilebilir olduğunu belirtmişlerdir.

Sonuç olarak; MBL E test, karbapenem dirençli *P. aeruginosa* izolatlarında MBL taraması için rutin laboratuvarlarda kullanılabilecek hızlı, güvenilir fenotipik tarama testi olarak önerilmektedir. Ancak testin yapılacağı besiyerinin seçimi önem arz etmektedir. Çalışmamızda MBL E test için beş farklı marka MHA besiyeri ile elde ettiğimiz sonuçlar testte kullanılan besiyerinin markasına göre farklılık göstermiştir. MBL E test için BBL ve Oxoid marka MHA besiyerleri ile alınan sonuçlar PZR sonuçları ile uyumlu bulunmuştur. Özellikle moleküler tanı yapma olanağı olmayan mikrobiyoloji laboratuvarlarda MBL E test araştırmalarında BBL ve Oxoid marka besiyerlerinin denenen diğer besiyerlerine oranla daha güvenilir bir şekilde kullanılabileceği sonucuna varılmıştır.

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Efficiency of Alvarado Score in Diagnosis of Acute Appendicitis

Akut Apandisit Tanısında Alvarado Skorunun Etkinliği

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Abstract

Aim: Acute appendicitis is the most common cause of abdominal pain resulting in surgery. This study aims to investigate the efficiency of Alvarado Score (AS) in diagnosis of acute appendicitis.

Materials and Method: The files of 185 patients operated due to acute appendicitis between January 2013 and February 2015 were retrospectively examined. The Alvarado Scores of the patients were calculated. The patients were divided into 2 groups as <7 and ≥7 according to their Alvarado Scores and their pathology results were compared.

Results: Of the185 patients included in the study, 44.8% (n: 83) were females and 55.2% (n: 102) were males. The average age was 27.12 (10-80) years. In terms of distribution, 63.8% (n: 118) of the patients had an Alvarado score of ≥7 and 36.2% (n: 67) had a score of <7. In the study, 16.7% (n: 31) of the patients had normal pathology results and the pathology of 83.2% (n: 154) patients operated with the pre-diagnosis of acute appendicitis were acute appendicitis patients. We also obtained the following results: specificity of Alvarado score: 90.3%; sensitivity: 74.6%; positive predictive value: 97.4%; negative predictive value: 18.1%; and accuracy ratio: 77.2%.

Conclusion: Alvarado Scoring is an affordable and effective method that is easy to use in the diagnosis of acute appendicitis.

Keywords: Acute Appendicitis; Alvarado Score; Abdominal Pain.

Öz

Amaç: Akut apandisit cerrahi ile sonuçlanan karın ağrısının en sık nedenidir. Bu çalışmanın amacı akut apandisit tanısında Alvarado skorunun (AS) etkinliğini araştırmak.

Gereçler ve Yöntemler: Ocak 2013-Şubat 2015 tarihleri arasında akut apandisit nedeniyle opere edilen 185 hastanın dosyaları geriye dönük olarak incelendi. Hastaların Alvarado Skor'u hesaplandı. Alvarado Skoru'na göre hastalar <7, ≥7 olarak 2 gruba ayrıldı ve patoloji sonuçları ile karşılaştırıldı.

Bulgular: Çalışmaya alınan 185 hastanın %44.8 (n: 83)'ü kadın, %55.2 (n: 102)'si erkekti. Ortalama yaş 27.12 (10-80) yıl idi. Alvarado skoru <7 olan %36.2 (n: 67) ve ≥7 olan %63.8 (n: 118) hasta mevcuttu. Çalışmada %16.7 (n: 31) hastanın patoloji sonucu normal ve akut apandisit tanısıyla opere edilen %83,2 (n: 154) hastanın patoloji sonucu akut apandisitti. Alvarado skorunun spesifitesi %90.3, sensivitesi %74.6, pozitif prediktif değeri %97.4, negatif prediktif değeri %18.1 ve doğruluk oranı %77.2 olarak hesaplandı.

Sonuç: Akut apandisit tanısında Alvarado Skorlaması, kullanım kolaylığı olan, ucuz ve etkin bir yöntemdir.

Anahtar Kelimeler: Akut Apandisit; Alvarado Skoru; Karın Ağrısı.

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INTRODUCTION

Acute appendicitis is one of the most frequent reasons for emergency abdominal surgery. Even though it has a high rate of incidence, there are no effective methods for diagnosing acute appendicitis. The negative laparotomy rates are high for patients undergoing surgery with the pre-diagnosis of acute appendicitis in spite of pre-operative physical examination and studies. Ultrasonography (USG), tomography (CT), magnetic resonance (MRI), laparascopy and scoring methods may be used for diagnosing acute appendicitis in suspected patients in order to reduce negative laparotomy ratios (1). The Alvarado scoring (AS) system is also one of the applicable scoring systems. The Alvarado score is calculated on the basis of patient anamnesis, examination findings and laboratory results. The migration of abdominal pain, lack of appetite, nausea/vomiting, rebound, fever, leukocytosis and neutrophilia (left shift) are evaluated and calculated on a scale of 10 points (Table 1) (2). While those who get a score in the range of 7-0 points with the Alvarado scoring system are recommended to undergo surgery, those who get a score in the range of 5-6 points are recommended to be evaluated with an additional method (3).

In this study, we aimed to investigate the effectiveness of AS system for the diagnosis of acute appendicitis.

Table 1. Alvarado score table

Clinical Sign	Points
Migration of pain	1
Nausea/Vomiting	1
Lack of appetite	1
Defense	2
Rebound	1
High Fever	1
Leukocytosis	2
Neutrophilia	1

MATERIALS and METHODS

The files of 185 patients who were operated between January 2013 and February 2015 due to acute appendicitis were retrospectively examined and their AS values were calculated. The patients were divided into two groups as <7 and ≥7 on the basis of their Alvarado scores. In scoring, leukocyte >10.000/mm^3, neutrophil percentage >75% and fever >37.5 ^{0} C were considered positive. The groups were calculated based on their pathology results. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy test (test validity) of the Alvarado score for the diagnosis of acute appendicitis in general, in women and men were separately calculated (Sensitivite = (RP / (RP+FN)) * 100 = % Spesifite = (RN / (FP+RN)) * 100 = %, positive predictive value = (RP / (RP+FP)) * 100 = %, negative predictive value= (RN / (FN+RP)) * 100 = %, diagnostic accuracy test (test validity) = ((RP+RN) / (RP+RN+FP+FN)) * 100 = %). The data collected were calculated using SPSS 15 for Windows, SPSS Inc., Chicago, Illinois, USA.

RESULTS

Among the patients included in the study, 83 (44.8%) were females and 102 (55.2%) were males. Their average age was 27.12 (10-80) years. There were 67 (36.2%) patients with AS<7 and 118 (63.8%) with AS ≥7. There were 34 (50.7%) women and 33 (49.3%) men with AS<7; 49 (41.5%) women and 69 (58.5%) men with AS ≥7 (Table 2).

Table 2. Distribution of patients according to Alvarado scores

Alvarado Score		Acute Appendicitis	Negative Appendectomy	Total (n)
< 7	Women	18	16	34
	Men	21	12	33
	Total	39	28	**67**
≥ 7	Women	47	2	49
	Men	68	1	69
	Total	115	3	**118**

In our study, the pathology of 154 (83.2%) patients operated with the pre-diagnosis of acute appendicitis were acute appendicitis patients. Among these patients, 65 (35.1%) were women and 89 (48.1%) were men. Of these patients, the Alvarado score of 39 people (18 women, 21 men) was <7 while 115 (47 women, 68 men) of them were in the group with an Alvarado score of ≥7. The pathology results of the remaining 31 (16.8%) patients were normal. Among these patients, 18 (9%) were women while 13 (7%) were men. The Alvarado score of 28 (16 women, 12 men) was <7 while 3 (2 women, 1 man) of them had an Alvarado score of ≥7. AS specificity was calculated as 90.3%, sensitivity as 74.6%, positive predictive value as 97.4%, negative predictive value as 18.1% and accuracy ratio as 77.2%. In our study, the sensitivity for women was found to be 72.3% and specificity 89.4% while the sensitivity for men was found to be 77.1% and specificity 92.3% (Table 3). The frequency at which the AS parameters of patients were identified is provided in the Table 4.

Table 3. Alvarado score rates for the diagnosis of acute appendicitis

Statistical Results	General	Women	Men
Sensitivity	74.6	72.3	77.1
Specificity	90.3	89.4	92.3
Positive predictive value	97.4	95.9	98.6
Negative predictive value	18.1	26.1	13.0
Diagnostic accuracy test	77.2	76.1	79.0

Table 4. Distribution of patients on the basis of parameters

Parameter	Number of patients (%, n)
Migration of pain	60.0 (111)
Lack of appetite	80.5 (149)
Nausea/vomiting	65.9 (122)
Defense	87.0 (161)
Rebound	83.7 (155)
Fever (37.5 ^{0} C)	30.2 (56)
Leukocytosis >10000/mm^3	67.0 (124)
Neutrophil percentage (>75%)	42.7 (79)

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DISCUSSIONS

Even though acute appendicitis is the disease that has the highest rate of incidence and requires emergency surgery, it is not always possible to make a timely and accurate diagnosis. Obtaining the patient history carefully and conducting a detailed physical examination are the most important tools in diagnosis. Acute appendicitis can be diagnosed at a great extent on the basis of clinical findings and physical examination. Given that AS is essentially based on clinical and physical examination, it offers an effective method for diagnosing acute appendicitis.

The most frequent sign of acute appendicitis is abdominal pain. It initially develops in the epigastric-periumbilical site and it migrates 1-12 hours later to become localized in the lower right quadrant of the abdomen. Another sign that is encountered in almost every patient is lack of appetite, which is generally the first sign. Nausea and vomiting are seen in 95% of the patients. The most important finding in physical examination is defense and rebound in the abdomen. The body temperature rarely exceeds 38^0C. The body temperature is normal in 25-50% of the patients. The white blood cell count is generally between 10.000 and 18.000. Left shift in the neutrophil count is another laboratory finding (4). In our study, lack of appetite was identified in 149 (80.5%) patients, defense in 161 (87.0%), rebound in 155 (83.7%) and leukocytosis in 124 (67.0%) patients (Table 4).

Acute appendicitis is confused with several diseases - primarily gynecological diseases- in spite of laboratory findings, imaging studies and physical examination. This situation has increased negative appendectomy rates. The rate of negative appendectomy identified in the literature changes between 11% and 19.4% (5,6). In our study, this was 16.8% (n: 31). Out of these patients, 9% (n: 18) were women, 7% (n: 13) were men. The AS of 28 patients was <7 (16 women, 12 men) while the Alvarado score of 3 patients was ≥ 7 (2 women, 1 man).

The difficulties in the diagnosis of acute appendicitis and prolonged duration before the operation increase the appendicitis perforation rate. This rate changes between 3.7% and 20% (5, 7). In our study, perforation was identified in 14% (n:26) of the cases. Of these cases, 7.5% (n: 14) were men and 6.4% (n: 12) were women. There were three cases with AS <7 and 23 cases with AS ≥ 7.

The combined use of multiple parameters for the diagnosis of acute appendicitis may provide better aid in the early and accurate diagnosis of the disease. In this way, perforation and negative appendectomy rates may be reduced. For this purpose, the Alvarado scoring can be used where the assessment is made on the basis of most frequent symptoms, physical examination findings and laboratory results for the diagnosis of acute appendicitis. Several studies have been conducted to assess the usability and reliability of this scoring since it was defined by Alvarado. These studies reported its sensitivity as 54-96.2% and specificity as 54-74.39% (8,9). In our study, specificity was calculated as 90.3%, sensitivity as 74.6%, positive predictive value as 97.4%, negative predictive value as 18.1% and diagnosis accuracy test as 77.2%. The sensitivity was found to be 72.3% while specificity and sensitivity in women was 89.4% and %77.1, respectively; specificity in men was 92.3%. In this study, the difference between female and male sex probably originates from the possibility that pelvic-gynecological diseases may lead to acute appendicitis findings in women.

In conclusion, Alvarado Scoring is a combination of physical examination, patient complaints and laboratory findings. We consider this scoring system to be a sensitive method for taking a decision to operate patients with the pre-diagnosis of acute appendicitis.

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The Effect of Callisthenic Exercises on Pain Threshold, Pain Severity and Muscle Strength on Sedentary Women Diagnosed with Upper Extremity and Low Back Pain

Üst Ekstremite ve Bel Ağrı Tanısı Konulan Sedanter Kadınlarda Kalistenik Egzersizlerin Ağrı Eşiği, Ağrı Şiddeti ve Kas Kuvveti Üzerine Etkileri

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Abstract

Aim: This study on sedentary women diagnosed with upper extremity and low back pain is conducted to analyze the effects of calisthenic exercises on pain threshold, pain severity, and muscle strength.

Materials and Methods: Our study included 80 sedentary women, aged between 40-60, who were diagnosed with upper extremity and low back pain; these patients were admitted to the outpatient physical therapy clinic of a private hospital in Malatya. Patients were randomly assigned to two groups. 40 patients underwent conservative therapy (US, HP, tens) as the control group and 40 patients received conservative therapy and calisthenic exercises as the training group. Both groups were administered a pre-test and post-test model. Pain threshold, pain severity, muscle strength of the subjects were assessed before and after the treatment. The data were evaluated using IBM SPSS Statistics 22.0 package software, and the level of significance was taken as $p<0.05$.

Results: Based on the results of this study, patients who were treated with conservative treatment together with calisthenic exercises had significantly increased muscle strength, pain threshold values ($p <0.05$) while they also showed significantly decreased pain intensity values ($p <0.05$). It was observed that all muscle strength variables were significantly improved compared to the baseline values after treatment with calisthenic exercise added to conservative treatment. There were significant differences found in muscle strength and pain threshold values between the two groups ($p<0.05$).

Conclusion: In conclusion, we believe that conservative treatment administered with calisthenic exercises increases muscle strength and muscle pain threshold values.

Keywords: Sedentary Women; Low Back Pain; Pain Threshold; Callisthenic Exercises.

Özet

Amaç: Üst ekstremite ve bel ağrısı tanısı konulmuş sedanter kadınların katılımı ile gerçekleştirilen bu çalışma, kalistenik egzersizlerin ağrı eşiği, ağrı şiddeti, kas kuvveti üzerine etkilerini incelemek amacı ile yapılmıştır.

Gereç ve Yöntemler: Çalışma grubumuzu Malatya ilindeki özel bir hastanenin fizik tedavi polikliniğine başvuran, yaşları 40-60 arasında değişen, üst ekstremite ve bel ağrı tanısı konulan, sedanter 80 kadın oluşturmuştur. Denekler rastgele iki gruba ayrılmıştır. Kontrol grubunda 40 deneğe konservatif tedavi (ultrason (US), hotpack (HP), tens), eğitim grubunda 40 deneğe kalistenik egzersiz ve konservatif tedavi uygulanmıştır. Her iki gruba ön test- son test modeli uygulanmıştır. Tedavi öncesi ve uygulanan tedaviler sonrası deneklere ağrı eşiği, ağrı şiddeti, kas kuvveti testi yapılmıştır. Veriler IBM SPSS Statistics 22.0 paket programı ile değerlendirilmiş ve anlamlılık düzeyi $p<0.05$ olarak alınmıştır.

Bulgular: Yapılan çalışma sonunda, konservatif tedavi ile kalistenik egzersizlerin bir arada uygulandığı terapilerde kas kuvveti, ağrı eşik değerlerinde artış görüldüğü ($p<0.05$), ağrı şiddeti değerlerinde azalma görüldüğü ($p<0.05$) tespit edilmiştir. Konservatif tedaviye ek olarak uygulanan kalistenik egzersizlerle birlikte bütün kas kuvvet değerlerinde tedavi sonrasında tedavi öncesine göre artış gözlemlenmiştir. Kas kuvvet değerleri ile ağrı eşik değerleri arasında iki grup arasında anlamlı farklar bulunmuştur ($p<0.05$).

Sonuç: Sonuç olarak; konservatif tedavi ile birlikte uygulanan kalistenik egzersizlerin kas kuvvetini artırarak, ilgili kasın ağrı eşiği değeri üzerinde etkili olduğu düşüncesi gelişmiştir.

Anahtar Kelimeler: Sedanter Kadın; Bel Ağrısı; Ağrı Eşiği; Kalistenik Egzersiz.

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INTRODUCTION

Chronic low back pain is very common in society and has already become a serious health problem that causes serious economic losses and even job loss. 65-80% of the world population is faced with low back pain during their lives (1).

Pain experienced by individuals affects sleep routine, family life, social life, efficiency in work life, and, in turn, reduces the quality of life. Controlling pain is important for providing relief to individuals, improving the quality of life, and reducing complications (2, 3). The most varied personal way of measuring physical pain is pain threshold level. In recent years, measurements of pain threshold help determine areas of pain and provides the ability to deliver the right treatment to patients (4, 5).

The International Association for the Study of Pain (IASP) has defined pain threshold in its terminological guide published in 1979 as the smallest stimuli intensity while pain tolerance is defined as the biggest stimulus an individual can bear (6).

Pressure pain threshold measurement provides insight into a person's sensitivity to pain and this can be useful for many clinical situations. For example, depending on underlying causes, it can be difficult to determine pain in the body caused by low force implementation apart from the sensitivity to pain. With pressure pain threshold and sensitivity level monitoring, underlying problems, pain levels, improvement speed and level can be followed. Since neuromuscular condition is generally associated with mechanical hyperalgesia, pressure algometry is used for diagnostic purposes in clinic practices (7, 8, 9).

Calisthenic exercises are aerobic and dynamic exercises. These are paced or low intensity exercises enabling the use of large muscle groups in the upper and lower extremities; as they can be modified, they are also handy and useful exercises. These exercises are performed rhythmically and in specific numbers. They can be adjusted according to the physical fitness level of the person. They are suitable for use in sedentary and elderly people. Calisthenic exercises consist of movements which increase the flexibility and strength of the body. At the same time, they increase both muscle endurance and cardiovascular fitness level. They allow the development of psychomotor skills such as coordination and balance as well. Calisthenic exercises are attractive due to their appropriate and functional nature in any environment and their applicability (7).

In this study, we aim to examine the effect of calisthenic exercises on pain threshold, pain severity and muscle strength in sedentary women diagnosed with upper extremity and back pain.

MATERIALS and METHODS

This study is approved by Inonu University Clinical Research Ethics Committee with the protocol number: 2013/56. To study the effect of calisthenic exercises on pain threshold in sedentary women diagnosed with upper extremity and back pain, we included in the study the patients who were admitted to the physical therapy clinic of a private hospital in Malatya, Turkey.

The study included a total of 80 sedentary women suffering from upper extremity and back pain between 40 and 60 years of age (48.20 ± 7.2 years; mean ± standard deviation). The patients who participated in the study were divided into two random groups. One of the groups (control group) were offered a combination of hot pack, ultrasound, conservative treatment (containing TENS) while the other group (study group) received conservative treatment along with calisthenic exercise training. We evaluated the patients before and after the treatment; the patients were also included in a physiotherapy programme at the start of treatment.

As part of the muscle test, we evaluated neck flexion, neck extension, elevation of the scapula, shoulder flexion, shoulder extension, shoulder abduction, back extensors, and anterior trunk flexors.

Muscle testing was conducted according to Dr.Robert W. Lovett's (10) manual muscle testing method. This test comprises the following categories:

Normal (5): muscle completes the range of motion with maximum resistance against gravity.
Good (4): muscle completes its normal range of motion with resistance less than maximum resistance against gravity.
Fair (3): muscle completes its normal range of motion against gravity.
Poor (2): muscle completes its normal range of motion in a position with gravity eliminated.
Trace (1): palpable contraction before disclosure of motion in the joint.
Total paralysis (0): No muscle contraction is felt.

Pain Intensity: Each patient was asked whether they had pain in the upper extremity and back and to mark the severity of pain on a 10cm scale. Then, these marks were measured with a ruler (11).

Pain Threshold: Pain threshold in the neck, cervical 3rd and 5th vertebrae spinous projections, trapezius muscle, deltoid muscle, lateral epicondyle area, 3rd metacarpal proximal of the dorsal aspect of the hand, and lumbar 3rd and 5th vertebrae spinous protrusions in the waist were determined with J-Tech digital algometer (J-Tech Medical Industries Algometer Commander). The applied force used for the calibration of the device was set to Newton (N). Each time the device is turned on, it automatically self-calibrates displaying zero. The measurement of the cervical regions were carried out with the 0.5 cm^2 probe tip; other regions were measured with the 1 cm^2 probe tip.

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Measurements were repeated three times at 5-second intervals and the average values were recorded. Each evaluation was applied first on the left side and then the right side in relaxation position. The patients were asked to say "Yes" each time they felt pain in each contact. Each time the patients said "Yes," the device was held back for 5 seconds to provide relief; the second and third measurements from the same spot were then carried out after the relaxation period (12, 13).

Pain threshold measurements were recorded twice for each patient, before and after the treatment for each region.

Treatment: Our research included 80 sedentary women with upper extremity and back pain in two groups. The control group patients only received conservative therapy (hot pack, ultrasound, TENS therapy) in the clinic. The conservative treatment (hot pack, ultrasound, TENS therapy) of the study group patients accompanied 3-days-a-week calisthenic workouts targeted at large muscle groups in the upper and lower extremities with a physiotherapist for 8 weeks. Conservative treatment consisted of 20 minutes of hot pack, 20 minutes of TENS, and 10 minutes of US for the first four weeks while the patients received a treatment of 20 minutes of hot pack and 20 minutes of TENS in the second 4 weeks. We applied conservative treatment to the study group before starting the exercise training programme.

The exercise programme applied to the study group was as follows:

1) Flexion of the shoulders in standing position
2) Shoulder abduction in standing position
3) Reciprocal trunk lateral flexion in standing position
4) Shoulder elevation in sitting position
5) Circular motion of the shoulder from front to back in sitting position
6) Scapular adduction in sitting position with hands on waist
7) Reaching forwards in long sitting position
8) Reciprocal straight leg raising in supine position
9) Reciprocal hip flexion and extension in supine position
10) Abduction in side lying position
11) Body extension in prone lying position (14).

The estimated difference between the study and control groups was 3.5; the estimated standard deviation of the training group was 4.2; the estimated standard deviation of the control group was 4.6; in case of Type I error (alpha) 0.05 and Type II error (beta) 0.20 (power = 0.80), it was calculated by power analysis that each group should at least have 34 individuals.

To improve the reliability of the results of the study, a total of 80 patients were included, including 40 patients in each group (MedCalc version 12.4.0.0 for Windows).

Data were summarized by mean ± standard deviation. The appropriateness of the data to the normal distribution was assessed by Kolmogorov-Smirnov test while the homogeneity control of variances was assessed by Levene test. To analyse the data, we used the t test for independent samples between the groups; to compare the groups, we also used the t-test for dependent samples. We used IBM SPSS Statistics 22.0 for Windows software package for analyses. $P<0.05$ was considered statistically significant.

RESULTS

Above, we present the mean age, weight, and height of the study and control groups. There is no statistically significant difference between the groups ($p>0.05$).

Table 1. Mean age, weight, and height of the study and control groups.

Variables	Study Group (n=40)	Control Group (n=40)	p*
Age (years)	48.52±7.90	47.47±6.90	0.53
Weight (kg)	71.36±12.33	69.06±13.30	0.42
Height (cm)	162.02±5.20	161.67±5.00	0.76

*: $p<0.05$ shows the significance level acoording to the t-test results of independent samples; the data are presented in mean±standard deviation.

Comparisons of pre- and post-treatment values of muscle strength of the study and control groups are given in Table 2. According to this and in terms of muscle strength values of the study group, there is a significant increase for all the muscle strength values after treatment compared to pre-treatment evaluation ($p<0.001$). Evaluating the data of the control group, we noticed significant improvement ($p<0.05$) in neck flexors and abdominal muscles while other muscle strength values did not show statistically significant values ($p>0.05$).

Table 3 presents the comparison between of pre- and post-treatment pain threshold values of the two groups. Studying the pain threshold values on the right and left sides, there is a notable increase in terms of pain threshold values ($p<0.001$) between the measurements before and after the treatment. In control group, except for the left hand pain threshold ($p>0.05$), all other pain threshold values ($p<0.001$) showed significant increase after treatment compared to pre-treatment values.

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Table 2. Comparison of muscle strength values of the groups before and after the treatment.

Variables	Study Group (n=40)			Control Group (n=40)		
	Before the treatment	After the treatment	p*	Before the treatment	After the treatment	p*
NF	3.47±0.55	4.10±0.49	<0.001*	3.60±0.49	3.80±0.40	0.008*
NE	3.22±0.42	3.80±0.40	<0.001*	3.32±0.47	3.40±0.49	0.453
SE right	3.95±0.63	4.52±0.59	<0.001*	3.70±0.56	3.77±0.47	0.257
SE left	3.67±0.72	4.35±0.57	<0.001*	3.60±0.59	3.65±0.53	0.317
ShF right	3.65±0.57	4.42±0.54	<0.001*	3.50±0.50	3.60±0.49	0.219
ShF left	3.52±0.59	4.15±0.53	<0.001*	3.40±0.49	3.47±0.50	0.250
ShE right	3.40±0.49	3.90±0.49	<0.001*	3.25±0.43	3.27±0.45	1.000
ShE left	3.32±0.47	3.67±0.52	<0.001*	3.20±0.40	3.25±0.43	0.500
ShA right	3.57±0.54	4.25±0.49	<0.001*	3.52±0.55	3.57±0.54	0.157
ShA left	3.45±0.55	4.02±0.53	<0.001*	3.42±0.54	3.42±0.54	1.000
BE	3.25±0.43	3.82±0.54	<0.001*	3.22±0.42	3.27±0.45	0.500
Abdominal	3.55±0.50	4.30±0.51	<0.001*	3.70±0.46	3.97±0.35	0.001*

*: p<0.05 shows the significance level acoording to the t-test results of dependent samples; NF: Neck flexion; NE: Neck extension; SE right: right scapular elevation; SE left: left scapular elevation; ShF right: right shoulder flexion; ShF left: left shoulder flexion; ShE right: right shoulder extension; ShE left: left shoulder extension; ShA right: right shoulder abduction; ShA left : left shoulder abduction; BE: back extension; the data are presented in mean±standard deviation.

Table 3. Comparisons of pain threshold values of the study and control groups before and after the treatment (Newton/ kg/ cm²)

Variable	Study Group (n=40)		p*	Control Group (n=40)		p*
	Before the treatment	After the treatment		Before the treatment	After the treatment	
Right C3	19.50±3.79	22.10±4.75	<0.001*	18.20±2.34	19.10±2.56	<0.001*
Right C5	20.00±4.28	22.70±5.10	<0.001*	18.30±2.30	19.00±2.48	<0.001*
Right trapezoid	25.20±5.87	27.60±6.73	<0.001*	23.40±5.95	24.00±6.08	<0.001*
Right deltoid	30.50±7.91	32.80±8.41	<0.001*	26.10±5.67	26.60±5.69	<0.001*
Right lat. epi.	25.00±7.72	27.00±8.48	<0.001*	20.80±3.30	21.40±3.56	<0.001*
Right hand	33.40±8.76	35.20±8.87	<0.001*	32.10±5.68	32.70±5.78	<0.001*
Right L3	58.20±9.98	62.20±1.08	<0.001*	58.10±4.99	58.80±4.89	<0.001*
Right L5	59.90±11.4	64.10±1.20	<0.001*	74.20±9.59	59.90±5.50	<0.001*
Left C3	21.00±4.30	23.50±5.11	<0.001*	18.90±2.75	19.80±2.86	<0.001*
Left C5	21.60±4.74	23.90±5.66	<0.001*	18.80±2.71	19.50±2.91	<0.001*
Left trapezoid	26.50±6.18	28.70±7.20	<0.001*	23.80±6.29	24.50±6.43	<0.001*
Left deltoid	31.80±8.28	34.00±8.93	<0.001*	26.70±5.76	27.30±5.81	<0.001*
Left lat.epi.	26.60±8.10	28.40±8.49	<0.001*	21.50±3.82	22.10±3.90	<0.001*
Left hand	34.80±9.12	36.50±9.52	<0.001*	32.60±5.95	33.00±5.92	0.13
Left L3	60.30±1.02	63.40±1.10	<0.001*	58.60±4.97	59.40±4.99	<0.001*
Left L5	62.00±1.15	65.30±1.23	<0.001*	59.90±5.12	60.60±5.32	<0.001*

*: p<0.05 shows the significance level acoording to the t-test results of dependent samples; Right C3: right cervical 3; Right C5: right cervical 5; Right lat. epi: right lateral epicondyle; Right L3: right lomber 3; Right L5: right lomber 5; Left C3: left cervical 3; Left C5: left cervical 5; Left lat. epi: left lateral epicondyle; Left L3: left lomber 3; Left L5: left lomber 5; the data are presented in mean±standard deviation.

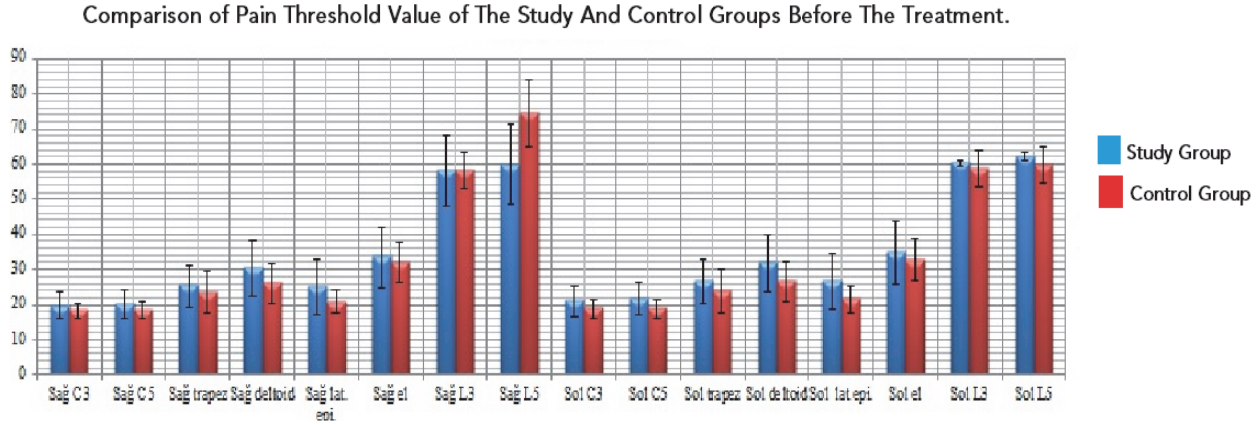

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Figure 1. Comparison of pain threshold value of the study and control groups before the treatment.

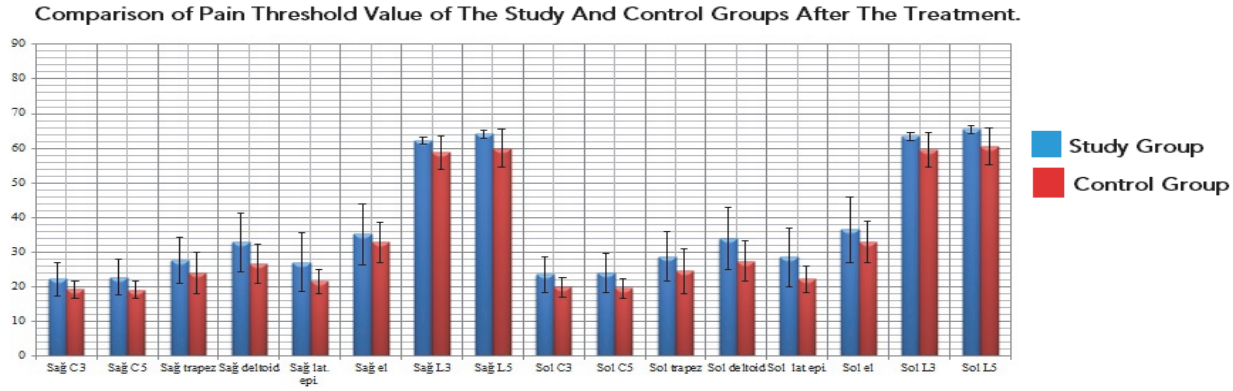

Figure 2. Comparison of pain threshold value of the study and control groups after the treatment.

Table 4 presents VAS measurements of both groups before and after the treatment. As seen in the table, the pre- and pos-treatment values of the study group reveal notable improvement in terms of VAS scores ($p<0.001$). In the control group, there was no statistically significant change in VAS scores after the treatment ($p\leq0.01$)

Table 4. Comparison of VAS scores of the groups before and after the treatment.

Variable	Study Group (n=40)		p*	Control Group (n=40)		p*
	Before the Treatment $\overline{X}$ ±SD	After the Treatment $\overline{X}$ ±SD		Before the Treatment $\overline{X}$ ±SD	After the Treatment $\overline{X}$ ±SD	
VAS (cm)	7.15±1.57	2.38±1.47	<0.001	7.71±1.33	4.46±1.65	<0.001

*: $p<0.05$ shows the significance level acoording to the t-test results of dependent samples; VAS: Visual Analog Scale; the data are presented in mean±standard deviation.

DISCUSSIONS

In this study, which aims to show the effect of calisthenic exercise - when it is applied together with conservative treatment - on threshold of pain, pain intensity and muscle strength, we adopted a pre-test and post-test model.

As a useful form of exercise, calisthenic exercises are aerobic and dynamic exercises and they can be modified for lower and upper extremities. Calisthenic exercises consist of movements which increase the flexibility and strength of the body. As a commonly used training model in rehabilitation and sports training, calisthenic exercises lead to stronger and more flexible bodies with high performance and lower injury rates if they are adopted in the early and late stages of training (15).

Examining the muscle strength values of our patients, we observed that all patients showed improvement in terms of muscle strength in all muscle groups after the calisthenic exercise training programme. Only neck flexors and abdominal muscle strength values were found to be significant in the control group.

Dividing 68 patients with an average age of 76 into two groups, Iwamoto et al. (16) have stated that a course of 3-days-a-week calisthenic exercise accompanied by balance-flexibility-walking exercises for five months have provided significant increase in terms of muscle strength and flexibility in their study group of 34 people. Keser et al. (17) have similarly divided 30 multiple sclerosis patients (mean age: 35 years) into two groups; their study group with multiple sclerosis patients were administered calisthenic exercises for 6 weeks (three days a week). Their study has shown that calisthenic exercises lead to decrease in VAS scores and increase muscle endurance. Our study also confirms the idea that calisthenic exercise programmes effectively increase muscle strength.

Therefore, regardless of the duration of exercises and different demographic characteristics of patients, our study confirms the significant increase in muscle strength due to calisthenic exercises reported in the literature.

Calisthenic exercises are used in many rehabilitation programmes, yet, there are only a few studies on the effect of these exercises on pain intensity and pain threshold. Analysing the pre-test and post-test values

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of VAS scores of patients who were trained with calisthenic exercises, there are significant differences in VAS scores between the groups. The VAS scores of the trained group were considerably lower than the VAS scores of the control group. This explains that calisthenic exercises have positive effect on pain intensity. Jespersen et al.'s study (18) on 22 women (mean age: 39 years) diagnosed with lateral epicondylitis shows that there is a strong correlation between VAS, assessed pain intensity, and pain threshold and pain tolerance.

Our study shows that sedentary women, who complained of pain and did calisthenic exercises 3-days-per-week for 8 weeks, had increased pain threshold and muscle strength values and reduced pain intensity. We also determined a relationship between decrease in pain intensity and pain threshold. Considering this relationship, pain threshold and pain severity should be considered together before and after the treatment.

Yürük and Gültekin's study (14) on patients with fibromyalgia syndrome, who received calisthenic exercise training, shows that pain threshold values were higher compared to the pre-treatment results after treatment. Jones et al's study (19) includes 24 individuals divided into two groups. They provide aerobic exercise training for 30-minute-a-day/3-days-a-week for 6 weeks. They report that they have observed positive change in the participants' pain threshold at the end of the training.

In our study, pain threshold values were lower in the preliminary tests than the final test results. There was significant difference between the two measurements. The age range and type of exercise in Yürük and Gültekin's research is similar to our study. The increase in pain threshold at the end of our work is also supported in the literature. In Jones et al's (19)'s study, physical exercise training programme was for 6 weeks while this was 8 weeks in our study; yet, our research has provided significant improvement in the pain threshold in this period. Jones et al's study is solely based on aerobic exercises whereas our study comprised calisthenic exercises with characteristics of aerobic exercises and this explains the development in a positive direction that we observed in our patients.

CONCLUSION

In conclusion, our study on sedentary women, who had pain and were treated with a combination of conservative treatment and 3-days-a-week calisthenic exercises for 2 months, has shown that calisthenic exercises increase pain threshold compared to application of conservative treatment alone. At this point, we hold the opinion that applying calisthenic exercises along with conservative treatment increases muscle strength and pain threshold while decreasing severity of pain, which in turn improve people's quality of life.

Patients usually avoid exercises for fear of increased symptoms such as pain and fatigue. However, as physical activity decreases, muscle strength and muscle endurance also diminish and muscles become more prone to traumas; at length, this situation creates a vicious cycle. Therefore, by offering less intense and applicable physical activities that would not aggravate symptoms of patients with pain, practitioners can contribute to the enhancement of the quality of life of patients.

Calisthenic exercises are not very common in treatment of sports injuries and rehabilitation, yet we believe that calisthenic exercises can be used both as an alternative treatment in rehabilitation and as an exercise method that improves muscle endurance and muscle strength.

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Effect of Type I Diabetes on Cognitive Functions of School-Age Children

Okul Çağındaki Çocuklarda Tip I Diyabetes Mellitusun Bilişsel Fonksiyonları Üzerine Etkisi

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Abstract

Aim: Carbohydrates have an important effect on the develpoment and function of the nervous system. We wish to determine the effect of type I diabetes on cognitive functions of school-age children.

Materials and Method: We conducted our research on 29 children with type I diabetes mellitus. Subjects were chosen from amongst the patients who were admitted to the pediatric endocrinology department of Turgut Özal Health Center (Malatya, Turkey). 28 children without any apparent health problems were chosen as controls.

Subjects were divided into four groups according to their age; two of these groups included children with diabetes and the other two the controls. Wechsler intelligence test, which was developed for children, was applied to control and patient groups by pediatric psychologists.

Results: We found that type I diabetes influenced the abilities of visual-spatial groups in different ways. We observed that it was influential on visual-hearing rememberance and ability to employ acquired knowledge of various ages groups of children with numerous intelligence types. In general, we noticed statistically significant differences in word sequencing, picture completion and designing the picture abilities between the groups. A positive correlation was identified between the cubical figure and performance scores of the two diabetic children groups.

Discussion: We reviewed the results in the light of the relevant literature. Diabetes was found to affect specific type of memory inversely. Therefore, it can be concluded that time of diagnosis and ensuring metabolic control in diabetes might have important consequences associated with the hazardous effects of diabetes on the development and function of the nervous system.

Keywords: Diabetes Mellitus (Type I); Cognitive Function; Schoolchildren; Wechsler Intelligence Scale For Children–Revised.

Öz

Amaç: Sinir sisteminin gelişimi ve fonksiyonları bağlamında karbonhidratlar büyük bir öneme sahiptir. Bu nedenle; okul çağındaki çocuklarda, karbonhidrat metabolizmasının bozulduğu tip I diyabet mellitus'un bilinçsel fonksiyonları üzerindeki etkisini saptamayı amaçladık.

Gereç ve Yöntem: İnönü Üniversitesi Tıp Fakültesi Araştırma ve Uygulama Merkezi Çocuk Endokrinoloji polikliniğine başvuran, tip I diyabet mellitus tanısı konulan 6-16 yaş aralığında diyabet dışında başka bir hastalığı olmayan 29 çocuk ve akranlarından seçilen 28 sağlıklı çoçuk, yaş aralıklarına göre dört gruba ayrıldı. Çalışmaya katılanlar iki diyabet ve iki kontrol grubu şeklinde ayrıldı. Hasta ve kontrol grubundaki çocuklara çocuk psikiyatrisine bağlı olarak çalışan uzmanlar tarafından ve çocuklar için geliştirilen Wechsler çocuklar için zeka testi uygulandı.

Bulgular: Tip I diyabetin, farklı yaş gruplarındaki çocuklar arasında görsel- mekansal yetenek ve görsel- işitsel uyaranların sırasını hatırlama ve kazanılan bilginin sorunları çözmede kullanma yeteneği bakımından zekanın değişik biçimlerini farklı düzeyde etkilediği saptandı. Gruplar arasında genel çerçevede söz dizisi, resim tamamlama ve resim düzenleme bakımından istatistiksel olarak farklılar saptandı. Her iki diyabet grubunda çocukların küplerle desen puanı ve performans puanı arasında pozitif bir korelasyon saptandı.

Sonuç: Bulgular literatüre göre tartışıldı. Çocuklarda; tip I diyabetin, belli zeka tipleri üzerinde olumsuz etki yaptığı saptandı. Bu nedenle erken tanı ve metabolik kontrolün sağlanması diabetin olası zararlı etkilerinin önlenmesi bakımından önemli olduğu düşünülmektedir.

Anahtar Kelimer: Tip I Diyabet; Bilişsel Fonksiyonlar; Okul Çağındaki Çocuklar; Wechsler Zeka Testi (Çocuklar İçin).

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GİRİŞ

Tip I Diyabet Mellitus; çocukluk ve adölesan dönemde görülen, insülin sentezleyen ve salgılayan pankreasın Langerhans adacıklarındaki β hücrelerinin otoimmun olarak tahrip edilmesi nedeni ile insülinin mutlak eksikliğinin sonucu olarak kan şekerinin yüksek olması ile karakterize yaygın bir metabolik hastalıktır (1-3). Bu hastalık karbonhidrat metabolizmasının bozulması ile birlikte, yağ ve protein metabolizmasının da bozulması sonucu olarak vücutta bir çok organ üzerinde olumsuz etkiler yapan bir hastalıktır (4). Sinir sistemi bu hastalığın hedef organlarından biridir (5). Sinir sisteminin normal fonksiyonları için glikozun kesintisiz sağlanması kritik bir öneme sahiptir. Bu özellikle çocuklar için daha büyük bir önem gösterir. Çocuklarda glikoz beynin büyümesi ve gelişmesi için gereklidir. Bu nedenle çocukların beyni bu dönemde ortada çıkan değişikliklere daha duyarlıdır (6). Diyabet bir taraftan diyabetik ketoasidoz, beyin ödemi ve hipoglisemi gibi akut etkiler yaparken diğer taraftan retinopati, nefropati ve nöropatinin de dahil olduğu birçok kronik değişmeye yol açmaktadır (2,5,7).

Beynin birincil enerji kaynağıdır glikozdur. Normal olarak kan akımı ile glikozun kesintisiz temini gerekir. Glikoz taşıyıcı proteinler tarafından kolaylaştırılmış difüzyonla beynin mikrovasküler endotel hücreleri vasıtasıyla sağlanır (8). Çocukluk ve adölesan dönemde ortaya çıkan hiper ve hipoglisemi bir taraftan sinir sistemini oluşturan hücrelerin gelişmeleri bağlamında olumsuz etkiler yaparken diğer taraftan Tip I Diyabetes mellitus ile bazı nörodejeneratif hastalıklar arasında bir ilişkinin saptanması diyabette erken yaşta tanı koymanın giderek önem kazanmasına yol açmaktadır (9).

Diyabettin sinir sistemi üzerindeki etkileri elektroensefalogram, gri ve beyaz madde yoğunluklarının miktarındaki değişmeler ve serebral korteks tabakasının kalınlığı üzerindeki etkiler bağlamında çeşitli radyolojik yöntemlerle çalışılmıştır (10).

Diyabetin hiper ve hipoglisemi durumlarının çocuklarda yol açtığı damar değişiklikleri ve nöronal hücrelerde hasarlanma ile başlayan değişmeler (3) çocukların akranlarına göre beynin büyümesi ve gelişmesinde geri kalmasına, buna bağlı olarak da okulda ve hayatta yaşıtlarından geri kalmalarına sebep olmaktadır. Bu nedenle çocuklarda diyabetin erken tanımlanmış olması ve gerekli tedavinin başlaması Tip I diyabetin daha sınırlı bir hasara yol açması bakımından önemlidir. Hastalığı erken yaşta başlamış olanların daha sonraki çocukluk ve ergenlik döneminde Tip I Diyabetin kognitif fonksiyonlar üzerindeki etkisinin saptanması bağlamında sağlıklı çocuklarla karşılaştırmalar yapılmıştır. Tip I Diyabetli çocukların zeka, okul başarısı, görsel -uzaysal yetenek, bellek, dikkat ve yönetici fonksiyonlar, hızlı karar verme, problem çözme becerileri, öğrenme, yazma, okuma, dikkatin sürdürülmesi ve psikolojik etkinlik bozulmalara yol açtığı (2, 11), ve diyabetik olmayanlarla magnetik rezonans görüntüleme tekniği ile yapılan değerlendirmelerde kortikal atrofi hızında ve daha çok subkortikal kısımlar olmak üzere beyin sapı lezyonlarında artış, beyin sapı uyarılmış potansiyelin iletiminde yavaşlama ve çoğu bölgesel kan akımı perfüzyonunda anormalliklere yol açtığı rapor edilmiştir (11).

Nöropsikolojik testlerle Tip I diyabetin beynin değişik bölgelerinde yaptığı değişmelerin etkilerinin tespiti ve değişik bölgelerin etkilenme düzeyleri ve bunların günlük hayattaki yansımaları için çok sayıda çalışma yapılmıştır. Bu testlerin her biri hem amaç bağlamında hem de beynin farklı bölgelerinin yürüttüğü işlevler bağlamında birbirinden farklıdır. Bellek zekayla ilişkisi en çok incelenen temel zihinsel yeteneklerdir (12). Ancak, bu konuda yapılan çalışmaların sonuçları çelişkilidir. Bu çelişkili veriler de göz önüne alınarak çalışmamızda Wechsler çocuklar için zeka ölçeği-gözden geçirilmiş formu ile Tip I diyabetli çocukların akranlarına göre zihinsel düzeyleri açısından yerini ve düzeyini tespit etmeye ve olası mekanizmasına açıklama getirmeyi amaçladık.

Gerek çocuklarda diyabet tanımlamanın ve metabolik kontrolün güçlüğü ve gerekse yüksek kalori diyet ile yaşam tarzındaki değişiklikler toplumda diyabetin prevalansında bir artışa neden olmaktadır. Amacımız erken tanı ve metabolik kontrol ile diyabetin nörokognitif fonksiyonlar üzerindeki etkisini göstermek ve diyabetli çocukların akranlarına göre zihinsel olarak bulunduğu düzeyi saptamaktır.

GEREÇ VE YÖNTEM

İnönü Üniversitesi Tıp Fakültesi Çocuk Endokrinoloji Polikliniğinde takip edilen başka bilinen hastalığı olmayan, nörolojik muayenesi normal olan, santral travma öyküsü olmayan Tip I diyabetli 29 çocuk hastada yapıldı. Kontrol grubu, sağlıklı olan 28 çocuktan oluşturuldu. Hastalar ve kontrol grubu yaşlarına göre, 6-11 yaş ve 12-16 yaş aralığında olmak üzere iki gruba ayrıldı.

Çalışmaya alınan diyabetli gruplardaki çocuklar cinsiyet, yaş, yaşadıkları bölge, anne -baba yaş, eğitim ve meslekleri, ailelerin kendi yorumlarınca sosyoekonomik durumları, yaşam alanları not edildi.

Çalışmaya alınan diyabetli ve yaşıtları sağlıklı çocuklar 6 - 11 yaş aralığında olanlar bir grup, 12-16 yaş aralığında olanlardan ikinci grup oluşturuldu. Diyabetli olan çocuklardan birinci grubu 12-16 yaş aralığında olan çocuklardan, ikinci grup ise 6-11 yaş aralığında olanlardan oluşturuldu. Kontrol grubundaki çocuklardan 6-11 yaş aralığında olanlar üçüncü çalışma grubunu oluştururken, 12-16 aralığında olanlar dördüncü çalışma grubunu oluşturdu. Çalışmaya katılan her çocuğa ve velisine / vasisine, katılım öncesi çalışmaya ilişkin ayrıntılı bilgi verildi, aydınlatılmış onam alındı. Çalışma, İnönü Üniversitesi Tıp Fakültesi Etik Kurulu'nca onaylandı.

Bilişsel işlevlerin değerlendirilmesinde, Wechsler çocuklar için zeka ölçeği-gözden geçirilmiş formu (WÇZÖ-R) kullanılmıştır. Söz konusu test, İnönü Üniversitesi Çocuk Psikiyatrisi Anabilim Dalı'na bağlı çalışan uzman psikolog tarafından uygulandı. Çocukların zeka düzeylerini belirlemek ve yaşadıkları sorunları tespit

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etmek için Wechsler'in çocuklar için geliştirdiği zeka ölçeği Formu kullanıldı (Wechsler Intelligence Scale for Children Revised - WISC - R). Wechsler tarafından 1949'da geliştirilen bu ölçek, 1974 yılında gözden geçirilmiş ve WISC - R (Revised) şekli ortaya çıkmıştır (12). WISC-R ölçeği sözel ve performans olmak üzere iki bölümden oluşmasına karşılık hesaplamalarda sözel, performans ve toplam zeka puan olmak üzere üç tür puan hesaplanır. Bu bölümlerin her biri altışar alt test kapsar ve toplam on iki alt testten oluşur. Sözel bölüm, Genel bilgi, Benzerlik, Aritmetik, Sözcük Dağarcığı, Yargılama ve Sayı dizilerinden oluşmaktadır. Performans bölümü; Resim Tamamlama, Resim Düzenleme, Küplerle Desen, Parça Birleştirme, Şifre ve Labirent alt testlerinden oluşmaktadır.

WISC-R'da bireyin bir alt testten aldığı puan, o alt testin maddelerine verilen puanların toplamından oluşmaktadır. Elde edilen ham puanlar, çocuğun takvim yaşına uygun standart puanlara çevirebilmek için, yaş ve aylık dilimlere göre düzenlenmiş olan tablolardan yararlanılmaktadır. Sözel alt testler için elde edilen standart puanların toplamından bireyin Sözel Zeka Bölümü (ZB), Performans alt testlerden elde edilen standart puanların toplamından Performans Zeka Bölümü elde edilmektedir.

Çalışmamızda sözel alt test puan hesaplanmasında Sayı dizisi alt testi puanı, sözel IQ ve toplam zeka puanların hesaplanmasında kullanılmamıştır. Aynı şekilde performans entellejinda ve toplam zeka puanın hesaplanmasında labirent alt test puan hesaplamaya dahil edilmemiştir. Sözel ve Performans puanların toplanmasından da toplam zekâ puanı hesaplanır.

WISC-R; ülkemizdeki standardizasyonu 1995 yılında Savaşır ve arkadaşları (12) tarafından yapılmış ve standardizasyon 6 ile 16 yaşları aralığında yer alan 1639 kişilik bir örnekleme üzerinde gerçekleştirilmiştir. WÇZÖ - R'nin Türk çocukları üzerinde yapılan güvenirlik çalışmasında testlerin yarı güvenirliği, sözel bölüm için 0.97, performans bölüm için 0.93, toplam bölüm için 0,97 olarak bulunmuştur. Bu değerler WÇZÖ - R'nin yüksek güvenirliğe sahip olduğunu göstermektedir (13).

WÇZÖ – R; Sözel alt testlerden biri, performans testlerinin ise tümü sürelidir. Test bu konuda özel eğitim almış kişilerce uygulanabilir. Wechsler'in geliştirdiği bu ölçek ile çocuğun yerini kendi yaşıtları içerisindeki yerini görebilmek, sözel ve görsel belleği ayrı ayrı değerlendirebilmek, her iki bellek alanında da yalnızca anlık bellek ve öğrenmeyi değil, aynı zamanda gecikmeli hatırlamaya da bakılabilmektedir. Değerlendirme sonucunda bireylerin sözel, performans ve tüm test zeka bölümleri katsayıları elde edilmektedir. Sözel zeka bölümü performans zeka bölümünden 15 puan düşükse dil alanında, performans zeka bölümü sözel zeka bölümünden 15 puan düşük ise görsel - motor - algısal alanda sorun olduğu düşünülebilir.

Zeka testi sonucunda elde edilen zeka puanına IQ denir. Bu sınıflamada 130 ve üzeri; çok üstün, 120 - 129 arası; üstün, 110 - 119 arası; ortalamanın üstü / parlak, 90 - 109 arası; ortalama/normal olduğunu gösterir. 80 - 89 arası puan bireyin düşük normal / künt, 70 - 79 arası; sınırlı düzeyde mental işlevsellik, 69 ve altı; zihinsel engelli olduğunu belirtir (13).

İstatistiksel değerlendirme için SPSS 13.00 versiyonu kullanıldı. Nicel değişkenlerin tanımlanmasında ortalama (Ort1)±standart sapma (SD)ve ortanca (ort2) (min-max), nitel değişkenlerde ise sayı ve yüzde kullanıldı. Nicel değişkenlere ilişkin verilerin normal dağılım gösterip göstermedikleri Shapiro Wilk normallik testi ile değerlendirildi. Normal dağılım gösteren nicel değişkenlerin karşılaştırılmasında bağımsız gruplarda tek yönlü varyans analizi ve en küçük önemli fark yöntemi uygulandı. Normal dağılım göstermeyenlerde ise Kruskal Wallis varyans analizi ve Benferonili Mann-Whitney U testi kullanıldı. Nitel değişkenlerin değerlendirilmesinde Pearson Ki-kare, Sperman Rank korelasyon analizi ve Fisher'in Kesin Ki Kare analizi ile değerlendirildi. $p \leq 0.05$ değerleri istatistiksel olarak anlamlı kabul edildi.

BULGULAR

Bu çalışma; iki yıldan uzun süreli takip edilen 29 adet Tip I Diyabetli ve 28 adet sağlıklı çocuktan oluşan kontrol grubu ile yapıldı. Hasta ve kontrol grubu yaş aralığı 72-192 ay, tip I diyabetli hastalar yaşlarına göre iki gruba ayrıldı. 12-16 yaş aralığında olanlar (1. grup) ve 6-11 yaş aralığında olanlar (2. grup) altında toplantı. Çalışmaya alınan çocukların 15'i (%51,7) 1. grupta, 14'u (%48,3) 2. grupta idi. 1. gruptaki çocukların yaş ortalaması 131,3 ay iken (alt-üst sınır: 144-192 ay), 2. gruptaki çocukların yaş ortalaması ise 118,8 aydır (alt-üst sınır:72-132 ay). 1. ve 2. gruptaki çocukların yaş ortalamaları arasındaki fark istatistiksel olarak anlamlıdır (p< 0,0001).

Çalışmanın üçüncü grubu; 6-11 yaş aralığında olan çocuklardır ve birinci kontrol grubunu oluşturur (72-132 ay), dördüncü grubu oluşturan çocuklar ise 12-16 yaş aralığındadır (144-192 ay). 4. çalışma grubu ile (kontrol grubu 2) grup 1 arasında yaş ortalaması istatistiksel olarak anlamlı değil iken, üçüncü çalışma grubu (kontrol grubu 1) ile 2. çalışma grubu arasında yaş ortalaması istatistiksel olarak anlamlıdır (p<0,0001).

Çalışmamızdaki hastaların tanı alma yaş ortalaması 1. grupta 44,4 ay (min: 12 ay max: 63 ay) iken, 2. grupta 97,2 aydır (min: 63 ay, max: 149 ay). Ortalama hastalık süresi 1. grupta 86,9 ay (min: 33 ay- max: 24 ay) olup 2. grupta 71,5 ay (min: 28 ay max: 132 ay).

Sözel alt testlerden aldıkları puan değerlendirildiğinde gruplar arası karşılaştırmada resim tamamlama ve resim düzenleme yönünden gruplar arasında istatistiksel fark saptandı (Tablo 3).

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Tablo 1. 6-16 yaş aralığındaki çalışma ve kontrol gruplarının genel bilgi, aritmetik, söz dizisi,resim tamamlama ve resim düzenleme puanları yönünden karşılaştırılması

	Grup 1 (Ort±SD)	Grup 2 (Ort±SD)	Grup 3 (Ort±SD)	Grup 4 (Ort±SD)	P
Genel Bilgi	7.07±2.3	7.26±3.7	8.64±2.7	9.35±3.1	0.153
Aritmetik	9.42±2.9	9.13±3.1	10.92±2.7	10.92±2.4	0.185
Söz dizisi	8.28±1.8	8.06±1.6	9.64±1.5	8.28±1.4	0.056
Resim Tamamlama	8.21±3.4	9.26±2.9	11.07±1.8	10.07±2.3	0.050
Resim Düzenleme	8.35±2.4	7.86±2.5	11.71±3.3	7.50±3.9	0.03

Gruplar arasında resim düzenleme, söz dizisi ve resim tamamlama bakımından istatistiksel olarak anlamlı fark saptandı.

Tablo 2. 6-16 yaş aralığındaki çalışma ve kontrol gruplarının benzerlik, söz dağarcığı, yargılama, küplerle desen, parça birleştirme ve şifre puanları yönünden karşılaştırılması

	Grup 1 (Ort2, min-max)	Grup 2 (Ort2 ,min-max)	Grup 3 (Ort2, min-max)	Grup 4 (Ort2,min-max)	P
Benzerlik	10.00(9-16)	9.00(6-15)	12.00(7-15)	10.00(4-14)	0.105
Söz dağarcığı	8.00(7-16)	8.00(1-13)	11.00(8-14)	9.00(6-12)	0.153
Yargılama	10.00(5-13)	11.00(5-15)	11.00(8-14)	11.50(7-12)	0.490
Küplerle desen	9.00(3-17)	10.00(4-15)	10.00(7-15)	10.00(5-15)	0.182
Parça birleştirme	9.50(7-17)	10.00(6-14)	10.00(7-13)	9.50(6-14)	0.823
Şifre	8.50(6-14)	10.00 (7-34)	10.00(7-15)	9.00 (5-17)	0.275

Normal dağılım göstermeyen nicel veriler bağlamında gruplar arasında istatistiksel bir fark saptanmadı.
Diyabetli gruplar arasında küplerle desen puanı ile performans puanı arasında pozitif bir korelasyon saptandı (Grup 1 r=0.657, p=0.011, Grup 2 r=0.836, p=0.0001).

Tablo 3. 6-11 yaş aralığındaki çalışma ve kontrol gruplarının genel bilgi, aritmetik, söz dizisi, resim tamamlama ve resim düzenleme puanları yönünden karşılaştırılması

	Grup 2(Ort,±,SD)	Grup 3(Ort,±,SD)	p
Genel bilgi	7.26±3.7	8.64±2.7	0.273
Aritmetik	9.13±3.1	10.92±2.7	0.110
Söz dizisi	8.06±1.6	9.64±1.5	0.014
Resim tamamlama	9.26±2.9	11.07±1.8	0.063
Resim düzenleme	7.86±2.5	11.71±3.3	0.002

Resim düzenleme ve söz dizisi bakımından gruplar arasında istatistiksel anlamlı fark saptandı.

Tablo 4. 12-16 yaş aralığındaki çalışma ve kontrol gruplarının genel bilgi, aritmetik, söz dizisi, resim tamamlama ve resim düzenleme puanları yönünden karşılaştırılması

	Grup 1 (Ort,±,SD)	Grup 4 (Ort,±,SD)	P
Genel bilgi	7.07±2.3	9.35±3.1	0.039*
Aritmetik	9.42±2.9	10.92±2.4	0.152
Söz dizisi	8.28±1.8	8.28±1.4	1.000
Resim tamamlama	8.21±3.4	10.07±2.3	0.107
Resim düzenleme	8.35±2.4	7.50±3.9	0.503

Her iki grup arasında genel bilgi alt testi bağlamında fark bulunmasına karşın diğer öğeler bakımından istatistiksel olarak anlamlı bir fark saptanmadı.

Tablo 5. 6-11 yaş aralığındaki çalışma ve kontrol gruplarının benzerlik, söz dağarcığı, yargılama, küplerle desen, parça birleştirme şifre, sözel ve toplam puanları yönünden karşılaştırılması

	Grup 2 (Ort2 - min-max)	Grup 3 (Ort2-min-max)	P
Benzerlik	9.00 (9-15)	12.00(7-15)	0.036
Söz dağarcığı	8.00(1-13)	11.00(8-14)	0.037
Yargılama	11.00(5-15)	11.00(8-14)	0.675
Küplerle desen	10.00(4-15)	10.00(7-15)	0.322
Parça birleştirme	10.00(6-14)	10.00(7-13)	0.424
Şifre	10.00(7-34)	10.00(7-15)	0.575
Sözel Puan	95.00 (58-120)	101.00(90-128)	0.080
Toplam puan	97.00 (63-121)	104.00(93-128)	0.038

İkinci ve üçüncü grup arasında benzerlik, söz dağarcığı ve toplam puan açısından istatistiksel fark saptanmasına karşın diğer değişkenler yönünden fark saptanmadı.

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Tablo 6. 12-16 yaş aralığındaki çalışma ve kontrol gruplarının benzerlik, söz dağarcığı, yargılama, küplerle desen, parça birleştirme şifre, sözel ve toplam puanları yönünden karşılaştırılması

	Grup 1 (Ort2, min-max)	Grup 4 (Ort2, min-max)	P
Benzerlik	10.00(9-16)	10.00(4-14)	0.376
Söz dağarcığı	8.00(7-16)	9.00(6-12)	0.671
Yargılama	10.50(5-13)	11.50(7-12)	0.420
Küplerle desen	9.00(3-17)	10.00(5-15)	0.044
Parça birleştirme	9.50(7-17)	9.50(6-14)	0.907
Şifre	8.50(6-14)	9.00 (5-17)	0.658
Sözel puan	90.50(81-126)	97.00(70-117)	0.333
Toplam puan	91.00(79-119)	95.00(73-123)	0.240

Birinci ve dördüncü gruplar arasında sadece küplerle desen bağlamında fark saptandı. İncelenen diğer veriler bakımından gruplar arasında önemli bir fark saptanmadı.

TARTIŞMA

Diyabetin nörokognitif fonksiyonlar üzerindeki etkisinin hastalık süreci ve hastalığın başlama yaşının önemli olması neden ile çocuklar 6-11 ve 12- 16 yaş aralıkları esas alınarak iki grup ayrıldı. Araştırmamızda, 6 yaş üstü ve 16 yaşı dahil tanı alan çocuklar ile yaşıtları olan sağlıklı çocuklardan oluşturulan kontrol grubundaki çocukların nörokognitif fonksiyonları incelendi. Nörokognitif fonksiyonların değerlendirilmesinde, WISC-R zeka ölçeği ile zeka tanı yaşı ve nörokognitif fonksiyonlar arasındaki ilişki incelendi. Normal olarak merkezi sinir sistemi normal nöronal fonksiyonları bağlamında; kesintisiz kan akımından glikoz temini bağımlıdır ve anormal kan glukoz konsantrasyonu merkezi sinir sisteminde geçici veya kalıcı değişmelere sebep olabilir. Bu özellikle çocuklar için gerçektir. Çocuklarda yaşamın ilk yıllarında beyinin büyümesi ve gelişmesi için glikoz enerji gereksinmesi artar. Uzun süre hiperglisemiye maruz kalma bir çok mekanizma ile nöronal hasara yol açabilir (8,14-16). Beyin metabolik olarak çok aktif ve büyüklüğüne orantısız olarak enerji tüketir. Yetişkinlerde vücut ağırlığının % 2 sini temsil etmesine karşın oksijen tüketimi, vücuttun tükettiği oksijenin %20'sine ve kalp debisinin %15'ine karşılık gelir. Çocukluk döneminde (5-6 yaşlarında) istirahat halinde beyin oksijen tüketimi total vücut oksijen tüketiminin yaklaşık olarak %50'si kadardır (14). Diyabetes mellitus, beynin hafif düzeydeki disfonksiyonu ile büyük ölçüde ilişkilidir (11,14-15). Yaşamın ilk 4-7 yılları arasında diyabet gelişmesi kognitif fonksiyonlarda bozulma riskini büyük ölçüde artırır (16). Diyabetin merkezi sinir sisteminde yol açtığı hasarın büyüklüğünü göstermek için zeka durumunu tespit amacı ile ilişkili çok çeşitli nöropsikolojik testlerden yararlanılır. Zeka; Kişinin yaşam çevresini algılaması ve yaşadığı ortamda karşılaştığı sorunlarla başa çıkmasını sağlayan ve değişik serebral bölgelerle ilişkili olan işlevleri gerçekleştirmeye yönelik genel doğal bir yetidir (17-18).

Wechsler Çocuklar için Zeka Ölçeği-Gözden geçirilmiş formu (WISC-R) çocuklarda özgün yeteneklerin belirlemede kullanılan testlerin başında gelmektedir. Bu test farklı nörokognitif işlevleri ölçen dört alt test'den oluşturulmuştur. Bu alt gruplar görsel-mekansal yetenek (Resim tamamlama+küplerle desen ve parça birleştirme), sözel kavramlaştırma yeteneği; bu yetenek dil işlevleri kavram ve soyut düşüncenin kullanımını ölçer (yargılama+benzerlikler+sözcük dağarcığı), sıraya koyma yeteneği, bu test sayesinde kısa süreli bellekte depolanan görsel ve işitsel uyarıları sırasını hatırlayabilme yeteneği tespit edilir (sayı dizileri+resim düzenleme+şifre) ve edinilmiş bilgiyi; sosyal yaşamda karşılaşılan sorunları çözebilmede kullanabilme becerisini değerlendiren testleri (genel bilgi+aritmetik ve sözcük dağarcığı) içermektedir. Toplam zeka bölümü ise bahsedilen tüm özellikleri kapsayarak genel zeka düzeyini göstermektedir (19). Çalışmaya katılan diyabetli grupların, normal zeka düzeyi puanının alt sınırına yakın olması aralarında bir farkın olmaması yanında kontrol grubunu oluşturan 6-11 yaş grubundaki çocukların toplam zeka puanı bağlamında çalışma grubundaki çocuklardan daha yüksek bir puan elde etmesi dikkat çekicidir. Genel zeka puanlarının donuk normal zeka puanı aralığında olması normal zeka düzeyinin alt sınırına sahip olmaları açısından dikkat çekici bir bulgudur (Tablo 5,6).

Araştırmamızda Wechlser zeka ölçeğinin sözel zeka bölümü, performans zeka bölümü ve toplam zeka bölümü puan ortalamaları açısından gruplar arasında istatistiksel olarak anlamlı farklılık bulunmadı (Tablo 5,6). Akademik başarının altın standartı olan WISC-R zeka ölçeğinin sözel zeka bölümü; okul ve kültürel ortam ile ilgili genel bilgi düzeyi, soyutlama, genelleme, dikkat, akıl yürütme, öğrenme ve muhakeme yeteneği ile işitsel belleği değerlendirmektedir. Testin performans bölümü; görsel dikkat, neden sonuç ilişkisi kurabilme, görsel-hareket-mekansal koordinasyon, psikomotor hızı ölçmektedir. Testin ölçtüğü tüm nörokognitif fonksiyonların hasta gruplarında farklı olmadığı görülmüştür (Tablo 5,6).

Zeka ile ilişkili nöropsikolojik çalışmalar, çok sayıda bilişsel işlevin durumunu göstermesi açısından önemlidir. Zeka testleri ise bu işlevlerin birlikte çalışıp tek bir deneyimi oluşturduğuna işaret etmektedir. Bu bakımdan, bilişsel işlevler hakkında bilgi edinmek için, çoğu durumda zeka testlerine başvurulmaktadır.

WISC-R'ın tüm alt testlerinin gruplar içinde hipoglisemi sıklığına göre karşılaştırılmasında; 5 yaş altında tanı alan çocukların bulunduğu grupta sadece küplerle desen alt testinin ölçtüğü görsel-hareketsel-mekansal fonksiyonu için anlamlı düzeyde bozukluk bulundu. Bu bulgu Bender Gestalt testi sonucu ile tutarlı olarak erken tanı alan DM'li çocuklarda görsel algı bozukluğu olduğunu düşündürmektedir. Hannonen ve arkadaşlarının (3) bir çalışmasında, WISC-R zeka ölçeğinin alt testlerinin, ciddi düzeyde hipoglisemi sıklığı öyküsü olan DM grubunun,

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hipoglisemi sıklığı öyküsü olmayan DM grubu ve kontrol grubu ile karşılaştırılmasında bizim çalışmamızı destekler nitelikte istatistiksel olarak anlamlı farklılık bulunmamıştır. Diğer taraftan bizim çalışma bulgularımızı desteklemeyen Hagen (20) ve arkadaşlarının yaptıkları bir araştırmada WISC-R zeka ölçeğinin işitsel kısa süreli belleği ölçen sayı dizileri alt testinde erken başlangıçlı DM grubunda anlamlı düzeyde kısalma bulunmuştur. Bu çalışmada DM'li çocukların özellikle de erken başlangıçlı DM grubunun kontrol grubuna göre bilgiyi hatırlama ve organize etme de sıklıkla bozuk stratejiler kullandıkları belirtilmektedir.

Sonuç olarak Tip I diyabetin çocuklarda gerek görsel-mekansal ve gerekse görsel- işitsel uyaranları sırası ile hatırlama belleğini olumsuz yönde etkilediği görülmektedir. Bu nedenle erken tanı ve metabolik kontrol, ortaya çıkması olası değişmelerin önlenmesi bağlamında önemlidir. Ancak bu şekilde bu çocukların yaşıtlarından okul ve günlük yaşamdaki performansları bağlamında geri kalmalarını önlemek mümkün olabilir.

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Our Clinical Experience in Iatrogenic and Traumatic Bile Duct Injury: A Retrospective Analysis

İyatrojenik ve Travmatik Safra Yolu Yaralanmalarındaki Klinik Deneyimlerimiz: Bir Retrospektif Analiz

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Abstract

Background: The purpose of this study is to present our experience of diagnosis, clinical course, treatment and outcome in iatrogenic and traumatic bile duct injury.

Methods: Sixteen patients, who were treated due to iatrogenic and traumatic bile duct injury between June 2009 and October 2014 at İnönü Universty, were analysed retrospectively.

Result: Of the sixteen patients with bile duct injury, 4 (%25) were males and 12 (%75) were females. 3 (%18.75) of the bile duct injuries occured due to trauma and 13(%81.25) occurred due to laparoscopic cholecystectomy. 2 (%12.5) patients were taken to emergency surgery due to trauma in our center. 14 (%87.5) patients were operated previously in other clinics and referred to our center due to complications. In the treatment of bile duct injury, 1 (%6.25) patient underwent duct to duct anastomosis while the others 15 (%93.75) were treated with Roux-en-Y hepaticojejunostomy. The average length of stay of patients in the hospital was18.9 days, and the average follow-up time was 25.6 months.

Conclusion: Bile duct injury may occur with iatrogenic or traumatic causes and can cause severe morbidity and mortality. Laparoscopic cholecystectomy is still the most common cause of bile duct injury.Regardless of their causes, bile duct injurys are serious conditions that require experienced treatment in terms of management. The time between onset of bile duct injury and surgical procedure is insignificant and treatment may give successful results in centers with experienced surgeons in hepatobiliary surgery.

Keywords: Bile Duct Injury; Iatrogenic; Cholecystectomy; Trauma; Hepaticojejunostomy.

Özet

Amaç: Bu çalışmanın amacı; iyatrojenik ve travmatik safra yolu yaralanmalarının tanı, klinik seyir, tedavi ve sonuçlarına ilişkin deneyimlerimizi sunmaktır.

Gereç-Yöntem: Haziran 2009- Ekim 2014 tarihleri arasında İnönü Üniversitesi Genel Cerrahi Kliniği'nde iyatrojenik veya travmatik, safra yolu yaralanması nedeniyle tedavi edilen 16 hasta retrospektif olarak incelendi.

Bulgular: Safra yolu yaralanması olan 16 hastanın 4 (%25)'ü erkek, 12 (%75)'si kadın idi. Safra yolu yaralanmalarının 3 (%18.75)'ü travmaya, 13 (%81.25)'ü laparaskopik kolesistektomi ameliyatına bağlı olarak meydana gelmişti. 2 (%12.5) hasta travma nedeniyle tarafımızdan acil ameliyata alınmıştı. 14 (%87.5) hasta ise başka merkezlerde daha önce ameliyat edilip, komplikasyon gelişmesi üzerine kliniğimize sevk edilmişti. Safra yolu yaralanmalarının tedavisinde 1 (%6.25) hastaya uç uca anastomoz, 15 (%93.75) hastaya Roux-n Y hepatikojejunostomi yapıldı. Hastalara ait hastanede kalış süresi ortalama : 18.9 gün ve ortalama takip süresi: 25.6 ay idi.

Sonuç: Safra yolu yaralanmaları iyatrojenik veya travmatik nedenlerle meydana gelebilir ve ciddi mortalite ve morbiditeye neden olabilir. Laparaskopik kolesistektomi ameliyatları halen safra yolu yaralanmalarının en sık sebebidir. Safra yolu yaralanmaları; nedeni ne olursa olsun, tedavi yönetimi açısından ciddi deneyim gerektiren bir durumdur. Safra yolu yaralanmasının oluş zamanı ile biliyer rekonstrüksiyonun yapılma zamanı arasındaki süreden bağımsız olarak, hepatobiliyer cerrahi konusunda tecrübeli klinikler tarafından yapılan biliyer rekonstrüksiyon işlemi ile başarılı sonuçlar alınabilir.

Anahtar Kelimeler: Safra Yolu Yaralanması; İyatrojenik; Kolesistektomi; Travma; Hepatikojejunostomi.

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INTRODUCTION

Bile duct injury (BDI) occurs due to iatrogenic and traumatic reasons. The most frequent reason behind iatrogenic BDI is cholecystectomy surgery. Nowadays, BDI occurs at an incidence rate of 0.5% during laparoscopic cholecystectomy operations (1). The most important local risk factors for BDI connected to cholecystectomy surgery are male patients, acute cholecystitis, acute biliary pancreatitis, bleeding in Calot's triangle, large stones located in Hartmann pouch, Mirizzi's syndrome, surgery lasting longer than 2 hours and fibrotic gallbladder. These factors are responsible for 15-35% of BDI cases (2). As the cause of more than half of these cases, the most important risk factor in BDI is inexperienced surgeons (3). Traumatic BDI constitutes less than 1% of all intra-abdominal injuries (4). The most common reconstruction process in surgical treatment of BDI is the Roux-n Y hepaticojejunostomy (HJ) (5).

In this article, we aim to share our clinical experience regarding the timing of surgical procedures

MATERIALS and METHODS

The study includes 16 iatrogenic or traumatic BDI patients who were treated at General Surgery Department, Inonu University between June 2009 and October 2014. We retrospectively evaluated the demographic data, causes of injury, diagnosis and treating time, clinical and laboratory results, bile duct injury types according to Strasberg classification, diagnostic tools, treatment methods, hospital stay, mortality, and early and late morbidity rates of these patients.

Except for 2 (12.5%) patients, who underwent emergency surgery in our clinic due to gunshot wounds (GSW) and blunt trauma, all the patients were operated in other centres before they were referred to our clinic.

RESULTS

There were 4 males (25%) and 12 (75%) female in our patient group with an age range of 16-68 years (mean age: 39 years). BDI development causes were as follows: in 1 (6.25%) patient due to GSW, in 2 (12.5%) patients due to blunt abdominal trauma, and in the remaining 13 patients (81.25%) due to laparoscopic cholecystectomy surgery. 5 (38,4%) of the laparoscopic cholecystectomy surgeries were conducted under emergency conditions due to acute cholecystitis while the remaining 8 (61.6%) were conducted under elective conditions due to cholelithiasis. In only 1 (7.9%) of the laparoscopic cholecystectomy operations we had to switch to open surgery during the operation.

14 (8.75%) of the 16 BDI patients were previously operated in other centres and then referred to our clinic. Of these 14 patients, 13 (92.8%) had bilious drained from the abdomen whereas 1 (1.2%) patient had hemorrhagic drainage. In the physical examination, all of the patients had abdominal distention, coordinate accuracy, and defence. Except for 2 (12.5%) patients, who underwent emergency surgery due to trauma, and 1 (6.25%) patient, who was operated under emergency conditions due to bleeding following laparoscopic cholecystectomy, all 13 (92.8%) patients had high fever.

We evaluated the preoperative complete blood count and blood biochemistry parameters of all the patients. The laboratory findings of the patients were as follows: 13 (81.25%) patients had high WBC values; 10 (62.2%) had high CRP values; 8 (50%) patients had high ALT and AST values; 9 (56.2%) patients had high total bilirubin values; and 10 (62.2%) patients had high GGT and ALP results. Of the 16 patients, 13 (92.8%) patients underwent abdominal ultrasonography (USG), computed tomography (CT), and endoscopic retrograde cholangiopancreatography (ERCP) for diagnostic purposes; two patients, who were operated under emergency conditions due to GSW and a motor vehicle accident, respectively, along with one more patient, who was admitted to the emergency service with intra-abdominal haemorrhage and hypovolemic shock after laparoscopic cholecystectomy, were examined only with abdominal ultrasound imaging.4 (25%) of our patients underwent magnetic resonance cholangiopancreatography (MRCP). In 12 (92.3%) of the 13 patients, the BDI diagnosis was confirmed with preoperative ERCP. In 1 (7.7%) patient only, who had right sectoral duct injury, was considered to have a leak in the cystic stump.

The time between the onset of BDI and reconstruction process varied between 0 and 90 days (mean: 18.8 days). In case of our GSW patient, who had liver laceration, vena cava inferior and renal injury, and hemo-pneumonia in the right side of the chest, BDI was detected during the operation. Given the patient's poor general condition, the operation was terminated and the patient was intubated and sent to the intensive care unit after packing. On the 2nd postoperative day, the patient was reoperated for depacking and the biliary reconstruction was then completed.

All the patients underwent intraoperative cholangiography prior to biliary reconstruction and after the reconstruction process. In the postoperative period, the check-up cholangiography processes were administered through catheters on the 15 postoperative day. All postoperative cholangiography results were normal and there was no anastomotic leakage. In ten (62.5%) patients, the feeding catheters were removed after this imaging process while 6 (37.5%) had to keep the catheters for the follow-ups until the postoperative 2nd month, when their cholangiography results were assessed normal. To determine the type of BDI, we used the Strasberg classification (Table 1) (6).

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Table 1. Strasberg classification

Type A	Bile leak in the cystic tract or accessory ducts in the gall bladder.
Type B	Binding proximal and distal sections of the aberrant right hepatic duct and their complete section with the gall bladder.
Type C	Binding distal section of the right aberrant hepatic duct and its complete section along with the gall bladder. Leaving the proximal of the aberrant right hepatic duct and bile leak from this point.
Type D	Lateral injury in the main bile duct.
TypeE1	Complete section of the bile duct with the remaining hepatic duct at a length of 2 cm or more.
TypeE2	Complete section of the bile duct with the remaining hepatic duct at a length of less than 2 cm.
TypeE3	Stenosis in the left and right hepatic duct bifurcation line.
TypeE4	Stenosis involvement in the left and right hepatic ducts.
TypeE5	Total stenosis in the main hepatic duct and complete section of the gal bladder along with binding the proximal and distal of the right aberrant hepatic duct

Table 2. Early and late complications and treatment approaches to these complications.

EARLY COMPLICATIONS	TREATMENT
Wound infection: 5(%31,25)	Medical dressing
Minimal bile leak (<30cc/day): 3(%18,75)	Monitoring, spontaneous recovery
Bilioma: 3(%18,75)	Percutaneous drainage
Pneumonia: 2(%12,5)	Medical treatment
Intraabdominal abscess: 1(%6,25)	Relaparotomy, surgery drainage
Pleural effusion: 1(%6,25)	Pleural drainage
Increase in total bilirubin level: 1(%6,25)	A single session of plasmapheresis
LATE COMPLICATIONS	**TREATMENT**
Anastomotic stenosis: 1(%6,25)	Balloon dilatation
Chronic liver disease: 1(%6,25)	Monitoring

Table 3. Types, etiology, surgical treatment, additional organ injuries, and treatment durations of BDI.

Injury type	Etiology	Surgical Treatment	Additional organ treatment	Duration between onset of BDI and reconstruction process
TypeE1	GSW	HJ on CHT plane	VCI, RV, PV, LV	2 days (Emergency surgery of VCI, RV, LV and choledochus repair; HJ on postoperative 2nd day)
TypeE1	LC	HJ on CHT plane	N/A	5 days
TypeE1	LC	HJ on CHT plane	PV	21 days
TypeE1	LC	HJ on CHT plane	RHA	4 days
TypeE2	LC	HJ on 0,5 cm below the right/left hepatic duct junction	RHA	4 days
TypeE2	LC	HJ on 0,5 cm below the right/left hepatic duct junction	RHA	10 days
TypeE2	LC	HJ on 0,5 cm below the right/left hepatic duct junction	RHA	4 days
TypeE2	LC	HJ on 0,5 cm below the right/left hepatic duct junction	N/A	7 days
TypeE2	LC	HJ on 0,5 cm below the right/left hepatic duct junction	N/A	5 days
TypeE3	LC	HJ the right/left hepatic duct junction	N/A	10 days
TypeE3	LC	HJ the right/left hepatic duct junction	N/A	12 days
TypeE3	LC	HJ the right/left hepatic duct junction	N/A	40 days
TypeE4	BAT	HJ in the left hepatic duct	LV	42 days
TypeE4	LC	HJ in the right hepatic duct	N/A	45 days
TypeE4	LC	HJ in the right hepatic duct	N/A	90 days
TypeE4	MVA	End-to-end anastomosis on the left hepatic duct	LV	0 days

GSW: Gunshot wounds; VCI: Vena cava inferior; RV: Renal vein; PV: Portal vein; LV: Liver; LC: laparoscopic cholecystectomy; HJ: Hepaticojejunostomy; RHA: Right hepatic artery; CHT: Common hepatic duct; BAT: Blunt abdominal trauma; MVA: Motor vehicle accident.

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According to the Strasberg classification, 4 patients (25%) had E1, 5 (31.2%) patients had E2, 3 (18.8%) patients had E3, and 4 (25%) patients had E4 injuries.
One of our patients, who had been in a motor vehicle accident, had full-thickness incision in the left biliary tract. As far as the reconstructive process is concerned, this patient underwent end to end anastomosis through the feeding catheter. The rest of the patients underwent Roux-n Y hepaticojejunostomy with 5/0 PDS and front-to-end sutures. All anastomoses were performed with 5F feeding catheters. One end of the catheter was placed in the proximal biliary tract while the other end was placed 4-5 cm from the jejunum out through the abdomen.

The data concerning the type of BDI, its etiology, surgical treatments, additional organ injuries, and the time between the onset of BDI and the biliary reconstruction are summarised in Table 3. The complications seen within 30 days after the biliary reconstruction process were regarded as early complications; complications after the first 30 days were regarded as late complications. The early and late complications as well as the treatment of these complications are given in Table 2.

Table 4. Data about the patients.

Age	16-68 years Mean: 39 year
Sex	Male: 4 (%25) Female: 12 (%75)
Etiology	Laparoscopic cholecystectomy: 13 (%81,25) Trauma: 3 (%18,75)
Strasberg classification	E1: 4 (%25) E2: 5 (%31,25) E3: 3 (%18,75) E4: 4 (%25)
Additional organ injury	Right hepatic artery: 4 (%25) Liver: 3 (%18,75) Portal vein: 2 (%12,5) Renal vein: 1 (%6,25) Vena cava inferior: 1 (%6,25)
Diagnosis time	0-20 days Mean: 3,9 days
Treatment time	0-90 days Mean: 18,6 days
Biliary reconstruction	Hepaticojejunostomy: 13(%93,75) End-to-end anastomosis: 1(%6,25)
Hospitalisation duration	0-35 days Mean: 18,9 days
Follow-up duration	2-66 months Mean: 25,6 months

DISCUSSIONS

BDI is caused by iatrogenic and traumatic reasons and leads to severe morbidity, in some cases, to mortality such as secondary bile peritonitis, sepsis, and even death. Laparoscopic cholecystectomy is the most frequently performed surgical procedure in symptomatic gallstone surgery. Although BDI incidence is lower in open cholecystectomy surgery, laparoscopic cholecystectomy has become the preferred procedure due to less postoperative pain, shorter hospitalisation and return duration by surgeons and patients alike (7).

The frequent application of laparoscopic cholecystectomy surgery has brought about some reduction in the BDI incidence. However, cholecystectomy and, particularly, laparoscopic cholecystectomy, have been subjects of lawsuits against surgeons for malpractice while researchers have started discussing the safety of cholecystectomy. The latter technique has also become a subject of training practices as it has also turned out to be an important cause of serious morbidity and even mortality. Indeed, 81.25% of our patients had to be treated due to laparoscopic cholecystectomy procedures. Although the risk of complications in emergency cholecystectomy surgery is higher than those encountered in elective surgery, it should be remembered that BDI may develop during elective surgeries, as it was the case in our series, and surgeons should be extremely careful about this matter.

Practitioners should be tactful as far as BDI-related risk factors are concerned. If they suspect the safety of a thorough cholecystectomy after initiating a laparoscopic procedure, we believe that practitioners should not act conservatively as to whether to switch the procedure to open surgery. Also, if the surgeon is inexperienced in terms of laparoscopic cholecystectomy, we think that a second and more experienced surgeon should be present in the operating room.

Only one third of BDIs can be noticed during surgery. If BDI id detected during laparoscopic cholecystectomy, there is an indication of switching to open surgery. In this case, the most significant point is to avoid excessive dissection during open surgery especially if surgeon is not sufficiently experienced in biliary reconstruction; in this picture, surgeon may consider draining surgery area and refer the patient to a different centre. Excessive dissection and administrating biliary reconstruction by inexperienced surgeons will reduce the success of reconstruction process (8, 9).

The most common signs and symptoms in patients suspected for BDI are abdominal pain, abdominal distention, fever, bilious drainage from the abdominal drain, abdominal tenderness on physical examination, rebound and deterioration in the defense and laboratory parameters (10). So, following cholecystectomy surgery, signs like fever, abdominal pain, abdominal distention, bilious drainage from the abdominal drain may cause increase in cholestatic enzymes like WBC and CRP and this increase should be kept in mind for a potential BDI picture.

For the diagnosis of BDI, the most commonly used imaging methods are ultrasound, CT, MRCP, ERCP and percutan transhepatic cholangiography (PTC). With USG, widening intrahepatic and extrahepatic bile ducts can be measured while it can also reveal abdominal fluid accumulation, abscesses, and biloma. CT is a more

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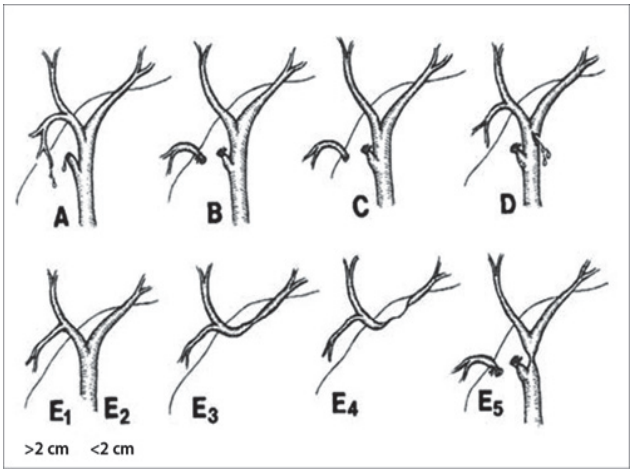
specific imaging modality in patients with suspected bile leak. PTC is an imaging method that is more useful in patients with proximal BDI. MRCP is a non-invasive method with a sensitivity rate of 85-100% and used in imaging the biliary tract. While ERCP is the most useful in imaging of wounded biliary tracts, it also leads to the treatment of BDI (10). In our series, except for 3 (18.75%) patients who underwent emergency surgery, the remaining 13 patients (81.25%) were administered preoperative ERCP; in 12 (92.3%) of the patients, ERCP proved to be diagnostic. For this reason, although it is a more invasive procedure than other imaging methods, we believe that ERCP is a very valuable and objective procedure in the diagnosis and treatment of BDI.

Iatrogenic BDI is often seen with other intra-abdominal organ injuries after blunt or penetrating abdominal traumas. In patients with intra-abdominal bleeding, BDI can be overlooked or, even if it is diagnosed, its treatment may be postponed until patients are more stable (11). As research in literature has taught us, we first administered primary liver repair, vena cava inferior and renal vein repairs for the patient who underwent emergency surgery due to GSW. During the operation, we also applied primary choledochal repair and packing to this patient. The patient was then intubated and taken to the intensive care unit for further depacking biliary reconstruction at a later time. In one of our patients, who underwent emergency surgery due to intra-abdominal haemorrhage after developing intra-operative portal vein injury during laparoscopic cholecystectomy at a different centre, we failed to detect BDI during the operation. This patient was diagnosed with BDI when we noticed postoperative leak from the abdominal.

As far as BDI classification is concerned, there are many classifications used in the literature (12, 13). We adopted the Strasberg classification for BDI classification in our study (Figure 1).

The first treatment option in iatrogenic and traumatic BDI is the endoscopic method. If this method proved ineffective, Roux-n Y hepaticojejunostomy is the most preferred method among many biliary reconstruction processes (14). A total of 15 (93.75%) patients underwent HJ in our series; for the remaining 1 (6.25%) patient, we applied end-to-end anastomosis. In this surgical technique, proximal biliary tracts are prepared for anastomotic and distal biliary tract is closed with sutures. In HJ, absorbable polydioxanone (PDS 4/0, 5/0) sutures are used. Low postoperative stricture rate is the reason why HJ is the most preferred method (15). For Terblanche et al. have stated that HJ has given them a success rate of 90% (16); Rossi and Tsao's study have indicated that end-to-end anastomosis may lead to a 40-50% rate of strictures in the long term (17). However, bypassing the saffron by using HJ may result in gastric hypersecretion, changes in pH values, and increased gastrin levels and, eventually, can cause increased incidence of duodenal ulcers. Increase in plasma triglyceride, gastrin, and glucagon-like immunoreactive levels along with decrease in gastrin and gastric inhibitory polypeptides and insulin levels are among the common laboratory findings in patients undergoing HJ. As the bile flow path changes due to HJ, fat metabolism impairment may take place, too, which is another frequently seen sign in these patients (18, 19). Another drawback of HJ is that it is not suitable for endoscopic examinations required for the diagnosis and treatment of biliary strictures that may develop in the postoperative period. An alternative solution to this issue can be preparing a long jejunal loop during the operation and locating this loop in the right subcostal area (permanent-access hepaticojejunostomy). This jejunal loop can be open or closed and enables endoscopic dilatation in case of biliary stricture development (20).

Figure 1. Strasberg classification



The timing of biliary reconstruction process after the onset of BDI, early or late, is an important factor affecting the success of the process. The success rate of reconstruction conducted within the first 4 days of injury is high whereas this rate is lower in processes applied between 4 days to a few weeks particularly because of inflammation in the tissues and narrow bile duct to be reconstructed; in the latter case, complication rates are also quite high (21).

However, in their study comparing the results of high intra-hepatic bilioenteric anastomosis in inflammation and scar free, well-vascularized bilioenteric anastomosis with cases undergoing anastomosis on the common hepatic duct level, Mercado et al. have reported a success rate of 97% in high intrahepatic repair group and of 85% in extra hepatic repair group regardless of the time of reconstructive surgery. For the bilioenteric anastomosis administration in this study, researchers have applied anastomosis on unscarred, well-vascularized segments with tension-free mucosa-to-mucosa technique along with one-to-one 4/0 absorbable sutures (22).

In our series, 10 (62.5%) of the 16 patients underwent biliary reconstruction process within the first 4-21 days of the onset of BDI, when tissues are most inflamed and swollen. Studying early and late complications in these 10 patients, we observed late onset of complications in

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only 1 (10%) patient. This case was the patient who had been admitted due to portal vein injury following laparoscopic cholecystectomy and undergone portal vein repair in our clinic; we noticed BDI 15 days after the repair and administered HJ on the postoperative 21st day. This particular patient was followed for 44 months and developed cirrhotic changes in the liver. As far as early complications are concerned, we observed self-repairing biliary fistula that did not require any additional intervention in 1 (10%) patient, high bilirubin levels that had started on postoperative day 2 and ended on postoperative day 3 with plasmapheresis requirement in 1 (10%) patient, wound infection in 1 (10%) patient, pneumonia in 1 (10%) patient, and biloma in 1 (10%) patient.

The time between the onset of BDI and biliary reconstruction for the remaining 6 patients of our series varied between 0-2 days and 40-90 days. In other words, this group comprised patients who underwent operations within the first 48 hours or 6 weeks of injury with considerably low intra-abdominal inflammation levels. Analysing early and late complications in these patients, we observed anastomotic stricture in 1 (10%) patient as a late complication and applied anastomosis dilatation to the patient with PTC. As early complications, we observed pleural effusion in 1 (16.6%) patient, pneumonia in 1 (16.6%) patient, wound infection in 4 (66.6%) patients, self-repairing biliary fistula without the need for further in 2 (% 33.2) patients, percutaneously drained biloma in 2 (33.2%) patients, and surgically drained drained intra-abdominal abscess in 1 (16.6%) patient.

The average hospitalisation time for patients who underwent biliary reconstruction during dense intra-abdominal inflammation was 14.7 days; this was 24.3 days in the other group.

Analysing complications and length of hospital stay in the two groups, we noticed no significant difference between the groups in terms of early or late complications; contrary to what is expected, patients undergoing biliary reconstruction during the inflammatory phase had shorter hospital stay.

Although research indicates a strong correlation between surgical success and biliary reconstruction process with emphasis on the relation concerning the duration between onset of BDI and HJ administration, clinical / surgical experience plays a very important role in successfull biliary reconstruction process regardless of the time elapsed between BDI onset and reconstructive treatment, as it can observed in our experience.

CONCLUSION

BDI may develop due to iatrogenic and traumatic reasons and may prove to be a serious cause of morbidity and mortality. Whatever the cause, BDI is a serious condition the treatment of which requires experience. Early diagnosis of BDI and experienced treatment decrease morbidity and mortality rates dramatically. Regardless of the time between the onset of BDI and surgical application, biliary reconstruction may give successful results if surgery is conducted by surgeons experienced in hepatobiliary surgery.

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Cerebral Venous Sinus Thrombosis-Related Epileptic Seizures and Their Clinical Features

Serebral Venöz Sinüs Trombozuna Bağlı Epileptik Nöbetler ve Klinik Özellikleri

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Abstract

Aim: Cerebral venous sinus thrombosis (CVST) is a severe neurological disease that may cause disability and death. Its clinical symptoms are varied. Epileptic seizures may manifest as early signs of the disease in 30-40% of patients. We aim to compare patients presenting with seizures with those presenting without seizures in CVST patients.

Materials and Methods: 50 patients diagnosed with cerebral venous sinus thrombosis were included in the study. The demographic characteristics, initial symptoms, etiologic factors, radiological findings and treatment were analyzed retrospectively. Patients with seizures were evaluated with all their clinical features.

Results: There were 10 patients with epileptic seizures (20%). Nine of the patients were females. All nine female patients had pregnancy-associated seizures. Patients with supratentorial lesions seen was greater than the frequency of seizures. All of the seizures were observed as early seizures (within 14 days). 4 patients focal seizures, secondary generalized seizures were observed in 6 patients. 7 patients who have seizures are also have sagittal sinus thrombosis. Transverse sinus structures affected in the second frequency.

Conclusion: Made in previous studies of patients with DVT reported that about half of the early episodes, in our study, this rate was found to be 20%. Patients who had seizures have similar outcomes with patients without seizures.But the attacks early with an effective antiepileptic treatment was considered to be the prevention of deaths and late seizure recurrence.

Keywords: Cerebral Venous Sinus Thrombosis; Seizure; Epilepsy.

Öz

Amaç: Serebral ven trombozu (SVT); özürlülük ve ölüme neden olabilen ciddi bir nörolojik hastalıktır. Klinik semptomlar çok çeşitlidir. Epileptik nöbetler hastaların %30-40'ında hastalığın ilk bulgusu olarak karşımıza çıkabilir. Bu çalışmada erken dönem nöbet ile gelen SVT hastalarında prognozunun nöbet olmayanlarla karşılaştırılması planlandı.

Gereç ve Yöntemler: Kliniğimizde takip edilmiş 50 SVT hastasının demografik özellikleri, başlangıç semptom ve bulguları, etiyolojik faktörleri, nöroradyolojik bulguları ve tedavileri retrospektif olarak incelendi. İlk klinik bulgusu epileptik nöbet olanlar ve/veya klinik izlemde nöbet geçiren hastalar tüm özellikleri ile değerlendirildi.

Bulgular:SVT hastalarımız arasında epileptik nöbet ile başvuran 10 hastamız (%20) vardı. Nöbet geçiren hastaların 9'u kadın, 1'i erkekti. Nöbet geçiren 9 kadın hastanın tamamı gebelik ile ilişkiliydi. Supratentoryal lezyonu olan hastalarda nöbet görülme sıklığı daha fazlaydı. Nöbetlerin tamamı erken dönem nöbet olarak gözlendi (ilk 14 gün içinde). Hastaların 4'ünde fokal nöbet, 6'sında sekonder jeneralize nöbet gözlendi. Nöbet geçiren hastaların 7 sinde süperior sagital sinüs trombusu vardı. İkinci sıklıkta etkilenen yapı transvers sinüstü.

Sonuç: Yapılan daha önceki çalışmalarda SVT'li hastaların yaklaşık yarısında erken dönem nöbet bildirilirken, bizim çalışmamızda bu oran %20 olarak saptandı. Erken dönem nöbet ile gelen SVT hastalarında prognozun nöbet olmayanlarla benzer olduğu görüldü.Fakat etkin bir erken dönem antiepileptik tedavi ile nöbete bağlı ölüm ve geç dönem nöbet nüksünün önlenebileceği düşünüldü.

Anahtar Kelimeler: Serebral Venöz Tromboz; Nöbet; Epilepsi.

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INTRODUCTION

Cerebral venous sinus thrombosis is a serious neurological disorder that can cause disability and death. It is more rarely seen compared to arterial stroke and often occurs in young ages (1, 2). Its incidence is not known exactly but it has been reported to be 1-3 per hundred thousand in western countries (3). It is responsible for 1-2% of adult stroke (1, 2).

Many reasons have been implicated in the etiology of cerebral venous sinus thrombosis. Pregnancy, post-partum infection, systemic inflammatory diseases, hereditary and acquired thrombophilia and antiphospholipid antibody syndrome, hematological diseases, tumours, neurosurgical procedures, medications, and trauma are among its possible causes (4, 6). Still, around 15% of the cases do not reveal any etiologic factors (7, 19). Table 1 presents the CVST-related risk factors.

There is a rich clinical symptomatology in cerebral venous sinus thrombosis. The most common complaint is headache, yet focal neurological deficits like focal or generalized seizures, hemiparesis, and hemihypoesthesia as well as papilloedema, isolated intracranial hypertension, loss of vision, dizziness, and aphasia can also be seen (2, 4, 5).

Seizures are the first signs of the disease in 30-40% of patients with cerebral venous sinus thrombosis. Poor prognostic factors in CVST patients are being a male >37 years of age, having a Glasgow coma scale score of less than 9 and damaged deep venous structures, detecting intracranial hemorrhage in CT or MRI, and having malignancy and central nervous system infection symptoms (3, 19). A meta-analysis has reported that mortality rate in CVST is 5,6%-9,4%. The complete remission rate is reported to be 88% (20). Seizures are one of the factors that negatively affect the prognosis of the disease. Disease-related mortality was found 3 times more than those patients without seizures (8). In this article, we retrospectively review the files of patients who were diagnosed with CVST between October 2010 and April 2015 in our clinic. We aim to evaluate the clinical features of seizures and seizure rates in these CVST patients.

Table 1. Risk factors associated with Cerebral venous sinus thrombosis.

Acquired risk factors
Infection (menengitis, otitis, tonsillit, sepsis, tuberculosis, HIV)
Pregnancy
Trauma and surgery (head trauma, spinal anaesthesia, radical neck surgery)
Drugs (OCSs, hormone replacemnet therapy, steroids, lithium, sildenafil)
Hereditary risk factors
Hypercoagulability (protein S, C, antithrombin deficiency, factor V leiden and prothrombin mutation)
Malignity (meningioma, leukemia, lymphoma)
Hematological disases (anemia, paroxysmal nocturnal hemoglobinuria, polisitemia)
Inflammatory diseases (Behçet's disease, SLE, Wegener granulomatosis, temporal arteritis)
ther
Thyroid diseases (hyperthyroid and hypothyroid)

MATERIALS and METHODS

We retrospectively evaluated the demographic characteristics, initial signs and symptoms, etiologic factors, neuro-radiological findings and treatment processes of 50 patients whose CVST diagnosis were confirmed with MRI and MR venography between October 2010 and April 2015 at the Neurology Clinic, Inonu University, Faculty of Medicine. Patients with initial clinical evidence towards epilepsy and/or those who had seizure during clinical follow-up were evaluated with all their characteristics. Only patients who were monitored for at least 5 months were included studied.

RESULTS

There were 50 patients who received CVST diagnosis in our clinic between April 2015 and October 2010. Of these patients, 37 were females (74%) and 13 (26%) were males. The age range of patients was 20-72 with a mean age of 39,24±13,08. Evaluating clinical characteristics of these patients, we found out that all the patients (98%), except for one, had headache complaint. Nausea and vomiting was the second most common (52%) complaint after headache. Focal neurological signs such as hemiparesis and hemihypoesthesia along with other visual symptoms were among other frequent (32%) findings. There were 10 patients (20%) who had applied with epileptic seizures. Unconsciousness was the least common (18%) finding. Clinical findings and percentages with regards to patients are summarised in Table 2. Considering the etiology of the patients, we observed that 22 patients had pregnancy-related issues, 5 patients had coagulation disorders while 4 patients had infection (otitis media in 3 patients and tonsillitis in one patient). 17 patients did not show any etiological signs.

9 of the 10 patients presenting with seizures were females. As the first clinical finding, we observed that all seizures were early period seizures. 4 of the patients had focal seizures while 6 showed secondary generalised seizures. None of the patients had status epilepticus. 7 of the patients experiencing seizure had superior sagittal sinus thrombus. The structure affected in the second frequency was the transverse sinus structure. 2 of the 10 patients having epileptic seizures had parenchymal

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involvement. Both patients showed hemorrhagic infarction in the posterior parietal region. All of the patients had multiple sinus thrombosis and 1 of the patients had affected deep venous structures. All 9 female patients had pregnancy associated seizures; 8 of these patients had presented in the early postpartum period (2 days to 3 weeks). One of them was in the 34th week of her pregnancy; she also had factor V Leiden mutation. In one of the male patients who presented with seizures, we could not detect any etiologic factors. All seizure patients were first given heparin therapy followed by a 6-month oral anticoagulant (warfarin) therapy along with antiepileptic treatment. 7 of these patients were treated with levetiracetam therapy while 2 patients received lamotrigine treatment. During the follow-up of the patients, we did not observe any late period seizures. There were no seizure-related deaths either.

Table 2. Clinical findings of the patients.

Clinical findings	Number of patients (n)	Percentage (%)
Headache	49	98
Nausea / vomiting	26	52
Impaired vision	15	30
Unconsciousness	9	18
Epileptic seizures	10	20
Focal findings (hemiparesis / hemihypoesthesia)	16	32

DISCUSSION

Epileptic seizures are the first symptom of cerebral venous sinus thrombosis in 12-31,9% of patients while this can raise up to 44.3% in the early stages of the disease (7, 8). In a series of 90 patients, onset ratio with clinical seizure was 46.7% although only 5.6% of the patients continued to have seizures. Kalita et al.'s study reports that patients with supratentorial lesions have 5 times higher rates for seizures. In particular, patients with lesions in the frontal lobe and parietal lobe have a higher risk to have seizures as the first symptom (9). Bousser and Russell have stated that rate of presenting with seizures is higher if patients have lesions around the anterior central sulcus or focal lesions (10). The mechanism behind frequent seizures in especially hemorrhagic lesions is not fully understood. However, studies on animals and people with traumatic brain damages have shown that degradation products such as hemosiderin cause focal cerebral irritation and, eventually, seizures (11, 12). The literature indicates that mortality rate of patients having seizures is significantly higher than seizure-free patients (13, 14). However, studies investigating the relationship between epileptic seizures and localisation of thrombosis have been unable to come up with a significant relationship (9).

7 of our patients who had seizures had superior sagittal sinus thrombus. The structures affected in the second frequency were the transverse sinus structures. All of the patients had multiple sinus thrombosis and one of the patients had affected deep vein structure. The frequency of seizures are more common in newborns and children compared to adults (15, 16). But the pediatric age group was not included in our study. Sensory and motor deficits particularly are important determinants for aphasia and deep coma seizures (17).

The CVST-related mortality rate is 12.5% in patients who have seizures while it is 6.3% in patients without any history of seizures (18). We did not observe seizure dependent death in our patients. None of the patients developed late period seizures during the follow-ups. This can be associated with the effective antiepileptic treatment our patients received in the early stages of the disease.

Antiepileptic therapy should be initiated immediately for patients who present with seizures in the acute phase, especially when these seizures are accompanied by supratentorial lesions (13). In patients without seizures, administrating prophylactic antiepileptic drugs is not recommended (19). Long-term risk of seizure is approximately 11% (7). To prevent seizure recurrence and status epilepticus in patients at the onset of seizures, antiepileptic drugs are recommended in the acute phase. In long-term persistent seizures, patients usually carry other risk factors for seizure such as supratentorial lesions or motor deficits (19). It is not exactly known how long antiepileptic treatment should be continued; the overall approach is to leave this decision to patients.

CONCLUSION

Previous studies on CVST report early onset of seizures in about half of the patients; this rate was found to be 20% in our study. The prevalence of seizures was higher in patients with supratentorial lesions. However, an early and effective antiepileptic treatment can prevent seizure-related deaths and seizure recurrence.

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Incidence of Thyroid Carcinoma in Patients Undergoing Thyroidectomy for Nodular Goiter in Bitlis Province

Bitlis İlinde Nodüler Guatr Nedeniyle Tiroidektomi Uygulanan Hastalarda Tiroid Kanseri İnsidansı

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Abstract

Objective: The most frequently observed endocrine cancer is thyroid malignity. It constitutes only one percent of all malignities. The aim of this study is to investigate the incidence of thyroid cancer in cases with nodular goiter who undrewent thyroidectomy performed by a single surgeon in Bitlis province (Turkey), an endemic goiter region.

Materials and Methods: Pathology reports with surgery indication of 940 patients, who underwent thyroidectomy administered by the same surgeon for nodular goiter at Bitlis State Hospital between September 2008 and March 2015, were studied retrospectively. Postoperative histopathologic examinations were evaluated.

Results: Female and male counts of our 940 patients were 827 (88%) and 113 (12%), respectively. The proportion of female to male patients was 7,3/1. 30 of 940 patients (3,2%) underwent one part total and the other part near total thyroidectomy and 910 patients (96,8%) underwent total thyroidectomy. Histopathological examination showed that 825 (87,7%) cases had nodular hyperplasia, 46 (4,9%) cases had lymphocytic thyroiditis, and 69 (7,3%) cases had thyroid tumors. 69 tumors in 18 (26%) cases were benign; 51 (74%) cases were malign. In terms of cancer type, 45 (4,7%) cases had papillary carcinoma, 5 (0,5%) cases had follicular carcinoma, and 1 (0,1%) case had medullary carcinoma.

Conclusion: In some cases in endemic goiter regions, received exogenous iodine can affect cytological results and cause changes in thyroid tissue morphology. The observed incidence of thyroid cancer was 5,4% in the cases who underwent thyroidectomy due to nodular goiter in Bitlis province; and papillary thyroid carcinoma was the most observed cancer type.

Keywords: Endemic Nodular Goiter; Thyroidectomy; Thyroid Carcinoma.

Öz

Amaç: Tiroid maligniteleri en sık görülen endokrin kanserlerdir. Tüm malignitelerin %1'ni oluştururlar. Bu çalışmanın amacı, endemik guatr bölgesi olan Bitlis ilinde tek cerrah tarafından tiroidektomi yapılan nodüler guatr olgularında, tiroid kanseri görülme sıklığını araştırmaktır.

Gereç ve Yöntem: Bitlis Devlet Hastanesinde, Eylül 2008 ve Mart 2015 tarihleri arasında nodüler guatr ön tanısıyla cerrahi endikasyonu konulan ve tek cerrah tarafından tiroidektomi yapılan toplam 940 hastanın patoloji raporları retrospektif olarak tarandı. Postoperatif histopatolojik bulgular değerlendirildi.

Bulgular: Hastalarımızın 827'si (%88) kadın, 113'ü (%12) erkek olup, kadın/erkek oranı 7,3/1 idi. Toplam 940 hastanın 30' una (%3,2) bir taraf total + diğer taraf totale yakın, 910' nuna (%96,8) bilateral total tiroidektomi uygulandı. Histopatolojik incelemede 825 (%87,7) olguda nodüler hiperplazi, 46 (%4,9) olguda lenfositik tiroidit, 69 (%7,3) olguda ise tiroid tümörü tespit edildi. 69 tümör olgusunun 18' i (%26) benign, 51' i (%74) ise malign idi. Kanser tipi olarak 45 (%4,7) olguda papiller karsinom, 5 (%0,5) olguda folliküler karsinom, 1 (%0,1) olguda ise medüller karsinom tespit edildi.

Sonuç: Endemik guatr bölgelerinde, ekzojen iyot alınması bazı olgularda tiroid dokusu morfolojisinde değişime neden olarak sitolojik sonuçları etkileyebilmektedir. Bitlis ilinde tiroidektomi yapılan nodüler guatr olgularında tiroid kanseri görülme sıklığı %5,4 olarak tespit edilmiş olup, en fazla kanser tipi olarak papiller tiroid karsinomu görülmektedir.

Anahtar Kelimeler: Endemik Nodüler Guatr; Tiroidektomi; Tiroid Kanseri.

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INTRODUCTION

As is the case all over the world, there are endemic goitre pictures as a result of iodine deficiency in some areas in Turkey. The pathogenesis of goiter in areas with iodine deficiency can show different characteristics in terms of both functional and organic ways. In these areas, exogenous iodine supplementation can cause changes in the morphology of thyroid tissues and, therefore, affect cytologic results (1). Studying endemic goiter pathogenesis initially reveals development of homogeneous hypertrophy (goitre) due to the growth of thyroid mass (2). In this study, we aim to investigate the incidence and type of thyroid cancer in nodular goitre patients operated by the same surgeon in Bitlis, one of the endemic regions in Turkey.

MATERIALS and METHODS

In this study, we evaluated a total of 940 patients who underwent thyroidectomy with nodular (solitary or multiple) goitre diagnosis at Bitlis State Hospital between September 2008 and March 2015. Cases with goitre recurrence, patients with malignant fine-needle aspiration biopsy, and patients requiring neck dissection in the same session were excluded from the study. The data of patients were retrospectively obtained and reviewed from patient epicrises, operation room records, notes taken by specialist physicians about patients, and hospital pathology archives. All patients were operated by the same surgeon in the same centre. The majority of patients were patients with increased thyroid nodules (in size and number) from Bitlis and surrounding countryside. There were even patients with plunging giant goitre and signs of pressure.

RESULTS

Of the 940 patients who underwent thyroidectomy, 827 (88%) were females and 113 (12%) were males with a female/male ratio of 7,3/1. The average age of the patients was 38,1 (14-77). Of the 940 patients, 30 of them (3,2%) underwent total + near total thyroidectomy while 910 (96.8%) patients underwent bilateral total thyroidectomy. Histopathological examination showed that 825 (87.7%) cases were diagnosed with nodular hyperplasia while 46 (4.9%) had lymphocytic thyroiditis and 69 (7.3%) received thyroid tumour diagnosis. In terms of cancer type, 45 (4.7%) patients had papillary carcinoma, 5 (0.5%) patients had follicular carcinoma, and 1 (0.1%) showed medullary carcinoma (Table 1).

Table 1. Number and percentages of patients according to Histopathological diagnosis.

Diagnosis	Number (n) (%)	Percentage
Nodular hyperplasia	825	87,8
Lymphocytic thyroiditis	46	4,9
Benign tumour		1,9
Follicular adenoma	18	
Malign tumour		
Papillary carcinoma	45	4,8
Follicular carcinoma	5	0,5
Medullary carcinoma	0,1	1
Total	940	100

Anaplastic carcinoma was not detected. 38 (84.4%) patients diagnosed with papillary carcinoma were females and 7 of these patients were (15.6%) were males. The youngest patient was 16; the oldest patient was 65 years old and the average age was 39.4. 3 (60%) patients diagnosed with follicular carcinoma were females and 2 (40%) of these patients were males. The youngest patient was 40; the oldest patient was 69 years old and the average age was 47.4. The only one case with medullary carcinoma was a 40-year-old woman. Among the patients undergoing thyroidectomy, a total of 51 (5.4%) - 42 (4.5%) females and 9 (0.9%) males - showed malignancies (Table 2).

Table 2. Sex distribution and age of malign cases.

Diagnosis - -	Female (n)	Percentage (%)	Male (n)	Percentage (%)	Youngest	Oldest
Papillary carcinoma	38	74,5	7	13,7	16	65
Follicular carcinoma	3	5,9	2	3,9	40	69
Medullary carcinoma	1	2	0			- -

DISCUSSIONS

In countries like Turkey, where thyroid pathologies are commonplace, the use of thyroidectomy is continuing to increase day by day. Several geographic regions have been noted for endemic iodine deficiency. These places are usually mountainous regions and the soil is poor in iodine (3). Bitlis and its surroundings is a mountainous place and is known to host iodine deficiency. In sufficient nutrition combined with iodine deficiency, genetic predisposition, environmental factors and personal characteristics are effective in the formation of goitre. Especially iodine deficiency is the most important factor in goitre formation in Turkey. For a long time, it has been aimed to eliminate iodine deficiency with food and

exogenous iodine supplementation in order to prevent goiter development. While exogenous iodine supplementation from birth reduces goitre prevalence in new generations, this supplementation may cause some changes in the spectrum and pathogenesis of the disease in individuals who previously had goiter and

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nodular development (4). Nodular goitre is more common in women and it occurs in 4-5% of the society. There are different opinions on this matter and its underlying reasons. It has been suggested that women are more prone to develop thyroid nodules because they have positive antithyroperoxidase antibody titres (TPOAb) and low iodine excretion (<50 microgram/day) (5). In our study, 88% of the patients who underwent thyroidectomy were females while only 12% of these patients were males.

Thyroid cancer is less common compared to other types of cancer in society and the course of the disease is quite good. With correct diagnosis and treatment, the disease can be eliminated completely and the patient can live for a long time. Having received longitudinal radiation on the neck, vocal hoarseness, vocal cord paralysis, and having thyroid cancer history in the family bring high probability of cancer of thyroid nodules detected (6). Rapidly growing thyroid nodules that do not respond to drug therapy (TSH suppression), nodules detected before 20 years of age or and those detected after 60 along with solitary, hard, cold, and fixed nodules with accompanying lymphadenopathy carry the possibility of cancer. Besides, thyroid nodules observed in men have higher cancer incidence than those detected in women. Thyroid cancer constitutes approximately 1% of all cancers. Thyroid cancers can be divined into subgroups as follows: differentiated (papillary and follicular), undifferentiated (medullary, anapaestic), and other (lymphoma, sarcoma, metastasis from other organs, etc.). 75% of these cancers are differentiated cancer types. Among these cancers, papillary cancer is the most common type with 80% (7).

In line with the epidemiology of thyroid nodules, thyroid cancer is more common in women. According to the literature, 74% of the newly identified patients are females (8). In our study, too, 42 (82.3%) of the newly diagnosed 51 malignant cases were females while there were 9 (17.7%) such male patients; the female/male ratio was 4.6/1. Although these rates are consistent with the literature, Belfiore et al. (9) have stated that <30-year-old and >60-year-old males have a higher risk of cancer.

One notable detail in endemic goitre regions is the change in malignant solid nodules. Experimental studies on animals have shown that prolonged iodine deficiency leads to a significant increase in thyroid epithelial cell cancers (10). Again, it is reported that incidence for follicular, poorly differentiated, and anapaestic cancer types are higher in regions where endemic goiter and iodine deficiency are common (11). In a study conducted in Düzce (Turkey) on 198 patients with nodular goitre, it has been observed that 1.5% of these patients had thyroid cancer after the operation; 2 of these patients had papillary carcinoma while 1 patient had poorly differentiated thyroid carcinoma (4). Lawal et al. (12)'s study on patients who underwent thyroidectomy due to nodular goitre reports a cancer incidence rate of 13%; 69% of these patients are reported to have follicular carcinoma diagnosis.

Several studies in the literature demonstrate that iodine prophylaxis helps prevent diseases related with iodine deficiency while it causes changes in the histologic subtypes of thyroid cancer as well as in its phases (13). As external iodine intake increases papillary thyroid carcinomas in well-differentiated tumours, it reduces follicular and anaplastic carcinomas. Slowinska-Klencka et al. (1) have similarly reported a decrease in follicular carcinoma rates with exogenous iodine intake in endemic regions while the intake has caused increase in papillary carcinoma rates. The reason why papillary thyroid carcinoma was more common in our study could be a result of the increase in the use of iodised salt as with the rising awareness.

The most common cause of re-operation in thyroid surgery is the presence of incidental malignancy in pathology results. Castro et al. (7) have reported that 5% of all thyroid nodules are malignant. Bozkurt and Bektas's (14) study on 241 patients operated due to nodular goitre reports a cancer rate of 4.6% while Üçer's (15) study on 1275 patients with nodular goitre reports this rate to be 7.8%. Similarly, Senyürek et al.'s (16) have observed a cancer rate of 6.5% in patients with thyroid nodules while Erbil et al. (17) reports that they observed a post-thyroidectomy thyroid cancer rate of 11% in patients with nodular goitre.In our study, we observed malignancy in 51 patients (5.4%) with a cancer rate compatible with those in the literature; of these cancer types, the most common type was papillary carcinoma (88.2%).

Surgery performed for nodular goitre should both treat patients and cause minimal postoperative complications. In recent years, thyroidectomy is widely applied due to the increasing number of cases with recurrence and complications following surgeries performed to treat recurrence. One of the most important advantages of total thyroidectomy is that there is no remaining normal thyroid tissue after the operation. This allows practitioners to determine and treat local and/or distant metastases by using post-opretaive radioactive iodine treatment if needed (18).

CONCLUSION

There are no previous studies investigating the incidence of thyroid cancer and types of cancer in Bitlis province. As it has been indicated in this study, the thyroid cancer incidence in patients undergoing thyroidectomy by the same surgeon, in the same medical centre in Bitlis province with a pre-diagnosis of nodular goitre was 5.4% while the most common type of cancer was, in line with the literature, papillary carcinoma.

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Comparison of Early and Mid-term Outcomes of Endovenous Laser Ablation (EVLA) Treatment Versus Traditional Surgical Treatment in Vena Saphena Magna Insufficiency

Büyük Safen Ven Yetmezliğinde Endovenöz Lazer Ablasyon (EVLA) ve Geleneksel Cerrahi Tedavilerinin Kısa ve Orta Dönem Sonuçlarının Karşılaştırılması

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Abstract

Objective: In this retrospective study, we aimed to compare the short- term and mid- term clinical outcomes of endovenous laser ablation with traditional surgical treatment (high ligation and saphenectomy of Vena Saphena Magna) in patients with isolated unilateral symptomatic Vena Saphena Magna insufficiency.

Materials and Methods: Sixty five patients who underwent traditional surgical treatment (Group 1; n: 35; 16 women, 19 men, mean age; 44.3 ± 12.6 years, range; 20 - 68 years) and endovenous laser ablation treatment (Group 2; n = 30; 20 women, 10 men, mean age; 39.8 ± 11.7 years, range; 20 - 65 years) between May 2013 and December 2013 were included in the study. Groups were compared according to their differences.

Results: Pain scores of EVLA patients were significantly lower at postoperative first week and first month ($p< 0.01$), whereas, there was no significant difference preoperatively. No patient stated to have pain at postoperative 6th month. Frequency of complication development of EVLA patients was found to be lower at postoperative first week follow up but there was no statistically significant difference at 1st month and 6th month controls. CEAP scores of EVLA patients were significantly lower at postoperative follow-ups but there was no significant difference preoperatively.

Conclusion: We observed that endovenous laser ablation is a better treatment modality with better short and mid-term outcomes than traditional surgical treatment in isolated symptomatic unilateral Vena Saphena Magna insufficiencies.

Keywords: Vena Saphena Magna Insufficiency; Saphenectomy; Endovenous Laser Ablation.

Öz

Amaç: Bu retrospektif çalışmada izole ve tek taraflı semptomatik büyük safen ven yetmezliği olan hastalarda, endovenöz lazer ablasyon ve geleneksel cerrahi tedavi (büyük safen vene yüksek ligasyon ve safenektomi) sonrası kısa ve orta dönem klinik sonuçların karşılaştırılması amaçlandı.

Gereç ve Yöntemler: Mart 2013 - Ağustos 2013 tarihleri arasında kliniğimizde geleneksel cerrahi tedavi (Grup 1; 35 hasta: 16 kadın, 19 erkek, ortalama yaş; 44. 3±12. 6 yaş, 20-68 yaş arası) ve endovenöz lazer ablasyon (EVLA) (Grup 2; 30 hasta: 20 kadın, 10 erkek, ortalama yaş; 39. 8±11.7 yaş, 20-65 yaş arası) tedavileri uygulanan 65 hasta bu çalışmaya dahil edildi. Her iki gruptaki hastalar özelliklerine göre karşılaştırıldı.

Bulgular: Postoperatif 1. hafta ve 1. ay ağrı skorları karşılaştırıldığında EVLA yapılan hastalarda, diğer gruba göre istatistiksel olarak ağrı skorlarının daha düşük olduğu saptandı ($p< 0.01$). Buna karşın endovenöz lazer ablasyon uygulanan hastalarda preoperatif ağrı skorları arasında farklılık yoktu. 6. ay kontrolünde her iki grup hastada ağrı gözlenmediği saptandı. Postoperatif 1. hafta takibinde komplikasyon gelişme sıklığı EVLA yapılan hastalarda daha düşük saptandı fakat 1. ay ve 6. ay kontrollerinde istatistiksel farklılık saptanmadı. CEAP skorları EVLA hastalarında postoperatif takiplerinde istatistiksel olarak anlamlı olarak daha düşük iken preoperatif her iki grup arasında farklılık gözlenmedi.

Sonuç: İzole, semptomatik ve tek taraflı büyük safen ven yetmezliklerinde, endovenöz lazer ablasyon tedavisinin kısa ve orta vadedeki daha iyi sonuçlarla geleneksel cerrahi tedaviye göre daha iyi tedavi metodu olduğunu gözlemledik.

Anahtar Kelimeler: Büyük Safen Ven Yetmezliği; Safenektomi; Endovenöz Lazer Ablasyon.

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INTRODUCTION

Chronic venous disorder (CVD) has a considerable socio-economic impact due to its high prevalence, investigations and treatment costs, and loss of working days (1). Varicose veins are present in 25 - 33% of female and 10 - 20% of male adults, while its incidence is 2.6% per year and 1.9% per year in men (1). The classical or traditional surgical strategy for incompetence of the Vena Saphena Magna (VSM), in other words, Great Saphenous Vein (GSV) is a high ligation and stripping (saphenectomy) at the saphenofemoral junction (SFJ) (2). In the last decade, several new minimally invasive treatment options like as foam sclerotherapy accompanied with ultrasound, endovenous laser ablation (EVLA) and radiofrequency ablation have been introduced as alternatives to classical surgical treatment for improving the efficacy and quality of life of patients, minimizing side effects, costs, and postoperative pain of treatment (2). Of these new therapies, EVLA therapy is one of the most widely accepted and used treatment options for incompetent VSM (2). However, traditional surgical treatment is the most frequent treatment modality in varicosity of VSM at present (3).

The CEAP classification for CVD was developed in 1994 by an international ad hoc committee of the American Venous Forum and clinical signs (C), etiology (E), anatomy (A), and pathophysiology (P) were defined in this classification (4). Rutherford et al. reported that the CEAP classification system is an excellent classification scheme for the evaluation of chronic venous insufficiency (5). Venous clinical severity scores (VCSS) is based on scoring of clinical complaints, symptoms and signs. VCSS is important for the evaluation of patients with CVD.

Some patients want to undergo EVLA treatment to avoid the disadvantages associated with the traditional surgery, like cosmetic reasons and possible complications. Also, some surgeons prefer the EVLA treatment for the same reasons. On the other hand, other surgeons prefer the traditional surgery because there is a risk for recanalization of VSM after the EVLA treatment.

In this retrospective study, we aimed to compare the short-term and mid-term clinical outcomes of endovenous laser ablation with those of traditional surgical treatment (high ligation and saphenectomy of Vena Saphena Magna) in patients with isolated unilateral symptomatic Vena Saphena Magna insufficiency.

MATERIALS and METHODS

The study includes sixty five patients who underwent traditional surgical treatment (Group 1; total 35 patients; 16 women, 19 men, mean age; 44.3 ± 12.6 years, range; 20 - 68 years) or EVLA treatment (Group 2; total 30 patients; 20 women, 10 men, mean age; 39.8 ± 11.7 years, range; 20 - 65 years) in our clinic for VSM insufficiency between May 2013 and December 2013. This study was approved by the local Institutional Review Board. Written informed consents were obtained from all subjects before the operations. All of the patients were symptomatic at the onset. Main complaints of the patients with VSM insufficiency were swelling of the legs, pain in the extremities, cramping and burning.

All patients underwent venous Doppler ultrasound examinations, and their source and level of the venous reflux were obtained in preoperative period. Patients demonstrating backflow lasting more than 1.5 seconds during Valsalva maneuvers and those with a VSM diameter more than 5 mm were included in the study and considered for operations.

Patients with deep venous insufficiency, history of deep vein thrombosis, acute deep vein thrombosis, high risk of pulmonary thromboembolism, acute superficial phlebitis, lymphedema, active malignancy, peripheral arterial occlusive disease (ankle / brachial indices < 0.8), diabetes mellitus, pregnancy, lactation and immobility were excluded from the study. Inclusion criteria and exclusion criteria are shown in Table 1. VSM reflux was confirmed with color flow Doppler ultrasound by the surgeon before the operation while the patients were on the table.

Table 1. Inclusion and exlusion criteria.

Inclusion criteria	Age; 20 to 68 years
	Insufficiency of VSM and SFJ with reflux (backflow lasting more than 1.5 seconds and those with a VSM diameter more than 5 mm)
	Symptoms of VSM insufficiency
	C2 in according to CEAP
Exclusion criteria	Pregnancy
	Active malignancy
	Arterial occlusive disease (ankle/brachial indices <0. 8)
	Acute deep vein thrombosis
	History of deep vein thrombosis
	High risk of pulmonary thromboembolism
	Deep venous insufficiency
	Diabetes mellitus
	Lactation
	Acute superficial phlebitis
	Lymphedema

VSM: Vena saphena magna, SFJ: Safeno femoral junction, CEAP: clinical (C), etiological (E), anatomical (A) and pathological (P) classification

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Groups were compared in terms of differences between clinical characteristics, age and gender, CEAP classification, VCSS and development of complications were recorded and compared at the preoperative, postoperative 1st week, 1st month, and 6th month.

Gender, clinical characteristics, CEAP classification and age were not statistically significant variables in the preoperative control. Clinically, all patients in both groups were classified in C_2 at the preoperative control. We mainly evaluated VCSS through pain scores of patients.

Surgical Technique

When the patients' files were investigated, we detected that the patients underwent EVLA at knee medial to SFJ with a wavelength of 1470 nm diode laser using laser catheter with fiber optic radial tip under spinal anesthesia in all EVLA patients. Tumescent anesthesia which containing 5 mg bupivacaine, 0.5 mg adrenaline, 6 ampules of 8.4% sodium bicarbonate, 500 ml and 4°C isotonic saline solution was applied before the EVLA application. Dependent on the diameter of the vein, we used laser energy with the mean value of total energy, power, and interval at 70 J/cm (range 60 to 75 J/cm), respectively. In traditional surgical operation, approximately 4 cm oblique and 3 cm transverse incisions were performed in inguinal region and knee region of the patient, respectively, and then VSM high ligation and partial stripping (saphenectomy) were performed as usual.

Also, we detected that both groups of patients were discharged after the intervention on the postoperative first day. Follow-up examinations were done at 1st week, 1st month and 6th months.

Data were analyzed using the Statistical Package for Social Sciences 15.0 for Windows (SPSS Inc., Chicago, IL) in our study. Parametric tests were applied to data of normal distribution, and non-parametric tests were applied to data of questionably normal distribution. Repeated-measure analysis of variance was used to compare variable parameters. The distribution of categorical variables in both groups was compared using Pearson's chi-square test. Spearman correlation coefficient followed by the Tukey post-hoc test was used to determine correlations between different variables. All differences associated with a chance probability value (p value) is less than 0.05 were considered statistically significant.

RESULTS

Preoperative pain scores of VCSS were not statistically significant, and these values were mean 2±0 in group 2 and mean 2±1 in the other group, respectively. Mean pain scores of group 1 patients were 2 ± 1, 1 ± 1 and 0 at postoperative 1st week, postoperative 1st and 6th months, respectively (Table 2). Pain scores of patients who underwent EVLA were statistically significantly lower than other group at postoperative 1st week and 1st month ($p < 0.01$). No patient stated to have pain within postoperative 6th months.

Table 2. Pain scores of the patients before and after the operation.

	VCSS	Pretreatment		1-week follow-up ($p < 0.01$)		1-month follow-up ($p < 0.01$)		6-months follow-up	
		n	(%)	n	(%)	n	(%)	n	(%)
EVLA TREATMENT (Group 2)	Absent (0)	0	(0%)	12	(40%)	30	(100%)	30	(100%)
	Mild (1)	6	(20%)	18	(60%)	0	(0%)	0	(0%)
	Moderate (2)	14	(47%)	0	(0%)	0	(0%)	0	(0%)
	Severe (3)	10	(33%)	0	(0%)	0	(0%)	0	(0%)
TRADITIONAL SURGICAL TREATMENT (Group 1)	Absent (0)	0	(0%)	0	(0%)	15	(42. 8%)	35	(100%)
	Mild (1)	8	(22. 8%)	23	(65. 7%)	20	(57. 2%)	0	(0%)
	Moderate (2)	15	(42. 8%)	12	(34. 3%)	0	(0%)	0	(0%)
	Severe (3)	12	(34. 3%)	0	(0%)	0	(0%)	0	(0%)

EVLA: Endovenous laser ablation; n: number of patients; p values < 0.05 were considered statistically significant.

In postoperative 1st week control; hematoma, in other words, ecchymosis, wound infection, induration and paresthesia were seen in nine, three, six and three patients in group 1, respectively. Ecchymosis, thrombophlebitis, induration and paresthesia were seen in three, three, five and two patient in group 2, respectively. On the other hand, thrombophlebitis wasn't seen in group 1 and wound infection wasn't seen in group 2. In addition to this, we detected that wound infection, ecchymosis and thrombophlebitis were found to be statistically significant between the two groups ($p < 0.05$). However, induration and paresthesia were not statistically significant difference between two groups; even they were found at higher frequency in group 1 in the 1st week control. Complications at 1st week control were shown in Table 3. Ecchymosis, wound infections, thrombophlebitis, induration and paresthesia were recovered with medical treatment in the 1st month

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control. During these controls, we detected 100% ablation of veins in EVLA patients. On the other hand, there was no statistically significant difference between the two groups by means of frequency of complication development at 1st month and 6th month controls. In the 6th month control; recanalization was detected in two (6.6%) patients in EVLA group but there was no recanalization in stripping group.

Table 3. Complications detected in the first week control.

	Ecchymosis ($p < 0.05$) n	Wound infection ($p < 0.05$) n	Thrombophlebitis ($p < 0.05$) n	Induration n	Paresthesia n
EVLA TREATMENT (Group 2)	3	0	3	5	2
TRADITIONAL SURGICAL TREATMENT (Group 1)	9	3	0	6	3

p values < 0.05 were considered statistically significant; n: number of patients, EVLA: Endovenous laser ablation.

Patients were analyzed in accordance with CEAP classification in the postoperative 1st week, 1st month and 6th month controls. In the postoperative 1st week control; 13 patients were at C_2 (varicose veins) and 22 patients were at C_1 (telangiectasia) in group 1 while 6 patients were at C_2 and 20 patients were at C_1, 4 patients were at C_0 in EVLA group though there was no patient at C_0 in group 1. In the postoperative 1st month control; 34 patients were at C_2 and 1 patient was at C_0 in group 1 and 22 patients were at C_1 and 8 patients at C_0 in EVLA group. In the postoperative 6th month control; 20 patients were at C_0 and 8 patients were at C_1 and 2 patients were at C_2 in EVLA group, on the other hand, 15 patients were at C_0 and 11 patients were at C_1 and 9 patients were at C_2 in group 1. Both groups were compared with each other statistically; there was no statistically significant difference between the two groups preoperatively. However, CEAP scores of the patients who underwent EVLA were significantly lower in the postoperative 1st week, 1st month and 6th month follow-ups ($p< 0.01$). Detailed clinical findings of the patients according to CEAP classification are shown in Table 4. There was no mortality in either group at the perioperative period and follow-ups.

Table 4. CEAP scores of the patients before and after the operation.

	CEAP	Pretreatment n (%)	1-week follow-up ($p < 0.01$) n (%)	1-month follow-up ($p < 0.01$) n (%)	6-months follow-up ($p < 0.01$) n (%)
EVLA TREATMENT (Group 2)	C_0	0 (0%)	4 (13. 3%)	8 (26. 6%)	20 (66. 6%)
	C_1	0 (0%)	20 (66. 6%)	22 (73. 4%)	8 (26. 6%)
	C_2	30 (100%)	6 (20. 1%)	0 (0%)	2 (6. 8%)
	C_3	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	C_4	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	C_5	0 (0%)	0 (0%)	0 (0%)	0 (0%)
TRADITIONAL SURGICAL TREATMENT (Group 1)	C_0	0 (0%)	0 (0 %)	1 (2. 8%)	15 (42. 8%)
	C_1	0 (0%)	22 (62. 8%)	0 (0%)	11 (31. 4%)
	C_2	35 (100%)	13 (37. 1%)	34 (97. 2%)	9 (25. 8%)
	C_3	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	C_4	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	C_5	0 (0%)	0 (0%)	0 (0%)	0 (0%)

n: number of patients, EVLA: Endovenous laser ablation, p values < 0.05 were accepted as statistically significant; n: number of patients; CEAP: clinical (C), etiological (E), anatomical (A) and pathological (P) classifications.

DISCUSSION

Nowadays, it is known that number of patients treated with methods alternative to stripping treatment is rapidly increasing. Radiofrequency ablation and endovenous laser ablation treatment have been introduced as important new endovenous ablative techniques for the minimally invasive treatment of superficial venous reflux and varicose veins (6). Minimally invasive techniques such as endovenous laser therapy, radiofrequency ablation, and ultrasound guided foam sclerotherapy are widely used in the treatment of varicosity of VSM (7). Furthermore, there are some studies in the literature that compare short and mid-term results and patient satisfaction in patients with VSM insufficiency treated with open surgery with saphenectomy or minimally invasive techniques; hence, such minimally invasive techniques appear to be at least

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as effective as open surgery (3, 7-11). Stirling and Shortel report that results of minimally invasive therapies are equal to or may even surpass conventional surgery and offer dramatically reduced recovery time and complication rates (6). On the other hand, we observed that EVLA is superior to surgery with respect to early term complication rates. Furthermore, both groups were compared statistically and the frequency of development of complication were found to be lower while clinical recovery of the patients was also found to be better in the EVLA group in the postoperative first week follow up. However, there was no statistically significant difference between the two groups in the 1st month and 6th month controls. Pain scores were estimated during the first week and first month controls and were statistically lower in the EVLA group ($p < 0.01$). We detected that recovery after treatment was significantly quicker in the EVLA group than the surgery group in the early postoperative period; yet both groups were similar in the latter follow ups. Moreover, EVLA procedure doesn't need surgical incision.

Doganci and Demirkilic (12) report that they found 100% ablation in the veins of both treatment groups during the six months controls with duplex ultrasound assessment. in their study performed with 980 nm laser, Bare-tip fibre 1470 nm laser, and radial fibre in the treartment of GSV varicosities. Etlik et al. (13) report 100% technical success and a 99% closure rate after six, and then twelve months. Also, it is known that one drawback of EVLA is recanalization. Proebstle et al. (14) report that early recanalization is observed in less than 10% of VSM after EVLA treatment. On the other hand, we detected 100% ablation of veins after the 1st month while we observed recanalization in two (6.6%) patients within 6th month after the EVLA treatment. There was no recanalization in the saphenectomy group. Due to some mild complaints, these patients were suggested to receive medical treatment and use elastic compression stockings.

Our study has three major limitations; limited sample size of the groups, lack of long-term follow-up data, and its retrospective nature. We think that prospective, randomized and multicenter studies with more participants and the long-term follow-up data may affect the results.

CONCLUSION

In VSM vein insufficiencies, EVLA is a treatment method that can be preferred by surgeons as well as patients since it offers a short recovery period with low pain scores, postoperative complication ratios, and no surgical scars. As a result, we conclude that EVLA treatment has better early and mid-term results in comparison to traditional surgical treatment and, thus, it is an efficient and safe alternative modality.

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Side-based Activation of Sympathetic Skin Responses Recorded from the Frontal Region in Idiopathic Parkinson's Disease

İdyopatik Parkinson Hastalığı'nda Frontal Bölgeden Kaydedilen Sempatik Deri Yanıtlarının Tutulum Tarafına Göre Etkilenimi

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Abstract

Objective: In a unilateral onset Idiopathic Parkinson disease, sympathetic skin responses elicited from previously and markedly affected and also from unaffected palm and forehead were recorded before and after the treatment. The difference (if any) in sympathetic skin responses recordings obtained from patients and control cases and the impact of Idiopathic Parkinson disease treatments on response sympathetic skin responses were investigated.

Materials and Methods: A total of 23 patients and 22 healthy volunteers were included in the study. The patients were examined for autonomic nervous system involvement and the patients with facial hyperhidrosis were determined. Sympathetic skin responses of the patients were recorded twice (before and after initiation of therapy) from both sides of the forehead and both hands and compared with healthy volunteers.

Results: A statistically significant difference was not detected between sympathetic skin responses amplitudes of left and right hands in Tests 1 and 2. Significantly lower sympathetic skin responses amplitudes were observed in Test 2. Correlations among amplitudes of hand sympathetic skin responses, Hoehn and Yahr Staging and Unified Parkinson's Disease Rating Scale scores demonstrated significant decreases in amplitudes of sympathetic skin responses in parallel with disease progression. Left side dominancy in patients with hyperhidrosis is statistically significant.

Conclusion: Detection of lower amplitudes in hand sympathetic skin responses after therapy may be due to habituation or used drugs. Significant decreases in amplitudes of sympathetic skin responses in parallel with disease progression were observed. No data concerning left side dominancy in the patient group with hyperhidrosis have been detected so far.

Keywords: Parkinson Disease; Sympathetic Skin Responses; Autonomic Dysfunction.

Öz

Amaç: Bu çalışmada, unilateral başlangıçlı İdyopatik Parkinson Hastalığı'nda, daha fazla tutulan tarafta sempatik deri yanıtlarında diğer tarafa göre fark olup olmadığı ve sempatik deri yanıtları üzerinde kullanılan tedavilerin etkisi araştırılmış ve sağlıklı gönüllüler ile karşılaştırılmıştır.

Gereç ve Yöntemler: Çalışmaya 23 hasta ve 22 sağlıklı gönüllü alınmıştır. Hastalar otonom sinir sistemi bulguları ve yüzde hiperhidrozis varlığı açısından sorgulanmıştır. Tedavi öncesi (test 1) ve tedavi sonrası (test 2) sempatik deri yanıtları iki yanlı frontal ve el bölgesinden kayıtlanarak kontrol grubuyla karşılaştırılmıştır.

Bulgular: El yanıtlarında Test 1, Test 2 ve kontrol grubunda sağ ve sol taraf arasında, aynı zamanda hasta-sağlam taraf arasında istatistiksel olarak anlamlı bir farklılık göstermemiştir. İlaç tedavisi sonrasında yanıt amplitüdlerinin istatistiksel olarak anlamlı olarak düştüğü kaydedilmiştir. El yanıt amplitüdleri ile Hoehn and Yahr Staging (H&Y) skorları ve Unified Parkinson's Disease Rating Scale (UPDRS) puanları arasında hastalık ilerledikçe negatif korelasyon gözlenmiştir. Sol taraf başlangıçlı olan hastalarda hiperhidroz varlığı sağ taraf başlangıç olanlara göre istatistiksel olarak anlamlı bulunmuştur.

Sonuç: Tedavi sonrasında tedavi öncesine göre el yanıtlarında amplitüdlerin düşmesi, habituasyona veya kullanılan ilaçlara bağlı olabileceği düşünülmüştür. Hastalık ilerledikçe amplitüdlerinin istatistiksel olarak anlamlı düştüğü gözlenmiştir. Hiperhidrozlu grupta sol taraf başlangıçlı hastalık olma olasılığının yüksek olması ile ilgili bu güne kadar literatürde herhangi bir bilgiye rastlanmamıştır. Bu konuda daha kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Parkinson Hastalığı; Sempatik Deri Yanıtları; Otonomik Disfonksiyon.

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INTRODUCTION

Idiopathic Parkinson disease (IPD) is a neurodegenerative disease related to age. It has an asymmetrical involvement pattern on the onset of the disease. Autonomic symptoms, which are considered to be non-motor symptoms, include constipation, frequent urination and urgency, impotence, sweating disorders, sialorrhea and orthostatic hypotension (1, 2). Motor symptoms demonstrate relatively asymmetrical involvement even in the advanced stages of the disease, however, asymmetrical involvement is not expected for such as symptoms as seborrhea, sialorrhea and thermoregulatory dysfunction. Numerous neurophysiological and neuropathological studies have analyzed autonomic nerve function in IPD (3-8). Recording sympathetic skin responses (SSRs) used in the evaluation of nervous system is an easily applicable method, which can be implemented by means of a standard electromyography device. During classical electrocardiographic examination, SSR are recorded from palms and soles where the skin resistance is at its lowest level. The most frequently used stimulation method is electrical stimulation of sympathetic and parasympathetic nerves of arms or legs (9). Previously, changes indicating asymmetry (if any) in SSR recorded from palms and in other autonomic tests in IPD have been investigated. Schestatsky *et al.* found SSR recorded from lower and upper extremities had significantly lower amplitudes in IPD patients when compared with the control group (7). Fusina *et al* made SSR recordings from both hands in cases with early stage IPD and detected decreased amplitudes consistent with the side with motor involvement (6). Giza *et al.* made recordings from both hands and could not detect any significant difference between IPD and the control group (10). SSR recordings obtained from the frontal region or forehand have not been analyzed before. In this study in a unilateral onset IPD, SSRs elicited from previously and markedly affected and also from unaffected palm and forehead were recorded before and after the treatment. The difference (if any) in SSR recordings obtained from patients and age-matched normal control cases and the impact of IPD treatments on SSRs were investigated. Besides, the presence of asymmetry, which is observed in motor symptoms, has been also investigated in SSR recordings obtained from hand and forehead.

MATERIALS and METHODS

The study has been conducted in accordance with the principles of the Helsinki Declaration and approved by the local Institutional Ethical Committee (2007/100–41). Informed consent was taken from each individual. Changes in SSRs which are recorded from bilateral forehead and hand in pre-treatment and after treatment and according to the affected side were investigated in this study.

A total of newly diagnosed treatment-naive IPD patients or patients on drug break (vacation) at least for two days [women (n=11) and men (n=12)] were included in the study. Diagnosis of IPD made according to the United Kingdom Parkinson' s Disease Society Brain Bank (UKPDSBB) citeria (11) differentiation of IPD patients from other Parkinson plus syndromes by National Institute of Neurological Diseases and Stroke (NINDS) guidelines (12).

In routine biochemical analyses and cranial images, we did not meet any pathology that might cause IPD-like symptoms. The patients were examined for autonomic nervous system involvement and the patients with facial hyperhidrosis were determined. SSRs of the all the patients enrolled in the study were recorded twice (at a median interval of 9.3 days (range, 24 hours to 21 days). First recording was made before the treatment (Test 1); the second recording was made after initiation of therapy (Test 2). In Test 2, the tests were performed at least one hour after the treatment of the patients was completed. SSRs of the patients were recorded from both sides of the forehead and both hands. These patients were started on L-Dopa, dopamine agonists and rasagiline therapy. For Test 2, we could contact with 20 [women (n=11) and men (n=9)] out of 23 patients.

Control group consisted of 22 healthy volunteers [women (n=7) and men (n=15)] selected among patients who applied to the outpatient clinic for any other reason or from patient's relatives. Bilateral frontal and hand SSRs of the control subjects were also recorded.

SSRs were recorded between 09.00 and 17.00 h. The subjects lay in a comfortable supine position in a quiet, well-lit air-conditioned room maintained at 24±1 degrees Celsius (°C). The skin temperature of each subject was > 32°C. The subjects were instructed to keep their eyes open, not to breathe deeply, cough, talk or move their head during the procedure. The experiment was performed with a Nicolet Viking IV channel electromyography. SSR recordings were made with standard surface electrodes made from Ag-AgCl (10 millimeter (mm) diameter, Nihon Kohden, NM-312S). Recording method was similar to the method mentioned by Yildiz *et al.* (13).

The frequency bandpass was 0.2– 100 Hertz (Hz). The time window for recording was 5 second (s) and the gain was 500 microvolt (μV) per division. The electrical stimulation (square pulse with 0.2 milisecond (ms) duration and 10-100 milliamps (mA) intensity) was applied over the right tibial nerve at the ankle. In subjects without any recordable response, we increased the intensity level by 10 mA (maximum 100 mA) until the responses occurred and reached a stable form. Subjects who showed no response on either side after receiving five consecutive electrical stimuli of an intensity of 100 mA were considered unresponsive. The recording location is shown in Figure 1.

In each subject, the right and left sides of the frontal region and hand were studied and bilateral F-SSRs were recorded. The stimuli were delivered at irregular intervals at least 20 s apart. Ten to twenty stimuli were delivered to each subject in every single examination

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(examinations 1, 2 and 3). SSRs were considered to be present when their amplitude was > 50 μV and its latency was similar for at least two of the subsequent stimuli. The peak-to-peak amplitude was measured for each response. Responses with maximum amplitude were calculated for each session in each subject. To avoid habituation, interval between impulses set on approximately 45-60 seconds. We observed that the responses appeared whenever the subjects laughed or were startled by a sudden noise. However, responses were distorted slightly because of movement artefact while laughing. Such responses were excluded from the analyses.

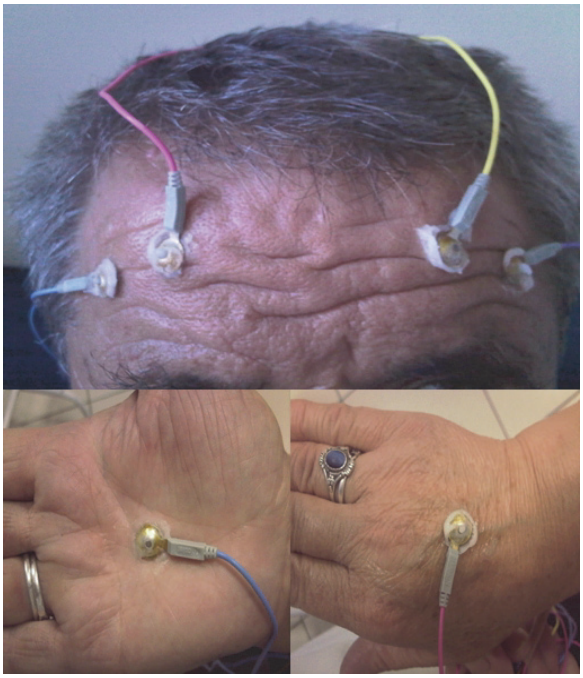

Figure 1. Sites of recording: A) Recording from the both sides of the forehead; B) Recording form hands (active electrode); C) Recording from hands (reference electrode)

In statistical analyses, maximum amplitudes of the right and left sides evoked by electrical stimulation in test 1 and test 2 evoked by electrical responses in patient groups, were compared using a two related sample test (Wilcoxon signed ranks test). Data from the control subjects and iPH patients were compared using the Mann–Whitney test. Latency responses were not use in statistical analyses. $P < 0.05$ was considered to be statistically significant.

RESULTS

Test 1 group consisted of a total of 23 patients with probable diagnosis of IPD. Their symptoms originated from the right and the left side whom symptoms begun from right in 12 and and from left in 11 of the patients. Test 2 could be applied on only 20 patients with symptoms originated from the right (n=11) and left (n=9) sides.
Median duration of the disease was 12 months (1-56 months), laterality of involvement was as follows; right in 12 and left in 11subjects. Median H&Y and UPDRS scores were 1,5 (0,5-2,5) and 30,74±11,28, respectively.

Control group consisted of 15 male and 7 female healthy individuals. Mean ages of the patients and the control subjects were 67.7±7.7 (Test 1, n=23) and 66.18±8.1 (n=22) years, respectively. A statistically significant difference was not found between ages of either group (p>0.05).

The characteristics of the patient group and diagnostic IPD criteria were based on UKPDSBB citeria. All 23 patients with IPD had bradykinesia while 15 of them had been asymmetrical onset. 20 of these patients had resting tremor and 16 had rigidity. Flexion posture was seen in 17 patients and 15 had postural instability. In terms of autonomic involvement; sweating, orthostasis, seborrhoea and urinary incontinence has been described by 7, 12, 5 and 12 subjects, respectively. One patient denied any autonomic symptoms, while constipation, sialorrhea have been described by 10 patients.

Bilateral hand SSRs were obtained from all patients in Test 2. Bilateral frontal SSRs could be recorded from 5 patients and from 2 out of 15 patients bilateral responses could not be elicited. In 13 patients, only right- sided responses could be obtained. In the control group, in 22 healthy volunteers, bilateral hand responses could be recorded. Bilateral frontal SSRs could be obtained from 6 persons, while in 6 healthy controls only unilateral SSRs could be elicited. Bilateral frontal SSRs could be recorded in 6 individuals, while in 6 individuals bilateral responses could not be acquired. In the remaining 10 individuals only right-sided SSRs could be elicited, while left –sided responses could not be obtained. Hand and frontal response patterns in Test 1, Test 2 and the control groups are shown in Table 1.

Table 1. Sympathetic skin response patterns elicited from hands and forehead in Test 1 and 2 and the control groups.

		Test 1 (n=23)	Test 2 (n=20)	Control (n=22)
Hand SSR	Bilateral responsive	23 (100%)	20 (100%)	22 (100%)
	Unilateral responsive*	0	0	0
	Bilateral non-responsive	0	0	0
Frontal SSR	Bilateral responsive	8 (35%)	5 (25%)	6 (27%)
	Unilateral responsive*	10 (44%)	13 (65%)	10 (46%)
	Bilateral non-responsive	5 (22%)	2 (10%)	6 (27%)

* In all cases with unilateral responses, any response could not be obtained from the left side.
SSR= Sympathetic skin response

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Two out of 4 patients with bilateral frontal SSRs were not examined in Test 2, while 2 patients with unilateral responses were observed in Test 2. Bilateral frontal responses could be recorded in one patient without frontal response in Test 1.

In Test 1, SSRs of both hands of all patients were recorded. Bilateral frontal SSRs could be elicited from 8 patients and from 5 out of remaining 15 patients bilateral frontal SSRs could not be obtained In 10 patients only right-sided SSRs could be elicited.

Descriptive data of hand SSRs elicited from Test 1, Test 2 and the control groups and comparisons between right and left sides and also affected and unaffected sides are shown in Table 2.

No statistically significant difference was detected between SSRs amplitudes of left and right hands in Test 1. (n=23, p>0.05). In the comparison between previously and more severely affected hand and the other (unaffected) hand (comparison between affected and unaffected side) a statistically significant difference could not be obtained. (n= 23, p> 0.05).

No statistically significant difference was detected between the right and left hand SSRs in Test 2 (n=20, p>0.05). No statistically significantly difference was detected between affected and unaffected hand SSRs (n= 20, p> 0.05). In the control group, no statistically significant difference was found between right and left SSRs amplitudes (n=22, p>0.05).

Amplitudes of hand SSRs in Test 1 and Test 2 were compared and statistically significantly lower SSRs amplitudes were observed in Test 2 (n=40, p=0.003; See Table 2).

Table 2. Comparison between involved and compact side sympathetic skin responses of hand recorded in Test 1, Test 2 and control groups.

Hand	Patient group				Control group	
Amplitüd (μV)	**Right**	**Left**	**involved side**	**compact side**	**Right**	**Left**
Test 1	n=23	n=23	n=23	n=23	n=22	n=22
Median	607	596	607	596	523	435
min-max	163-2012	136-1854	163-1854	122-2012	169-2536	140-2301
	p=0.083		p=0.394		p= 0.559	
Test 2	n=20	n=20	n=20	n=20		
Median	378	464.5	360	487.5		
min-max	147-1409	99-1384	147-1384	99-1409		
	p=0.161		p=0.641			
	Test 1- Test 2 n=40					
	* p=0.003					

SSR= Sympathetic skin response
*Amplitudes of hand SSRs obtained in Test 2 were significantly lower relative to Test 1.

No statistically significant difference was detected when amplitudes of hand SSRs in Test 1 and the control group were compared (n=90, p>0.05). Significant differences were not detected between hand SRRs of the right hands of the control group (n=22) and affected right hands of the patients (n=12) and also between the left hand SSRs of the control group (n=22) and affected left hands of the patient group (n=11) (n=34 and n=33, for both p>0.05; See Table 4).

Descriptive data of frontal SSRs obtained in Test 1, Test 2 and control groups and also comparisons between right and left and also affected and unaffected sides are shown in Table 3.

When data of only patients with bilateral responses in Test 1 were compared, we did not observe any statistically significant difference between amplitudes of the right and the left frontal SRRs (n= 8, p=0.017, amplitudes of the left frontal SRRs were lower when compared with those of the left SRRs). No statistically significant difference was detected between previously and much more affected side and the other side (affected and unaffected sides) (patients with bilateral responses, n=8, p>0.05).

In Test 2, right and left frontal SRR amplitudes were compared and amplitudes of the left side were found to be significantly lower than those of the right side (patients with bilateral responses (n= 5) (p=0.043); amplitudes of the left frontal SRRs were lower than those of the right side). No statistically significant difference was detected between amplitudes of the affected and the unaffected side SRRs (patients with bilateral responses n=5, p>0.05).

In the control group, amplitudes of the left frontal RSSs were significantly lower than those of the right side (patients with bilateral responses, n= 6, p=0.028, amplitudes of the left frontal SRRs were lower than those of the right side).

Since a statistically significant difference was detected between left and right frontal SRRs recorded in Test 1,

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Test 2 and the control groups (left side SSRs amplitudes were relatively lower or absent), data related to the right and the left sides were compared individually (see Table 3).

We failed to record right frontal SSRs in one patient and left frontal SRRs in two patients in Test 1. However, in Test 2, these responses could not be obtained. Contrarily, patients with undetectable right (n=4) and left (n=4) frontal SSRs demonstrated recordable responses in Test 2.

In the comparisons between frontal SSRs elicited in Tests 1 and 2, the patients who responded on the side to be examined were included in the analysis. In both tests on a total of 18 patients, right and left frontal SSRs could be recorded. No statistically significant difference was recorded between Test 1 and Test 2 as for frontal SSRs (n=18, p>0.05). When we investigated whether only right frontal or solely left frontal SSRs changed significantly between Test 1 and 2 and we still did not observe any statistically significant difference for either side (right frontal SSRs, n=14, left frontal SSRs, n=5, for both p>0.05; See Table 3).

In the comparison between amplitudes of frontal SSRs in Test 1 and the control group, right and/or left frontal SSRs could be obtained in a total of 26 patients. When these data were compared with 22 right and/or left frontal SSRs elicited in the control group, no statistically significant intergroup difference was detected (n= 48, p>0.05). When amplitudes of the right frontal SSRs recorded in Test 1 (n=18) were compared with the amplitudes of the left frontal SSRs of the control group (n=16 a statistically no significant difference could be detected (n=34 and n=14, respectively; for both p>0.05; See Table 3).

Right frontal SSRs amplitudes in patients whose right side was more severely affected (in only 9 out of a total of 12 patients right frontal SSRs could be recorded) recorded in Test 1 and those of the control group (right frontal SSRs could be obtained in 16 out of 22 control subjects) were compared and any statistically significant intergroup difference was not detected (n=25, p>0.05; See Table 3).

Table 3. Comparison between involved and compact side of frontal sympathetic skin responses recorded in Test 1, Test 2 and control groups.

Frontal	**Patient group**				**Control group**	
Amplitude (μV)	Right	Left	involved side	compact side	Right	Left
Test 1	n=18	n=8	n=14	n=12	n=16	n=6
Median min-max	166,5 56-1393	98 67-267	148,5 56-517	137 57-1393	219.5 50-1835	124 78-629
	n=23, p=0.000 *n=18, p=0.000 **n= 8, p=0.017		n=23, p=0.862 *n=18, p=0.862 **n= 8, p=0.889		n=22, p=0.000 *n=16, p=0.000 **n= 6, p=0.028	
Test 2	n=18	n=5	n=13	n=10		
Median min-max	193 53-818	73 58-111	111 53-818	180.5 58-768		
	n=20, p=0.000 *n=18, p=0.000 **n= 5, p=0.043		n=20, p=0.913 *n=18, p=0.913 **n= 5, p=0.225			
	Test 1- Test 2					
Responsives in both tests	p=0.420 (n=18)					
Right frontal SSR	p=0.826 (n=14)					
Left frontal SSR	p=0.080 (n=5)					

SSR= Sympathetic skin response
* Bilaterally unresponsive patients were not included in the analysis
** Only bilaterally responsive patients were included in the study

In patients with more severely affected left side (in only 5 out of a total of 11 patients frontal SSRs could be recorded) in Test 1, amplitudes of the left frontal SSRs and the data of the control group in Test 1 were compared without a statistically significant difference between groups (left frontal SSRs could be elicited in 6 out of 22 control subjects) (n=11, p>0.05; See Table 4).

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Table 4. Comparison of hand and frontal SSRs in Test 1 and the control groups.

		Test 1 (n=23) Control (n=22)
Hand SSR	All data	p=0.725 (n=46, n=44)
	Right hand SSR and control right hand SSR in right side diseases	p=0.466 (n=12, n=22)
	Left hand SSR and control left hand SSR in left side diseases	p=0.317 (n=11, n=22)
Frontal SSR	All data	p=0.878 (n=46, n=44) *p=0.321 (n=26, n=22)
	Right frontal SSR	p=0.784 (n=23, n=22) *p=0.384 (n=18, n=16)
	Left frontal SSR	p=0.825 (n=23, n=22) *p=0.181 (n=8, n=6)
	Right frontal SSR and control right frontal SSR in right side diseases	p=0.631 (n=12, n=22) *p=0.357 (n=9, n=16)
	Left frontal SSR and control left frontal SSR in left side diseases	p=0.510 (n=11, n=22) *p=0.537 (n=5, n=6)

*Unattainable SSRs were not included;
SSR= Sympathetic skin response

DISCUSSIONS

In some studies where sudomotor activities have been evaluated in IPD, abnormalities including prolonged latency (14), decreased amplitudes (3,15) or loss of responses have been reported, Conversely, some studies reported that SSRs had not changed in IPD (10). Still, some studies have reported abnormalities in SSRs in the involved side when compared with the intact side (18) or lack of any difference between the intact and the affected side. Surprisingly, in studies performed on groups with IPD, multiple system atrophy and the control groups and many studies cited in the literature presence of SSRs abnormalities have been reported in IPD. However, presence of normal SSRs has been also indicated in IPD and its inmeasurable value in the differential diagnosis between multiple system atrophy and IPD coursing with marked autonomic symptoms have been also emphasized (19,20). In other words, in the discrimination of clinical conditions progressing with parkinsonism from IPD, presence of symptoms of autonomic involvement and abnormal SSRs detected during electrophysiologic examinations have been considered in the exclusion criteria for IPD. In this study, amplitudes of hand SSRs did not differ between the right, and the left hand and also between the affected and the unaffected sides in Test 1, Test 2 and the control groups Insignificant differences between SSRs recorded from symmetric organs or regions (hands and feet etc) are also an expected condition which has been already supported by many studies cited in the literature (13). In a neuropathological study performed by Break *et al.* in patients with IPD inclusion bodies in the form of α-sinuclein aggregates had been demonstrated in pre- and postganglionic neurons of parasympathetic and sympathetic nervous systems (21). In none of the neuropathological studies, asymmetric involvement - excluding extrapyramidal system- has not been detected in IPD. Conversely, pathological findings are detected in a symmetrical pattern. As a prerequisite for the diagnosis of IPD, asymmetric onset of motor findings and maintenance of this asymmetry even during disease progression should be detected. From the perspective of findings suggestive of autonomic involvement this asymmetry is not an expected or previously reported condition (22). In patients with asymmetric IPD, entirely symmetrical distribution of sweating was reported. In this dissertation study, no significant difference could be found between amplitudes of SSRs recorded from the affected and unaffected sides.

Amplitudes of SSRs of Test 1 and Test 2 were compared and significantly, lower SSRs amplitudes were observed after drug therapy. This condition may be explained in two mechanisms. Habituation of SSRs is a known condition. Since surprising effects of stimulation in Test 2 will decrease relative to Test 1, lower amplitudes of the responses might be recorded in Test 2. Frontal SSRs are also exposed to habituation as have been demonstrated previously in our laboratory studies (13). In this case, decrease in amplitudes of frontal SSRs in Test 2 is anticipated. However, such a decrease in frontal SSRs was not detected. A decrease in hand SSRs secondary to the use of antiparkinson drugs constitutes the second explanation. However, lack of any effect of antiparkinson and anticholinergic drugs on SSRs and perspiration has been already indicated (3,18,23,24).

Yet, critical importance of dopamine on autonomic regulation of brainstem and diffuse population of immunoreactive fibres in these centers are also known (25). Hand and face may demonstrate different sweating patterns or they may be controlled by different centers. Indeed, sweating is realized in two different patterns as thermoregulatory and mental sweating; a third explanation is not valid for our investigation.

Progression of the disease and decrease in the amplitudes of SSRs has been thought to be unlikely because of very short interval between Test1 and Test 2 (min. 24 hrs, max 21 days). Reports released up to now have yielded controversial results on variations in SSRs in patients with IPD. In some of these reports, SSRs were analyzed while drug therapies were maintained and in some others SSRs were recorded during drug-free period. Our outcomes have suggested that some of the

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controversial reports may stem from these diverse applications. In the comparison of amplitudes of hand SSRs in Test 1 and the control groups, no statistically significant intergroup difference was detected. A considerably important proportion of patients included in this study consisted of cases with very mild IPD (H&Y < 1, n=8, 8/23, 35%). Correlations among amplitudes of hand SSRs, H&Y and UPDRS scores demonstrated significant decreases in amplitudes of SSRs in parallel with disease progression. Therefore, the group of cases with a mild IPD was excluded from the statistical evaluation and when statistical evaluation was repeated SSRs with still lower amplitudes were detected albeit lack of statistical significance (p=0.084). Decrease in the number of patients and as stated above, application of Test 1 during treatment-naive period might explain this marginally insignificant result. In the comparison of hand SSRs between Test 2 and the control group, mild and severe cases were evaluated in combination and still a significant result could not be elicited. When these 8 cases with mild IPD were excluded from analyses and the remaining cases were re-evaluated, SSRs with significantly lower amplitudes were observed in the patient group relative to the control group ($p<0.05$). This outcome revealed the presence of a significant correlation between increasing severity of the disease and decreases in the amplitudes of SSRs. Besides this outcome is in compliance with the correlation between increasing severity of the disease and decrease in SSRs amplitudes and also with electrophysiological SSRs abnormalities and abnormal findings in cases with IPD under treatment cited in the literature.

We have limited information about frontal SSRs. Very few studies have systematically studied facial SSRs. Besides, almost all of them were performed in our laboratory on young patients (13). When facial SSRs were recorded symmetrically just like hand SSRs, similar responses could be elicited. However, different from hand SSRs this symmetry is not so obvious as hand SSRs. Facial responses are exposed to habituation. However, if this habituation is technically blocked, under constant stimulation, gradually increasing amplitudes called progressive increase in amplitudes is encountered. Detection of lower amplitudes only in hand SSRs in Test 2 contrary to frontal SSRs suggested the responsibility of an independent causative factor for habituation. Besides, it was thought that some peripheral or central characteristics are different between hand and facial SSRs. Amplitudes of frontal SSRs increase in line with the duration of the disease. One of the reasons underlying facial hyperhidrosis described in IPD might be this condition.

Independent from the affected and unaffected sides, loss of frontal SSRs has been detected in both patients and the control groups. Loss of left frontal SSRs is statistically significant. Even when the residual responses were analyzed, significantly lower amplitudes were observed on the left frontal SSRs. This finding, which is thought to be independent from IPD, detected in advanced age remains to be unexplained. Further studies may try to explain how and why the left frontal SSRs are lost. Sweating occurs in mental and thermal patterns. Mental sweating occurs in hands and feet, and thermal sweating is seen all over the body. Hand SSRs measure more frequently mental sudomotor activity, while frontal SSRs will measure mental sudomotor activity. Excessive sweating in IPD usually occurs on face, head and trunk. In a study by Schestatsky *et al.* on IPD patients with hyperhidrosis, SSRs recorded from hands were of lower amplitudes and they could be elicited less frequently when compared with cases without IPD (7). These findings were interpreted as a decrease in perspiration of hands leading to development of hyperhidrosis on face, head and trunk with a compensatory mechanism. In our study, hyperhidrosis was detected at an anticipated incidence. We did not observe any statistically significant difference between hand and frontal SSRs. The reason for this finding, which was incompliant with the literature data, might be related to our patient group, which consisted of the patients with early and late onset IPD, higher percentage of early onset IPD patients and scarce number of patients in two separate subgroups, each of which was insufficient to attain any level of statistical significance. For example, the group without hyperhidrosis apparently contained higher number of patients who demonstrated bilateral SSRs or conversely, the group with hyperhidrosis consisted of unresponsive patients or those displaying only unilateral SSRs. Indeed, these groups did not reach any level of statistical significance. Further investigation on this issue in a larger-scale study with more numerous patient populations will help resolve this problem.

Evaluating the patients complaining from hyperhidrosis, we observed motor symptoms with left side dominancy. Left side dominancy in the group of patients with hyperhidrosis is statistically significant. However, we have not come across any relevant data in the literature on this issue. With further studies, association between left-side dominant motor findings and hyperhidrosis can be easily enlightened. However, highly comprehensive studies in the field of neuropathology should be conducted in order to elucidate pathophysiology underlying different behavioural patterns between hand and facial SSRs can be also explained by heterogenous distribution of sympathetic denervation among various organs in IPD (26) and different degrees of involvement of sympathetic fibres (27). When all the reports presented so far are reviewed, controversial outcomes have been reported as for changes in SSRs in IPD. These incompliant results may result from diverse study designs, maintenance of treatments for antiparkinsonism, disregarding disease duration and severity and inability to construct subgroups based on the presence of symptoms related to autonomic involvement.

This study was presented in 10. National Congress of Parkinson's and Movement Disorders (Ela Quality Resort, Antalya) in 1-5 May 2013 as Poster 29 with the name of 'Sympathetic Skin Responses Obtained from the Affected Hand in İdiopathic Parkinson's Disease'.

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Evaluation of İntra-Articular Hip Pathology: Comparison of CT Arthrography And MR Arthrography

Kalça İntraartiküler Patolojilerinin Değerlendirilmesinde BT Artrografisi ve MR Artrografisinin Karşılaştırılması

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Abstract

Aim: To compare computed tomography arthrography (CTA) and magnetic resonance arthrography (MRA) in the evaluation of intra-artcular hip lesions.

Material and Methods: 42 CTA and MRA procedures were performed for 41 patients who have arthrography indications after standard hip MR examinations. All imaging findings were evaluated by a single musculoskeletal radiologist. Data regarding the presence of labral tear, paralabral cyst, cartilage damage, the femoral head-neck morphology and the acetabular retroversion were noted for each examination. Eight patients were operated. The McNemar chi-square test was used to compare radiological examinations.

Results: Labral tears and cartilage damages were the most common findings. Labral tears were visualized at 23 of 42 (%55) hips on MRA and most common site of location was anterosuperior quadrant (21/23, %91.3), on the other hand they were visualized at 17 of 42 (%40) hips on CTA with the most common site as anterosuperior quadrant (15/17, %88.2). Cartilage lesions were visualized 10 of 42 (%24.80) hips on MRA while 11 (%26.19) cartilage lesions were shown on CTA. %9.5 (4/42) patients have acetabular cartilage lesions and %14.3 (6/42) patients have both acetabular and femoral cartilage lesions on MRA. Meanwhile %11.9 (5/42) patients have acetabular cartilage lesions, %2.4 (1/42) patients has femoral cartilage lesions alone, and also %11.9 (5/42) patients have both acetabular and femoral cartilage lesions on CTA. Statistical analysis shows that CTA and MRA are compatible with each other for the evaluation of intraarticular hip lesions ($p>0.05$).

Conclusion: CTA can be used as an alternative imaging method to MRA for the detection of intra-articular pathologies in appropriate patients especially who have imaging challenges due to surgical hardwares and contraindications of the MRI procedure.

Keywords: Hip; CT arthrography; MR arthrography.

Öz

Amaç: Kalçada eklem içi ve eklem ile ilişkili patolojik durumlarda bilgisayarlı tomografi artrografisini (BTA) manyetik rezonans artrografisi (MRA) ile karşılaştırmak.

Gereç ve Yöntem: Standart MRG incelemesinin sonrasında artrografi endikasyonu bulunan 41 olguda BTA ve MRA incelemeleri (42 işlem) yapıldı. Görüntüler tek bir radyolog tarafından değerlendirilerek labral yırtık, paralabral kist, kıkırdak hasarı, femur baş-boyun bileşkesinde kemik çıkıntı ve asetabuler retroversiyon varlığı her bir inceleme için not edildi. Bu olgulardan 8 tanesi opere oldu. Radyolojik tetkiklerin karşılaştırmaları için Mc Nemar ki-kare testi uygulandı.

Bulgular: En sık saptanan bulgular labral yırtık ve kıkırdak hasarı idi. Labral yırtık bulgusu MRA tetkikinde 42 kalçanın 23'ünde (%55) ve en sık anterosüperior kadranda (21/23, %91.3), BTA tetkikinde ise 17'sinde (%40) ve en sık anterosüperior kadranda (15/17, %88.2) tespit edildi. Kıkırdak lezyonları MRA tetkikinde 42 kalçanın 10'unda (%24.80), BTA tetkikinde ise 11'inde (%26.19) tespit edilmiştir. Bu lezyonlar MRA'da %9.5 (4/42) olguda asetabular, %14.3 (6/42) olguda asetabular ve femoral tarafta birlikte, BTA'da ise %11.9 (5/42) olguda asetabular %11.9 (5/42) olguda asetabular ve femoral tarafta birlikte, %2.4 (1/42) olguda ise femoral tarafta tespit edildi. İstatiksel değerlendirmeye göre kalçada eklem içi ve eklem ile ilişkili lezyonların tanısında BTA ve MRA'nın birbirleri ile uyumlu olduğu ($p>0.05$) sonucuna ulaşıldı.

Sonuç: Öncelikle MR kontrendikasyonu bulunan veya cerrahi donanıma bağlı görüntüleme zorlukları yaşanacak olgularda olmak üzere, uygun hastalarda eklem ve eklemle bağlantılı lezyonların değerlendirilmesinde BTA, MRA'ya alternatif bir görüntüleme yöntemi olarak kullanılabilir.

Anahtar Kelimeler: Kalça; BT artrografisi; MR artrografisi.

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GİRİŞ

Kas-iskelet sisteminin sıklıkla karşılaşılan sorunlarından biri olan kalça ağrısının radyolojik değerlendirmesinde manyetik rezonans görüntülemesi (MRG) kemik ve yumuşak dokuları birlikte görüntülemesi ve çok düzlemli görüntüleme özelliği sayesinde bu eklemin bir dizi patolojisinde kullanılmaktadır. Ancak eklemi oluşturan (kapsül, kıkırdak vb.) veya eklem içi (bağ, fibrokartilajinöz yapı vb.) yapıların değerlendirilmesinde MRG her zaman yeterli olmamaktadır (1, 2).

Eklem ve eklem ile ilişkili patolojilerin değerlendirilmesinde manyetik rezonans artrografisi (MRA) en yaygın tercih edilen görüntüleme yöntemidir (2). Bilgisayarlı tomografi artrografisi (BTA) ise genellikle MR kontrendikasyonu gibi bazı özel durumlarda MRA'nın yedek sistemi olarak kulllanılmaktadır. Ancak son yıllarda bu konuda yapılan bazı araştırmalarla özellikle tetkik süresinin kısalığı, yüksek uzaysal rezolüsyonu ve submilimetrik skalada farklı düzlemlerde görüntü elde edilebilmesi gibi avantajları sayesinde BTA ön plana çıkmaya başlamıştır (3–9).

Bu çalışmada kalçada eklem içi ve eklem ile ilişkili patolojik durumlarda BTA'yı MRA ile karşılaştırarak bu tetkikin tanısal üstünlüklerini tespit etmeyi amaçladık.

GEREÇ ve YÖNTEM

Hasta popülasyonu ve seçimi

Yaklaşık iki yıl süresi içinde (Haziran 2012-Temmuz 2014) toplamda 41 olguda 42 tetkik olmak üzere standart MRG incelemesini takiben BTA ve MRA incelemeleri yapıldı.

Etik kurul onayı alınan bu çalışmada artrografi için klinik endikasyonu (labrum patolojisi, kıkırdak lezyonları, eklem içi serbest cisim varlığı vb.) bulunan ve bu işlemler için onamı alınan hastalar çalışmaya dahil edildi. Gebelik veya gebelik şüphesi bulunan ve emziren kadınlar, ilgili eklemde şiddetli dejeneratif eklem hastalığı, geçirilmiş cerrahi öyküsü veya aktif enfeksiyon ile artrografi için giriş yüzeyinde selüliti bulunan ve kontrast madde alerjisi öyküsü olan hastalar çalışmaya dahil edilmedi.

Hasta hazırlığı, artrografi işlemi ve görüntüleme protokolü

Eklem içi enjeksiyonlar olguların 29'unda floroskopi (Philips Allura XPER FD 20, Hollanda), 13'ünde ultrason (LOGIQ S8, General Electric, ABD) eşliğinde yapıldı. Ultrason rehberliği sırasında 9 MHz lineer ve cilt altı doku kalınlığı fazla olanlarda 5 MHz konveks prob kullanıldı.

Artrografi işlemine başlarken ilk olarak eklem içine verilecek kontrast madde karışımı hazırlandı. Eklem enjeksiyonu için 100 mL serum fizyolojik (SF; %0.9 NaCl) içerisine 1 mL gadopentetate dimeglumine (Magnevist, Schering, Berlin, Almanya) ilave edilerek dilüe paramanyetik kontrast madde solüsyonu hazırlandı. Hazırlanan dilüe kontrast maddeden 7 mL, noniyonik iyotlu kontrast maddeden, (Omnipaque (iohexol), Winthrop-Sterling, New York, ABD) 7.5 mL ve eklem içi analjezik ajandan (Marcaine (%0.5 bupivakain), Astra Zeneca, Luton, İngiltere) 3 mL aynı enjektöre çekilerek toplamda 17-18 mL'lik kontrast madde karışımı hazırlandı.

Eklem içi enjeksiyonu için hastalar sırt üstü (supin) pozisyonda iken floroskopi eşliğindeki işlemlerde femurun baş ile boyun bileşkesinin süperolaterali işaretlenerek, ultrason eşliğindeki işlemlerde ise femurun baş ile boyun bileşkesi hedef alınarak anterior yaklaşımla eklem aralığına ulaşıldı.

Eklem içi enjeksiyonlar rutin işlem alanı cilt temizliği ve lokal anestezi uygulamasını takiben 22 gauge (G) spinal iğne ile yapıldı. Hazırlanan karışımdan test dozlarında verilerek iğnenin eklem içerisinde olduğu doğrulandıktan sonra hastaların ağrı eşiği ve vücut yapılarına göre kalça eklemi için ortalama 12-18 mL SF çözeltisi eklem aralığına verildi.

Tetkikin ikinci aşamasında enjeksiyonu tamamlanan hastalar öncelikle BT (ortalama 17.7 dk içerisinde), daha sonra ise MR (ortalama 38.7 dk içerisinde) cihazlarına alındı. Artrografi incelemeleri 1,5 Tesla MR (Avanto, Siemens, Erlangen, Almanya ve Achieva, Philips, Best, Hollanda) ve 64 kesitli BT (Aquillion 64, Toshiba, Tokyo, Japonya) cihazları ile yapıldı.

BTA görüntüleri 64x0,5mm kolimasyonda gerçekleştirildi (çekimin teknik parametreleri kalça eklemi için: 120 kVp; 66 mAs; yüksek çözünürlüklü filtre; pitch,0.8; kesit kalınlığı, 0.5-1mm; görüntü alanı, 24 cm; matriks, 512x512). Volümetrik inceleme yapılarak çekim sonrasında 0.5 mm ve 1mm kesit kalınlığıyla aksiyel, koronal ve sagital düzlemlerde reformasyonlar yapıldı.

Kalça MRA tetkikinde koronal, sagital ve aksiyel oblik düzlemlerde yağ baskılı T1 ağırlıklı (TR/TE, 524/13 msn; matriks, 207x320 ;NEX, 1 ; FOV, 20 cm; kesit kalınlığı, 3 mm, kesit aralığı, 0.6 mm); koronal yağ baskılı T2 ağırlıklı (TR/TE, 2900/46 msn; matriks, 207x320 ;NEX, 2 ; FOV, 20 cm; kesit kalınlığı, 3 mm, kesit aralığı, 0.6 mm) ve koronal 3D gradient eko T1 ağırlıklı (TR/TE, 31/4.76 msn; FA, 20; matriks, 205x256 ;NEX, 1 ; FOV, 20 cm; kesit kalınlığı, 1.2 mm) görüntüler elde edildi.

Görüntülerin değerlendirilmesi

BTA ve MRA görüntüleri kas-iskelet radyolojisinde 3 yıllık deneyimi bulunan bir radyolog tarafından değerlendirildi.

Kalça olgularında labral yırtık, paralabral kist, asetabular retroversiyon, femur baş-boyun bileşkesinde kemik çıkıntı ve kıkırdak hasarı varlığı değerlendirildi. BTA ve MRA'da labral yırtık labrum içine kontrast madde geçişi, kıkırdak kaybı ise kıkırdak hasarına bağlı kontrastın kıkırdak içine geçişi ile eklem yüzeyinde düzensizlik olarak tanımlandı.

Labral yırtıkların ve kıkırdak lezyonlarının yerleşimi asetabular labrum saat kadranına göre altı bölgeye ayrılarak lokalize edildi. Bu bölgeler 3 ile 9 arası bir hat olarak belirlendi ve bu hattın üzeri süperior, aşağısı ise inferior olarak değerlendirildi. Buna göre 1 ile 3 arası anterosüperior, 11 ile 1 arası süperior, 9 ile 11 arası

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posterosüperior olarak değerlendirildi. Kıkırdak lezyonlarının değerlendirilmesinde bu üç bölgenin hepsinin etkilendiği durumlarda diffüz tanımlaması yapıldı. Bunun dışında kıkırdak lezyonları için asetabular ve femoral tarafın hangisini/lerini ilgilendirdiği de not edildi.

İstatiksel analiz

İstatistiksel analizler SPSS 15.0 versiyonunda değerlendi. Lezyonların tespitinde BTA ve MRA karşılaştırmaları için Mc Nemar kikare testi uygulandı.

BULGULAR

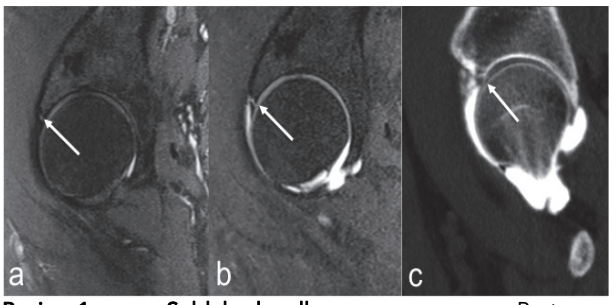
Çalışma grubunda yer alan 42 işlemin 22'si (%48.78) kadın, 20'si (%51.22) erkek cinsiyete ait olup yaşları 19-66 (ortalama 39.12) arasında değişmekte idi. Olguların 8 tanesi opere oldu (5'i açık cerrahi, 3'ü artroskopik cerrahi olmak üzere).

Görüntülerin değerlendirilmesinde labral yırtık, paralabral kist, asetabular retroversiyon, femur baş-boyun bileşkesinde kemik çıkıntı ve kıkırdak hasarı olmak üzere 5 farklı lezyonu her kalça için MRA ve BTA'da ayrı ayrı tespit edip karşılaştırdık. Her üç yöntemde de en sık tespit edilen bulgular sırasıyla labral yırtık, kıkırdak hasarı ve femur baş-boyun bileşkesinde kemik çıkıntı idi. Tüm olgulardaki farklı lezyonların MRA ve BTA'daki sayısal dağılımları **Tablo 1'de** gösterilmektedir.

Tablo 1. Tetkiklerde saptanan patolojilere göre MRA ve BTA'da lezyonların dağılım ve sayıları

	MRA	BTA
Labral yırtık	23	17
Paralabral kist	7	5
Femur baş-boyun bileşkesinde kemik çıkıntı	7	7
Asetabular retroversiyon	4	4
Kıkırdak kaybı	10	11

Labral yırtık bulgusu MRA tetkikinde 42 kalçanın 23'ünde (%55), BTA tetkikinde ise 17'sinde (%40) tespit edildi. Bu yırtıklar MRA'da %50 (21/42) olguda anterosüperiorda, %2.4 (1/42) olguda süperiorda, %1 (1/42) olguda ise hem anterosüperior, hem de posterosüperiorda; BTA'da %35.7 (15/42) olguda anterosüperiorda, %2.4 (1/42) olguda süperiorda, %1 (1/42) olguda ise hem anterosüperior, hem de posterosüperiorda tespit edildi. Opere olan 8 olgudan 7'inde labral yırtık saptandı. Bu sonuçlara göre istatiksel olarak labral yırtık tanısında ve yerleşimlerinin belirlenmesinde MRA ve BTA sonuçlarının birbirleri ve cerrahi sonuçları ile uyumlu olduğu sonucuna ulaşıldı (p>0.05). Radyolojik ve cerrahi sonuçlarının uyumsuz olduğu iki olgudan birinde MRA ve BTA'da anterosüperiorda labral yırtık tanımlamasına rağmen operasyonda bu lezyonun labral yırtık yerine sublabral sulkus varyasyonu olduğu anlaşıldı (Resim 1).



Resim 1. a–c. Sublabral sulkus varyasyonu: a. Proton dansite (PD) yağ baskılı sagital MR, b. T1 yağ baskılı sagital MRA, c. sagital BTA görüntülerinde anterosüperior labrumda izlenen lineer sinyal artışı ve kontrast sızıntısı *(oklar)* yırtık olarak değerlendirildi. Ancak operasyonda labral yırtık saptanmadı.

Diğer bir olguda ise yırtık yerleşimi MRA ve BTA'da anterosüperior ve posterosüperior olarak belirlenmişken cerrahi bulgulara göre yırtık anteriorda yerleşimli olarak tanımlanmıştır. Olguların radyolojik tetkiklere göre labral yırtık yerleşimleri ile MRA, BTA ve varsa operasyon sonuçları Tablo 2'de verilmiştir. Toplam 7 olguda labral yırtığa paralabral kist eşlik etmekte olup MRA bunların hepsini gösterirken BTA'da olguların ancak 5 tanesinde paralabral kistlerin varlığı belirlenebildi (Resim 2).

Tablo 2. Labral yırtık varlık ve yerleşimleri ile MRA, BTA ve mevcutsa operasyon sonuçları

Olgu no	Yaş Cinsiyet	MRA	BTA	Operasyon
1	7 E	Var (AS)	Yok	-
2	6 K	Var (AS)	Yok	Var (AS)
3	6 K	Var (AS)	Var (AS)	-
4	8 E	Var (AS)	Var (AS)	Var (AS)
5	9 K	Var (AS, PS)	Var (AS, PS)	Var (A)
6	6 E	Var (AS)	Yok	Var (AS)
7	1 E	Var (AS)	Var (AS)	Yok
8	0 K	Var (AS)	Var (AS)	-
9	5 E	Var (AS)	Var (AS)	-
10	1 K	Var (AS)	Yok	-
11	7 K	Var (AS)	Var(AS)	-
12	1 K	Var (AS)	Var (AS)	-
13	9 E	Var (AS)	Yok	-
14	6 K	Yok	Var (AS)	-
15	4 E	Var (AS)	Yok	Var (AS)
16	7 K	Var (AS)	Var (AS)	Var (AS)
17	7 K	Var (AS)	Var (AS)	-
18	3 K	Var (S)	Var (S)	-
19	6 E	Var (AS)	Var (AS)	-
20	9 E	Var (AS)	Var (AS)	-
21	0 E	Var (AS)	Var (AS)	-
22	0 E	Var (AS)	Var (AS)	Var (AS)
23	1 K	Var (AS)	Yok	-
24	1 K	Var (AS)	Var (AS)	-

AS: anterosüperior; PS: posterosüperior; S: süperior; A: anterior

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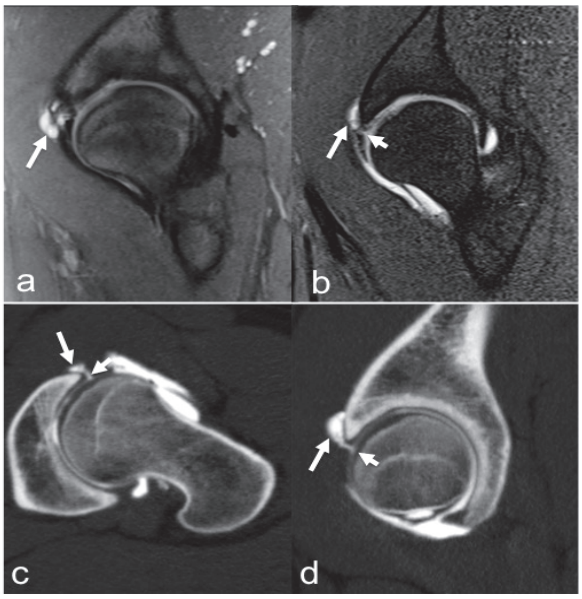
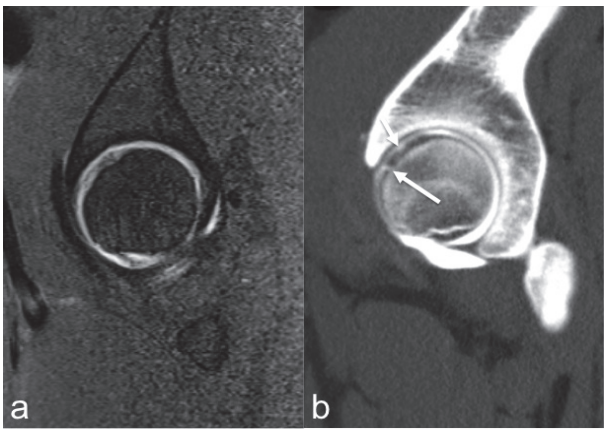


Resim 2. a–d. Labral yırtık-paralabral kist: a PD yağ baskılı sagittal MR görüntüsünde anterosüperior labrumun komşuluğundaki paralabral kist *(uzun ok)* izlenmektedir, T1 yağ baskılı sagital MRA görüntüsünde anterosüperior labrumdaki yırtığa *(kısa ok)* bağlı kontrast sızıntısı ve komşuluğundaki paralabral kiste *(uzun ok)* bağlı kontrast dolusu görülmektedir, c-d. Aksiyel ve sagital BTA görüntülerinde paralabral kistin *(uzun oklar)* labral yırtık *(kısa oklar)* ile bağlantısı açıkça görülmektedir. Operasyonda labral yırtık varlığı doğrulandı.

Kıkırdak lezyonları MRA tetkikinde 42 kalçanın 10'unda (%24.80), BTA tetkikinde ise 11'inde (%26.19) tespit edilmiştir. Bu lezyonlar MRA'da %9.5 (4/42) olguda asetabular (hepsinde anterosüperiorda), %14.3 (6/42) olguda asetabular ve femoral tarafta birlikte (3'ünde diffüz, 2'sinde anterosüperiorda, 1'inde ise hem anterosüperior hem de posterosüperiorda); BTA'da ise %11.9 (5/42) olguda asetabular (4'ünde anterosüperiorda, 1'inde hem anterosüperior hem de posterosüperiorda), %11.9 (5/42) olguda asetabular ve femoral tarafta birlikte (2'sinde diffüz, 1'inde anterosüperior, 2'sinde ise hem anterosüperior hem de posterosüperiorda), %2.4 (1/42) olguda ise femoral tarafta (anterosüperiorda) tespit edildi. Opere olan olgulardan 7'sinde kıkırdak hasarı tespit edildi. İstatiksel değerlendirmeye göre kıkırdak lezyonlarını ve yerleşimlerini göstermede bu iki tetkik birbirleri ve cerrahi sonuçları ile uyumlu bulundu (p>0.05). Cerrahi korelasyonu bulunan hastalardan yalnızca bir tanesinde asetabular taraftaki lezyon görüntüleme yöntemleri ile gösterilmedi. Bir başka hastada ise BTA'da femoral tarafta saptanan kıkırdak lezyonu MRA ile gösterilemedi (Resim 3). Asetabular ve femoral tarafta birlikte eklem kıkırdağı lezyonu saptanan başka bir olguda ise bu lezyon MRA'da tespit edilebilmesine karşın BTA'da–olasılıkla eklem içi enjeksiyon sonrası görüntülerin ortalamaya göre daha geç alınmasına bağlı olarak–gösterilemedi. Olgulardaki kıkırdak lezyonlarının yerleşimleri ile MRA, BTA ve varsa operasyon sonuçları Tablo 3'de verilmiştir.



Resim 3. a-b. Kıkırdak lezyonu: a. T1 yağ baskılı sagital MRA ve b. Sagital BTA görüntüleri. BTA incelemesinde femoral tarafta anterosüperiorda kıkırdak defektine bağlı kontrast sızıntısı *(uzun ok)* kolayca saptanırken aynı düzeyden geçen MRA görüntüsünde kontrast sızıntısı ayırt edilemiyor. Ayrıca yine BTA görüntüsünde bu lezyonun daha posterior komşuluğunda femoral tarafta yüzeyel kıkırdak hasarını düşündüren kontrast sızıntısı görülüyor *(kısa ok).*

Tablo 3. Kıkırdak lezyonlarının varlık ve yerleşimleri ile MRA, BTA ve mevcutsa operasyon sonuçları

Olgu no	Yaş Cinsiyet	Radyolojik tetkiklere göre lokalizasyonu	MRA	BTA	Operasyon
1	56 K	Asetabular	Var (AS)	Var (AS, PS)	
2	18 E	Femoral	Yok	Var (AS)	Femoral
3	29 K	Asetabular/femoral	Var (AS)	Var (AS, PS)	Asetabular
4	46 E	Asetabular/femoral	Var (AS)	Var (AS)	Asetabular
5	51 E		Yok	Yok	Asetabular
6	50 K	Asetabular	Var (AS)	Var (AS)	-
7	41 K	Asetabular/femoral	Var (diffüz)	Var (diffüz)	-
8	57 K	Asetabular	Var (AS)	Var (AS)	-
9	41 K	Asetabular	Var (AS)	Var (AS)	-
10	38 K	Asetabular	Yok (AS)	Var (AS)	Asetabular
11	24 E	Asetabular/femoral	Var (diffüz)	Yok (diffüz)	Asetabular/femoral
12	27 K	Asetabular/femoral	Var (AS, PS)	Var (AS, PS)	Asetabular/femoral
13	31 K	Asetabular/femoral	Var (AS)	Var (AS)	-

AS: anterosüperior; PS: posterosüperior

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Bunların dışında toplam 7 olguda femur baş-boyun bileşkesinde kemik çıkıntı, 4 olguda asetabular retroversiyon tespit edilmiş olup bu lezyonların gösterilmesinde de istatiksel analizlere göre her iki tetkik birbirleri ile uyumlu idi (p>0.05).

Güvenlik paremetreleri
Eklem içi enjeksiyonu hastalar tarafından rahatlıkla tolere edilebilmiş olup hiçbir hastada orta veya ciddi düzeyde komplikasyon ile karşılaşılmamıştır. Enjeksiyon sonrasında kalça işlemlerinin 4'ünde (%9.52) olasılıkla eklem kapsülünün gerilmesine ve bazı olgularda eşlik eden iyatrojenik kas içi kontrast madde sızıntısına bağlı olarak ağrı ve basınç hissi tarif edildi. Bu hastalardan birinin şikayetleri ertesi güne kadar devam ederken diğerleri enjeksiyondan birkaç saat (6-8 saat) sonra şikayetlerinin azalarak kaybolduğunu ifade ettiler.

TARTIŞMA

Kalça ekleminde BTA ve MRA'yı karşılaştırdığımız bu çalışmadaeklem içi veya eklemle ilişkili lezyonların tanısında bu iki tetkikin birbirleri ile uyumlu olduğunu ortaya koyduk.Literatürde kalça eklemi patolojilerinde MRA'nın etkinliğini değerlendiren çok sayıda araştırma bulunmasına rağmen aynı konuda BTA ile ilgili çalışmalar daha az sayıda yer almaktadır (2–10). Ancak son yıllarda modern çok sıralı BT teknolojisininsağladığı yüksek uzaysal rezolüsyon gibi avantajları sayesinde kalça artrografisinde MRA'nın yanısıra BTA ile ilgili çalışmaların da sayısı artmaya başlamıştır(3–9).

Standart MRG ve BT görüntüleme tetkikleri kalça patolojileri açısından önemli bilgiler vermekle birlikte bazı sınırlılıkları vardır (1).MRA ve BTA iyatrojenik olarak artrografik etki yaratarak eklem içi yapıların daha ayrıntılı gösterilmesi amacıyla geliştirilmiş olupinvaziv işlemler olmakla birlikte eklem aralığına verilen SF çözeltisi ile distansiyon sağlandığı için eklem içi patolojilerin saptanmasında MRG'ye göre daha üstün olan görüntüleme yöntemleridir (2).

Literatürde kalçada labral patolojilerin tespitinde MRG ve MRA'nın gücünü ortaya koyan çok sayıda çalışma vardır (2).Bu çalışmalara göre labral yırtığın tespitinde MRG'nin duyarlılık ve özgüllük değerleri %0-100 gibi çok geniş bir aralıkta değişmektedir (2). Bu konuyla ilgili çalışmalarınaz sayıda kısmında MRG'nin duyarlılık değeri %90'nın, özgüllük değerleri %80'nin üzerinde (2, 11–17) bulunmuştur. Bu çalışmalardan bazılarının 3 Tesla (T) ile yapıldığı (13, 18) gözönünde bulundurulduğunda çalışmalar arasındaki farklı oranların yüksek Tesla gücü ve koil sistemlerindeki değişiklikler gibi teknolojik gelişmelerin sağladığı farklılıklar ile ilişkili olduğu söylenebilir.Literatürdeki çalışmalara görelabral yırtık tespitinde MRA'nın duyarlılık ve özgüllük değerleri ise sırasıyla %69-100 (çoğu %90'nın üzerinde olmak üzere) ve %0-100 (çoğu %80'nin altında olmak üzere) arasında değişmektedir (2).Bu sonuçlara göre 3 T MRG ile 1.5 T MRA görüntülerini karşılaştırıldığı bir çalışma (12) dışında labral yırtığı tespit etmedeki duyarlılıkları açısından MRA'nın, MRG'ye üstün olduğu, özgüllükleri arasında ise her iki görüntüleme yöntemi arasında küçük farklar olduğu ortaya konmuştur (2). Literatürdeki çok sayıda çalışma labral patolojilerin saptanmasında MRA'nın mükemmel sonuçlar ortaya koyduğunu (12, 14, 16, 18) göstermesine rağmen uzaysal çözünürlüğünün düşük olması nedeniyle küçük labral yırtıkların saptanmasında zorluklar olabilir (3). Keeney ve arkadaşları tarafından yapılan bir çalışmada labral yırtık ile uyumlu klinik semptomları bulunan 101 hastaya (102 kalça) MRA tetkiki ve bunlardan konservatif tedaviden fayda görmeyenlere artroskopi yapılarak MRA'nın labral patolojileri saptamada %71 duyarlılık, %44 özgüllük, %93 pozitif kestirim değeri, %13 negatif kestirim değeri ve %69 doğruluk oranlarına sahip olduğu bulunmuştur (19). Bu çalışmada yazarlar MRA'nın labral yırtık tanısında mükemmel pozitif kestirime sahip olmasına rağmen duyarlılığının sınırlı olduğunu ve negatif bulunan bir görüntülemenin önemli bir eklem içi patolojiyi dışlayamayacağı sonucuna varmışlardır (19).BTA ise yeni bir tetkik olmamakla birlikte teknolojik gelişmelerle birlikte MRA'ya alternatif olmuştur.Nishii ve arkadaşları kalça displazisi bulunan 29 hastada (41 kalça) artroskopi bulguları ile karşılaştırmalı değerlendirme sonucunda BTA'nın labral yırtık tespitinde oldukça başarılı olduğunu ve duyarlılık, özgüllük ve doğruluk oranlarının sırasıyla %97, %87 ve %92 olduğunu bildirmişlerdir (4). Son yıllarda yapılan başka bir çalışmaise BTA'nın labral yırtık tespiti yanısıra yırtık ve sulkus varyasyonu ayrımında da %87.5-%93.8 duyarlılık, %95.2-%97.6 özgüllük ve %93.1-%96.6 doğruluk oranları ile oldukça başarılı olduğu göstermiştir (5).

Literatürde kalça patolojilerinde BTA'nın MRG ve MRA ile karşılaştırıldığı az sayıda çalışma vardır (6–9).Son yıllarda bu konu ile ilgili yapılan iki çalışmanın sonuçları MRA'da labral yırtık saptanabilirliği açısından birbirleri ile uyumludur.Ancak BTA'da labral yırtık saptanabilirliği açısından oldukça farklı sonuçlardan bahsedilmektedir. Şahin ve arkadaşlarının yaptıkları çalışmada (7)duyarlılık, özgüllük ve doğruluk oranlarının hepsi %100 olarak belirlenmişken nispeten daha eski tarihli olan çalışmada ise (6)bu oranlar sırasıyla %15, %13 ve %14 olarak bildirilmiştir. Çalışma grubunda yer alan hasta sayıları arasında belirgin fark bulunmayan bu iki çalışma arasındaki uyumsuz sonuçlar BT incelemesinin teknik parametreleri ile ilgili olabilir. Bizim çalışmamızda operasyon sonuçları ile uyumlu olarak MRA ile daha fazla olguda labral yırtık tanısı konulabilmesine karşın cerrahi korelasyonu olan sınırlı sayıda olgu bulunması nedeni ile duyarlılık, özgüllük ve doğruluk oranları belirtilmemiştir.

Labral yırtığın tespitinin yanısıra yerleşiminin ortaya konması da önemli olup radyoloji raporlarında bunun belirtilmesi cerraha kolaylık sağlar.Blankenbaker ve arkadaşları 65 hastada (65 kalça) görüntüleme bulgularını artroskopik bulgular ile karşılaştırarak labral yırtık yerleşimini belirlemede MRA'nın etkinliğini araştırmışlardır (20).Saat kadranlarına göre yırtık yerleşimlerini belirledikleri bu çalışmada olguların %85'inde labral yırtığı saat 1 (anterosüperiorda) düzeyinde tespit etmişlerdir (20).Literatürde bu konu ile ilgili yapılan diğer araştırmalarda da labral yırtıkların en sık yerleşim yerleri anterior ve anterosüperior olarak belirlenmiştir (3, 4, 7).Bizim çalışmamızda da labral yırtıklar en sık anterosüperiorda tespit edilmiş olup

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operasyon sonuçları ile karşılaştırıldığında MRA'nın bunu daha fazla olguda saptadığı ortaya kondu.
Kalça eklemindeki kıkırdak lezyonlarının tanısında standart MRG ve MRA'nın kullanımını değerlendirenaraştırmalardakigenel kanı bu lezyonların tanısında MRG ve MRA'nın duyarlılıklarının düşük iken, özgüllüklerinin yüksek olduğu yönündedir (2). Bu çalışmaların sonuçlarına göre kıkırdak lezyonları için duyarlılık ve özgüllük değerleri sırasıyla MRG için %0-94 ve %50-100 iken, MRA için %22-92 ve %25-100 arasında değişmektedir (2). Literatürde henüz yeterli veri bulunmamasına rağmen3T MRG'lerin modern çok kanallı koil teknolojisi gibi yenilikleri sayesinde MRA'ya alternatif olabileceğinden de bahsedilmektedir (12, 13).BTA'da ise kalça kıkırdak lezyonlarının tespiti daha az sayıda araştırmaya konu olmakla birlikte bu çalışmalarkalçada kıkırdak lezyonlarının tespitinde BTA'nın MRA'ya benzer ya da daha iyi duyarlılık oranlarına sahip olduğuna işaret etmektedir (3–9). Christie-Large ve arkadaşları eklem içi patoloji şüphesiyle BTA yapılan 96 hastanın 27'sinde BTA bulgularını cerrahi sonuçları ile kıyaslayarak hem femoral, hem de asetabular taraf kıkırdak patolojilerinde BTA'nın %88-94 duyarlılık, %100 özgüllük değerlerine sahip olduğunu ve cerrahi sonuçları ile mükemmel uyum gösterdiği sonucuna varmışlardır (3). Şahin ve arkadaşları tarafından yapılan yakın zamanlı başka bir çalışmada ise kıkırdak kaybını göstermede BTA'nın duyarlılığı femoral tarafta MRA ile benzer iken (BTA ve MRA için sırasıyla %75 ve %100) asetabular tarafta daha düşük (BTA ve MRA için sırasıyla %56 ve %89) bulunmuştur (7).Kalçada kıkırdak kalınlığının nispeten daha ince olması, kalça ekleminin küresel şekline bağlı parsiyel volüm artefaktı, diğer eklemlere göre daha derinde yerleşmesi nedeniyle sinyal/gürültü oranının düşük olması ve etkin yüzey koillerinin kullanılamaması gibi faktörlere bağlı olarak MRG'de kıkırdak lezyonlarının tanısı sınırlıdır (21).Bizim çalışmamızda operasyon sonuçları ile uyumlu olarak kıkırdak lezyonu tanısında BTA ve MRAbulguları birbirleri ile uyumlu bulunmuştur.Ancak cerrahi korelasyonu olan sınırlı sayıda olgu bulunması nedeni ile duyarlılık, özgüllük ve doğruluk oranları belirtilmemiştir.

Bu çalışmada femur baş-boyun bileşkesinde kemik çıkıntı, asetabular retroversiyon bulguları da görüntüleme yöntemleri ile kolaylıkla tespit edilmiş olup MRA ve BTA arasında uyumluluk vardı.

Çalışmamız bazı sınırlılıklara sahiptir.İlk olarak radyolojik görüntüler tek bir radyolog tarafından bir defa değerlendirildiği için gözlemci içi ve gözlemciler-arası uyumun belirlendiği bir güvenirlik analizi yapılmadı.İkincisi toplam hasta sayısının yanısıra özellikle cerrahi korelasyonu olan olguların sayısının azlığı nedeniyle tanısal doğruluk oranları belirtilemedi.Son olarakeklem içi enjeksiyon sonrasında aynı zaman aralıklarında BT ve MR cihazlarına alınamaması optimal karşılaştırmaya engel oldu.

Sonuç olarak bu çalışmada kalçada ekem içi ve eklem ile bağlantılı lezyonların tanısında BTA'nın MRA ile uyumlu olduğu sonucuna vardık. İyonizan radyasyona maruziyet gibi dezavantajlarına rağmen yüksek uzaysal rezolüsyon, submilimetrik skalada birçok farklı düzlemde görüntü elde edebilmesi, tetkik süresinin kısalığı ve buna bağlı hareket artefaktlarının azaltılması ve düşük maliyet gibi avantajları gözönünde bulundurulduğunda başta klastrofobi gibi MR kontrendikasyonu bulunan ve cerrahi donanımına bağlı görüntüleme zorlukları yaşanacak hastalarda olmak üzere kalçada eklem içi ve eklem ile ilişkili lezyonların tanısında BTA'nın MRA'ya alternatif bir görüntüleme yöntemi olduğunu düşünmekteyiz. Spesifik lezyonlara yönelik cerrahi sonuçlar ile karşılaştırmalı yapılacak prospektif çalışmalar ile bu görüntüleme yönteminin güçlü ve zayıf yönlerinin daha iyi şekilde ortaya konacağı kanaatindeyiz.

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Acute Diseminated Encephalomyelitis: A Case Report and Review of Literature

Akut Disemine Ensefalomiyelit; Olgu Sunumu Ve Literatür İncelemesi

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Abstract
Acute disseminated encephalomyelitis (ADEM) is an autoimmune and monophasic central nervous system disease that principally affects brain and spinal cord by causing non-vasculitic inflammatory diffuse demyelination. ADEM is one of the rare causes of impaired consciousness in childhood. Incidence of the disease under the age of 20 is 1.5-3 / 100000 per year and it mostly occurs in children between the ages of 5-8 years. Underlying causes aren't defined clearly yet, however, infections and vaccinations are known as predisposing factors for the disease. Multifocal white matter lesions on magnetic resonance imaging (MRI) are characteristic signs of ADEM. In our case, hyperintense lesions in cerebrum were detected on cranial MRI subsequent to impaired consciousness and convulsion. No specific feature was found in cerebrospinal fluid analysis of the patient. In this paper, we present a three-year-old boy who developed ADEM subsequent to viral upper respiratory tract infection and had full recovery after high dose steroid therapy.
Keywords: Acute Disseminated Encephalomyelitis; Cranial MRI; Multiple Lesions; High Dose Steroid Treatment.

Öz
Amaç: Akut disemine ensefalomiyelit (ADEM) otoimmün, monofazik, vaskülitik ve inflamatuvar olmayan yaygın demiyelinizasyon ile seyreden, özellikle de beyin ve spinal kordu etkileyen bir santral sinir sistemi hastalığıdır. ADEM çocukluk çağının nadir görülen bilinç bozukluğu nedenlerinden biridir. 20 yaştan önce hastalığın görülme sıklığı 1.5-3/100000'dir ve sıklıkla 5-8 yaş arasında görülür. Altta yatan neden tam olarak bilinmese de enfeksiyonlar ve aşılamalar hastalığın ortaya çıkmasında önemli faktörlerdir. Multifokal beyaz cevher lezyonları manyetik rezonans görüntülemede (MR) hastalığın karakteristik özelliğidir. Bizim hastamız da bilinç bulanıklığı ve nöbet sonrası yapılan beyin MR'da serebrumda beyaz cevherde hiperintens lezyonlar saptandı. Hastanın beyin omurilik sıvı incelemesinde hastalığa ait bir özellik saptanmadı. Bu yazıda yüksek doz steroid tedavisi sonrası tam düzelme gösteren, viral üst solunum yolu enfeksiyonu sonrası ADEM gelişen 3 yaşındaki erkek hasta sunulmuştur.
Anahtar Kelimeler: Akut Disemine Ensefalomiyelit; Beyin MR; Multiple Lezyonlar; Yüksek Doz Steroid Tedavisi.

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INTRODUCTION

Acute disseminated encephalomyelitis (ADEM) is an acute autoimmune, monophasic, nonvasculitic inflammatory demyelinating disease. Symptoms that are related to central nervous system (CNS) like convulsion, ataxia, paraparesis can bring about this disease while it also affects the white matter of the brain (1). The first case was defined in the 18th century as an uncommon presentation of measles and smallpox (2). The etiology is still unclear but the reasons behind the condition are thought to be immune-mediated since the cases generally have a history of viral infection or immunization (1). The incidence of this syndrome throughout the world is unknown but it may be approximately 1.5-3/100,000 in the USA. ADEM is more common in winter and spring and 80% of the cases occur in the first decade of life (2). Male–female ratio of ADEM is unknown but a study conducted in Japan showed a ratio of 2.3:1 (3). Geographical differences are still unknown and no study confirms the differences according to the geographical areas (4). There are no available definitive tests for this disease, thus the diagnosis is mostly made by depending on the clinical course, magnetic resonance imaging (MRI) characteristics and by excluding other disorders. Although ADEM is a rare disease, it should be distinguished from any other acute neurological diseases. MRI is the most sensitive method to show the number of lesions and extent of involvement; electroencephalography (EEG), cerebrospinal fluid (CSF) analysis and viral etiologic factors surveillance can also be useful for diagnosis (2). The outcome and prognosis are mostly good especially after using gamma globulin, steroids, plasmapheresis and immune suppressive treatments. Most of the cases present without any neurological deficits. Sometimes convulsion, ataxia, paraparesis and headache can persist and rarely it can progress to acute hemorrhagic leukoencephalitis, acute hemorrhagic encephalitis or acute necrotising hemorrhagic leukoencephalitis, all of which are considered as hyperacute forms of ADEM (1). Fulminant forms of ADEM have very poor prognosis and high mortality rate although there are reported cases that have revealed complete recovery using mild hypothermia therapy and high doses of steroids (5).

CASE REPORT

A 3 year-old boy was admitted to our emergency room (ER) in January with generalized convulsion, reduced response to stimulations, drowsiness, fever with history of cough and vomiting. Physical examination showed that he had the signs and symptoms of upper respiratory tract infection; other systems were normal with worsened general condition. On presentation, he was febrile to 38, 8 ^{0}C with normal blood pressure; he was also irritable and the abdomen was a little tender but also soft with no organomegaly. There was no guarding or any sign of peritoneal irritation. A number of tests were performed including blood tests, MRI, chest radiography in ER. The evaluation revealed significantly elevated count of white blood cells (WBC count up to 47.400/mm^{3}), a C-reactive protein (CRP) level of 50.5g/dL and an ammonia concentration of 48.5µmol/L with normal lactate (1.87 mmol/L) level. He had normal metabolic panel with negative blood and urine cultures and urine analysis was completely normal as was the chest radiograph. Lumber puncture and CSF analysis demonstrated normal erythrocytes, glucose (59 mg/dL; serum glucose: 83mg/dL), protein (263 mg/L; N: 150-430), culture, immunoglobulin G, and negative oligoclonal bands. The patient was treated with ceftriaxone and vancomycine for concerns of partially treated meningitis. The presumed diagnosis was ADEM which could be viral in origin so acyclovir was started. Cranial MRI showed hyperintense lesions in right cerebellar hemisphere, right middle cerebellar peduncle, bilateral globuspallidus predominantly on right, left internal capsule, frontotemporoparietal regions, in subcortical white matter, corpus callosum right hemisphere and in bilateral thalami. In addition, hyperintense lesions similar to those in thalami were observed in both nucleus caudatus and nucleus lentiformis inferior parts, too (Figure 1).

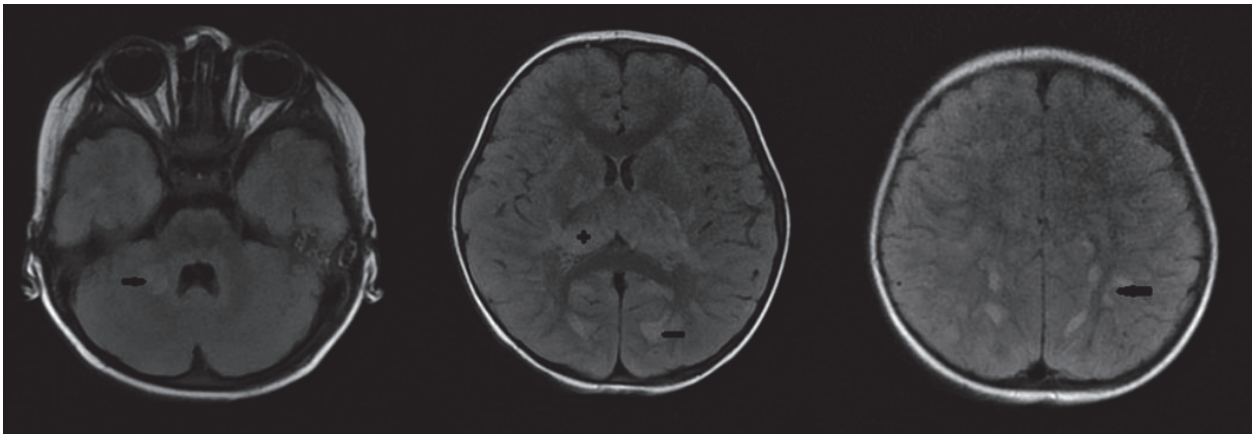

Figure 1. (a) Axial T2A section, right nucleus dentatus; (b) basal ganglions; and (c) on convex plan, subcortical white matter hyperintense lesions.

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Imaging was compatible for eudema and inflammation in both temporal lobes, at right parahippocampal gyrus localization and in both parietal lobes. Patient was diagnosed with ADEM with these findings. Three days after the admission, the patient had no fever and his WBC count was 10.900/mm^3, CRP was 3.45 g/dL, but intentional tremor was observed. High dose corticosteroid (methyl prednisolone) was started at the dose of 30 mg/kg/day for three days followed by oral prednisolone treatment at a dose of 2 mg/kg/day for tapering over 6 weeks. The patient was kept under motorization for 10 days. On discharge, the patient was completely normal. The first follow–up visit was 6 weeks after the discharge; the steroid treatment was completely stopped after 6 weeks and the patient was completely normal. After 6 months, MRI scans were performed to see the degree of improvement, new lesions and enhancement and there were no pathological findings on MRI (Figure2).

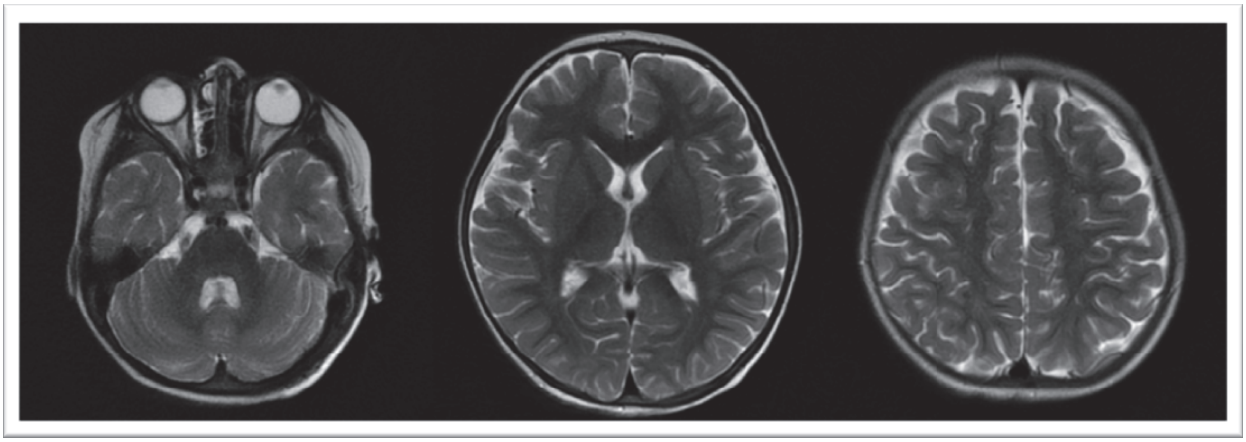

Figure 2. Post-treatment control cranial MRI, axial T2A image (2a) on nucleus dentatus location; (2b) on basal ganglions location; and (2c) on convex plan subcortical white matter lesions disappered.

DISCUSSION

ADEM principally involves the white matter tracts of the cerebral hemispheres, brainstem, optic nerves, and spinal cord. It is a disease of the young, with an estimated incidence of 1.5-3/100 000/year among people less than 20 years old. The mean age at presentation in children ranges from 5 to 8 years (6). Our patient was under the mean age of the onset of the disease. ADEM is post or peri-infectious reaction and it is usually preceded by an infection such as mycoplasma, Epstein-Barr virus (EBV), measles, rubella, varicella or mumps. It may even occur consequent to vaccination. There are reported cases of non-vaccinated patients who had underwent splenectomy that developed ADEM after bacterial meningitis. ADEM may arise secondary to molecular mimicry in which similarity between pathogenesis and myelin protein starts an autoimmune reaction against central nervous system. The cause of the disease is unknown in 1/3 of the cases (5, 7, 8). It is considered that the responsible factor for the case that was presented in this paper was a viral agent that may have caused upper respiratory tract infection symptoms. It affects especially cerebrum and spinal cord, so any patient with ADEM can express widespread of motor and sensory deficits, symptoms like ataxia, paraparesis, hemiparesis, monoparesis, loss of tonus, or generalized or focal convulsion. Eye aches, visual disturbances, oculomotor nerve palsy and urinary symptoms like transient retention of urine, dysarthria and nystagmus may be seen in the spectrum of clinical manifestations as well. These symptoms are mostly seen within 7-14 days following a viral infection or immunization (1, 2, 5). Ocular examination was normal in our patient and encephalopathy and convulsion came out without any paralytic condition. On the third day of admission, tremor manifested.

In the cerebrospinal fluid, lymphocytic pleocytosis and mild elevation of protein, oligoclonal bands, Ig G or myelin basic protein can be detected. In our case, CSF did not show any abnormality, which might indicate ADEM. EEG may show focal discharge and slowing visual evoked potential may be seen. Cerebral MRI is considered to be the most helpful technique, by showing focal or multifocal hyperintense lesions that mainly affect CNS (8). The most commonly acquired demyelinating diseases of CNS are ADEM and multiple sclerosis (MS). MS is an acquired, chronic inflammatory demyelinating disease of the brain (9). ADEM can be distinguished from MS by its monophasic character, prepubertal onset and presence of encephalopathy. The disease affects specific anatomical fields and some cases of recurrent or multiphasic courses have been reported. Demyelinating lesions may be seen after three months from the onset of ADEM or four weeks after completing steroid therapy (7, 10, 11). Recurrence of clinical or radiological findings is more frequent in MS and may exist after many years from the first manifestation. Therefore, patients who are suspected for MS should be followed-up for a long time (1, 2). International MS Study Group monophasic ADEM criteria:

- No history of prior demyelinating events

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- First clinical event with presumed inflammatory or demyelinating cause
- Acute or subacute onset
- Affects multifocal areas of central nervous system
- Must be polysymptomatic
- Must include encephalopathy (i.e., behavioral change or altered level of consciousness)
- Neuroimaging shows focal/multifocal lesion(s) predominantly affecting white matter
- No neuroimaging evidence of previous destructive white matter changes
- The event should be followed by clinical/radiologic improvements (although may be residual deficits)
- No other etiology can explain the event
- New or fluctuating symptoms, signs or magnetic resonance imaging findings occurring within 3 months are considered to be a part of the acute event (12).

Clinical international pediatric MS work team criteria of Miller et al. for ADEM are

1- Subacute encephalopathy
2- Clinical course from 1 week to 3 months
3- Improvement (but neurological deficit can remain)
4- MRI, white matter lesions
- Acute
- Multiple
- At least one lesion (1-2 cm)
- Supra and infra-tentorial lesions
- Gadolin enhanced lesions (not necessary)
- Lesion of basal ganglion (not necessary) (13).

The most important MRI finding of ADEM is multifocal hyperintense lesions. In our case, multifocal lesions were seen as settled in the supratentorial area, cerebrum, thalamus, capsulainterna, nucleus caudatus and nucleus lentiformis. The lesions that had settled in infratentorial area were 4-12 mm in diameter and those in the supratentorial area were 5-24 mm. Gadolin enhanced lesions were not seen. Some lesions were placed in basal ganglions.

The prognosis of ADEM is generally favorable. Farag et al. suggested that 76,2% of children were neurologically normal on the discharge and 23.8% were completely neurologically normal after the first year of follow-up and relapses had occurred in 9.5% of the children and no relation were present between relapse and tapering steroid treatment (2). In another study, 57-89% of children showed full recovery while the rest developed widespread neurological deficits like epileptic seizures that required antiepileptic drug treatment, headache, abnormal behaviors and hemiparesis (1). In our patient, we observed tremor at first but there were no clinical findings on discharge. Six months later, there were still no clinical or MRI findings. Prognosis of this patient was well and we did not observe any recurrences.

Cranial MRI is the most important method for the diagnosis of ADEM. Patients may recover without any sequellae with corticosteroid treatment. ADEM is one of the rare causes of impaired consciousness and it should be considered in children with sudden neurological deficit and encephalopathy.

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Cryptogenic Organizing Pneumonia Diagnosed with Transbronchial Parenchymal Biopsy: A Case Report with Accompanying Histopathological Images

Transbronşial Parankim Biyopsisi ile Tanı Konulan Kriptojenik Organize Pnömoni Olgusu: Histopatolojik Görüntüleriyle Birlikte Olgu Sunumu

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Abstract
Cryptogenic organizing pneumonia (COP) is an idiopatic condition characterized by granulation tissue extending to alveolar ducts and alveoli in small airways. Here, we present an exemplary case for COP which is uncommon in clinical practice of chest diseases. A 48-year-old male was admitted to our clinic with shortness of breath and cough. In arterial blood gas collected at room air, pH was 7.43, PaCO2 was 41.2 mmHg, PaO2 was 49.1 mmHg, and HCO3 was 24mEq/L. In thorax HRCT, ground-glass-opacities accompanied by bilateral consolidation areas were present especially in peripheral areas of the right lung and bilateral upper lobes. COP was reported histopathologically in transbronchial biopsies performed with bronchoscopy. Significant clinical improvement and radiological regression were observed in the patient with 80 mg/day methylprednisolone treatment. We share the case of our patient, who was diagnosed with bronchoscopic procedure without the need of open lung biopsy, to remind the importance of bronchoscopy in the diagnosis of COP.
Keywords: Consolidation; Cough; Cryptogenic Organizing Pneumonia; Shortness Of Breath.

Öz
Kriptojenik organize pnömoni (KOP), sebebi bilinmeyen, alveoler kanal ve alveollere uzanan küçük hava yolları içinde granülasyon dokusuyla karakterize bir durumdur. Göğüs hastalıkları klinik uygulamalarında çok sık karşılaşılmayan KOP'a örnek teşkil eden bir olgu sunuyoruz. 48 yaşında erkek hasta, polikliniğimize nefes darlığı ve öksürük ile başvurdu. Oda havasında alınan arteriyel kan gazında pH: 7.43, PaCO2: 41.2 mmHg, PaO2: 49.1 mmHg, HCO3: 24 mEq/L olarak bulundu. Toraks HRCT tetkikinde sağ akciğerde ve bilateral üst loblarda özellikle periferal alanlarda daha yoğun bilateral konsolidasyon alanlarının eşlik ettiği buzlu cam görünümü mevcuttu. Hastaya yapılan bronkoskopik inceleme ile alınan transbronşiyal biyopside histopatolojik olarak KOP tanısı raporlandı. 80 mg/gün metilprednizolon tedavisi başlanana hastada radyolojik olarak regresyon ve belirgin klinik düzelme gözlendi. Açık akciğer biyopsisine gerek kalmadan, bronkoskopik yöntemle tanı koyduğumuz bu olguyu, KOP tanısında bronkoskopinin önemini hatırlatıcı olması bakımından histopatolojik görüntüleri ile birlikte paylaşıyoruz.
Anahtar Kelimeler: Konsolidasyon; Kriptojenik Organize Pnömoni; Nefes Darlığı; Öksürük.

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INTRODUCTION

Cryptogenic organizing pneumonia (COP) is a rare pulmonological clinical picture. In case of the lack of any underlying causes, histopathologically defined "organising pneumonia" is defined as "idiopathic / cryptogenic organising pneumonia." It is assumed that COP is caused by abnormal granulation tissues that develop during the healing of an inflammatory process extending from the alveolar ducts to the alveoli due to an unknown cause (1).

The major histopathological finding for COP is the presence of granulation tissue buds formed by fibroblasts, collagens and fibrinous exudates within the alveolar ducts and alveoli (2). In addition to these histopathological findings that help differentiate the diagnosis of COP from other organising pneumonia signs, the most common symptoms are persistent dry cough, exertional dyspnea, and weight loss (2, 3). Open lung biopsy is the gold standard for its histopathological diagnosis. It is more difficult to identify COP by bronchoscopical methods. While COP, which is rarely mortal, responses to corticosteroids weakly, early histopathological diagnosis with lung biopsy and high-dose corticosteroid therapy can be life-saving (2, 4). In this report and with accompanying histopathological images, we present the case of a patient diagnosed with COP though bronchoscopical procedures without the need for an open lung biopsy in order to set an example for this rare phenomenon and to remind clinicians the importance of bronchoscopy.

CASE REPORT

A 48-year-old male patient presented with complaints of shortness of breath, cough, and fatigue. The symptoms had begun 2 weeks ago and had started a 500 mg/day-levofloxacin (PO) treatment prescribed by a health care provider where he had consulted with the same complaints and been diagnosed with lower respiratory tract infection. Due to ongoing complaints, the patient had been referred to our clinic. On admission, the patient was in good condition, conscious, cooperative, and oriented. Fever was 36.4°C, pulse was 98 beats/min, arterial blood pressure was 125/75mmHg, and SpO2 was 85% at room air. In the physical examination of the respiratory system, we auscultated crepitant rales around the bilateral borders. The laboratory examination revealed the following data: WBC: 13800; HGB: 13; HCT: 38.5; PLT: 467 000; and ESR: 73. The routine biochemical test results were within normal limits. PA chest X-ray revealed bilateral non-homogenous density on the right and around the peripheral areas (Figure 1a).

We administered a thorax HRCT. The HRCT results showed loss of volume in the right side of the chest, intra- and interlobular septal thickening with visible peripheral involvement especially in the upper lobes of both lungs and more intensely in the right lung, areas of consolidation, and extensive ground-glass opacities (Figure 1b).

The transbronchial parenchyma biopsy obtained by diagnostic bronchoscopy confirmed organising pneumonia (OP) (Figure 2). The examination for mycobacterial bronchoalveolar lavage showed that the direct examination for mycobacterium tuberculosis and the culture test result we acquired after 8 weeks were both reported negative. We referred the patient to Rheumatology clinic for possible connective tissue diseases but the rheumatological examination and test results pointed to no rheumatological diseases. Failing to identify any signs that could lead to OP, we concluded that the patient had COP and started a 80 mg/day methylprednisolone (IV) therapy. Within 2 weeks we observed clinical regression and after 4 weeks the patient showed radiological regression (Figure 1c). With a follow-up dose of steroids for six months, we planned to follow up the patient in the coming months.

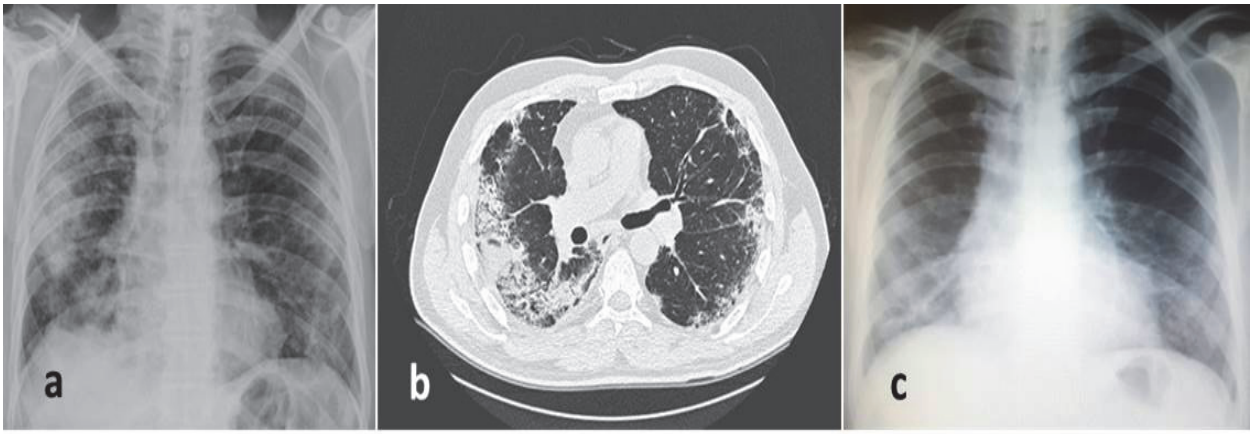

Figure 1. Radiological images of the patient.
1a. PA chest X-ray on admission (increased bilateral non-homogenous density),
1b. thorax HRCT (peripheral and interlobular septal thickening, areas of consolidation, and extensive ground-glass opacities),
1c. PA chest X-ray of the 4th week of the treatment (visible radiological regression).

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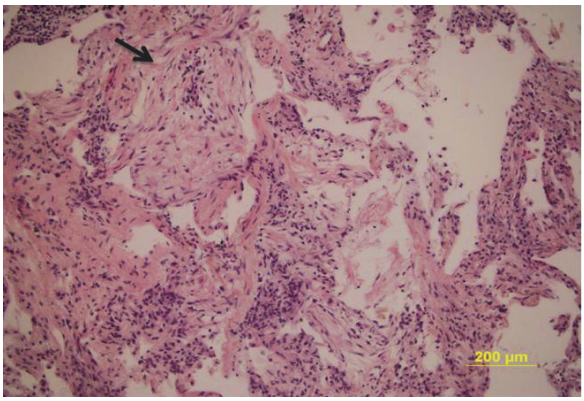

Figure 2. The transbronchial parenchyma biopsy view; fibroblasts filling in the distal airways (alveolar ducts and alveoli) and loose fibrous connective tissues (masson body) with collagen, fibrinous, and lymphocytic cells (HE X200).

DISCUSSIONS

COP is thought to result from incomplete healing of inflammatory response in the alveoli due to unknown damage. It has a similar incidence in men and women alike and it is more common in the 50-60 age range (3, 5). Our patient can also be evaluated in this age group.

COP can be confused with many diseases both in clinical practice and histopathological aspects. Diagnosis can be made by exclusion method. Although the gold standard is open lung biopsy for a histopathological diagnosis of COP, practitioners can make use of less invasive methods such as transbronchial lung biopsy as we have administered in our case (2, 6). Generally showing a subacute course, the most common symptoms of COP are cough, shortness of breath, fever, sputum, loss of appetite, and weight loss (3). In our case, too, the medical picture of the patient showed dry cough and shortness of breath. Increase in leukocytosis and acute phase reactants, both of which were observed in our patient, are often present with COP while these can also be misleading for clinicians as they often bring to mind infectious pneumonia in differential diagnosis (7). Peripheral multifocal consolidations are the major radiological findings that must be kept in mind in differential diagnosis. This view is typical for COP as it was the case in our patient. However, they may look like lower grade pulmonary lymphomas and bronchoalveolar carcinomas in some cases. This is why identifying histopathological findings are essential for the diagnosis (8). The standard therapy for COP is corticosteroid administration and treatments for 6-12 months have proved to give very good results (4).

Consequently, COP, a rare entity in itself, should be considered in differential diagnosis of many different respiratory pathologies due to its identifiable clinical and radiological findings. We have shared this case report to emphasize the role of bronchoscopy, which is a less invasive procedure in the diagnosis of COP compared to open lung biopsy.

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Aortic Bypass Surgery Simultaneously Performed with Coronary Artery Bypass Grafting and Mitral Valve Replacement in a Patient with Takayasu Arteritis: A Case Report

Takayasu Arteritli Bir Hastada Koroner Bypass ve Mitral Kapak Replasmanıyla Eş Zamanlı Uygulanan Aorta-Bisubklavian Bypass Operasyonu: Olgu Sunumu

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Abstract

Initially characterised by involvement of the aorta and its main branches, eye disorders, and weakening of the upper extremity pulses, Takayasu arteritis is a vascular disease with unknown etiology. There are several surgical options for its treatment. A 54-year-old man with Takayasu arteritis presented in our clinic with unstable coronary artery disease. The patient underwent operation with a diagnosis of ischemic mitral regurgitation. Turunkus brakiosefalikus and left subclavian artery osteal were occluded and we also observed signs of subclavian steal syndrome. For a safe surgery and to maintain cerebral perfusion we first performed ascending aorta bypass with a dacron graft. Then we simultaneously performed aortic-coronary bypass and mitral valve surgery. Prior to the operation, we initiated a steroid therapy, which continued post-operatively. We did not observe any complications. In order to maintain cerebral perfusion, we believe that open heart surgery and vascular procedures can be simultaneously and safely applied in patients with Takayasu arteritis who are in their remission process.

Keywords: Takayasu Arteritis; Aortabisubklavian Bypass; Coronary Artery Disease.

Öz

Takayasu arteriti, temelde aorta ve büyük dallarını tutan göz bozuklukları ve üst ekstremite nabızında belirgin zayıflamayla karakterize etiyolojisi bilinmeyen bir damar hastalığıdır. Bu hastalıkta cerrahi tedavi seçenekleri farklı özelliklere göre şekillenebilmektedir. 54 yaşında Takayasu arteriti olan erkek hasta kliniğimizde unstable koroner arter hastalığı ve iskemik mitral yetmezliği tanılarıyla opere edilmiştir. Hastada turunkus brakiyosefalikus ve sol subklavian arterin osteal tıkalı olduğu ve subklaviyan steal sendromu olduğu izlenmiştir. Operasyonda güvenli bir cerrahi için serebral perfüzyonun devamı açısından öncelikle dacron greftle asendan aorta bisubklavian bypass yapılmıştır. Sonrasında eş zamanlı olarak aortakoroner bypass ve mitral valve operasyonu gerçekleştirilmiştir. Operasyon öncesi remisyonda olan hastaya steroid tedavisi başlanmış ve operasyon sonrası da devam edilmiştir. Hastada herhangi bir komplikasyon izlenmemiştir. Remisyon dönemindeki Takayasu arteritli olgularda serebral perfüzyonun devamı açısından açık kalp cerrahisiyle eş zamanlı vasküler prosedürlerin güvenle uygulanabileceğini düşünüyoruz.

Anahtar Kelimeler: Takayasu Arterit; Aortabisubklavien Bypass; Koroner Arter Hastalığı.

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GİRİŞ

Takayasu arteriti (TA), aort ve ana dalları ile pulmoner arteri etkileyen nadir bir büyük damar vaskülitidir. Torasik aort ve dalları, abdominal aort ve dallarından daha fazla tutulur. Tutulan damarın beslediği organa ilişkin iskemik belirtiler gözlenir. Beyine giden damarlar etkilenmişse geçici iskemik atak, inme v.b. nörolojik belirtiler ve görme bozuklukları, extremiteleri besleyen damarların tutulumuna bağlı kladikasyo görülebilir (1). Hastalığın başlangıcında halsizlik, ateş, kilo kaybı gibi nonspesifik belirtiler nedeniyle tanı zordur ve gecikmeler olabilir. Tedavide kortikosteroitlere yanıt iyi olmasına karşın immünsupresif tedavi de eklenebilir. Bu hastalıkta cerrahi tedavi seçenekleri farklı özelliklere göre şekillenebilmektedir. Darlık derecesinin fazla olduğu veya tam tıkanıklık durumunda by pass, endovasküler stent veya anjioplasti gibi yöntemler uygulanabilir (2).

Yıllık insidansı 2.6/ milyon yeni olgu, prevalansı ise 2.6-6.4/ milyon arasındadır. Genç kadınlarda fazla görülmekte ve etyolojisi günümüzde tam anlaşılamamıştır. Tüm ülkelerde görülmesine karşın asya ülkelerinde daha sık görülmektedir. Takayasu arteriti ilk defa 1908'de Takayasu' nun (3) olgu takdiminden sonra Shimizu ve Sano (4) tarafından tarif edilmiştir. Aortun vasovasorumundan başlayan ve panarteritis şeklinde adventisya ve mediaya yayılan granülomatöz enflamasyonun koroner arter tutulumu ilk defa Frövig ve Löken (5) tarafından tesbit edilmiştir. Takayasu arteritinde, klinik olarak teşhis edilmiş veya otopside rastlanmış koroner arter lezyonlarının insidansının %10'u geçmemesi (6,7) bizi semptomatik koroner arter tutulumu teşhis edilen ve cerrahi yoldan tedavi edilen olgumuzu sunmaya yöneltti. Ancak bu olgumuzdaki koroner arter tutulumunun arteritten ziyade ateroskleroz kaynaklı olduğu düşüncesindeyiz. Hastadan biyopsi alınmamasının bir eksiklik olduğu ancak daha önce Takayasu arteriti tanısı konulduğu için buna gerek duyulmamıştır.

OLGU SUNUMU

Temmuz 2014 tarihinde, 54 yaşında Takayasu arteritli erkek hasta kliniğimize unstable koroner arter hastalığı ve iskemik mitral yetmezliği tanılarıyla operasyon amaçlı interne edildi. Hastanın göğüs ağrısı (usap), nefes darlığı (NYHA Class-3), kollarda eforla çabuk yorulma (cladicasyo) şikayetleri vardı. Hasta kronik sigara içicisiydi. Fizik muayenesinde, hastanın dört ekstremitesinden de tansiyon ve nabız alınamamaktaydı. Hastanın öncelikle rutin tetkikleri, EKG ve Telegrafisi istendi. Rutin tetkiklerinde akut faz reaktanlarının hafif yüksekliği dışında anlamlı bir patolojik bulguya rastlanmadı. EKG'de nsr'de, rate:76/ dk, tele'de hafif mediasten genişliği saptandı. Karotis doppler usg'de, sağ CCA ve ICA kalibrasyonunda azalma, (ICA'da distal oklüzyon?), sol vertebral arterde ters yönde akım (subklavian stell sendromu), sağ vertebral arterde çap azalması saptandı. Bunun üzerine hastaya çok kesitli karotis BT Anjiografi planlandı. Hastanemiz Radyoloji kliniğinde çekilen BT Anjiografide, truncus brachiocefalicus ve sol subklavian arterin arcus aortadan çıkış yerinden osteal tıkalı olduğu gözlendi. Transtorasık Ekokardiyografide, EF:%30, sol kalp boşluklarında genişleme, sol ventrikül sistolik ve diyastolik disfonksiyonu, orta-ileri iskemik mitral yetmezlik saptandı. Koroner Angiografide, LMCA; normal, LAD; proksimalinden total tıkalı, LAD distali CX'den gelen kollaterallerle retrograt dolmakta, CX; dominant olup normal yapıda, RCA; ortasından total tıkalı olup Cx'den gelen kollaterallerle retrograde dolmakta, Sol subklavian arter ostiumuna yakın segmenttentten itibaren total tıkalı olarak izlenmiştir. Bunun üzerine, remisyon dönemindeki TA'li hastaya CABG+mitral kapağa müdahale kararı alındı. Ancak operasyonda güvenli bir cerrahi için serebral pefüzyonunı açısından öncelikle dacron Y greftle asendan Aorta-Bisubklavian bypass planlandı. Operasyon öncesi remisyon döneminde olan hastaya steroid tedavisi başlanmış ve operasyon sonrası da devam edilmiştir. Operasyona alınan hasta; arter monitörizasyonu femoral arterden yapıldıktan sonra genel anestezi altında midsternal insizyon ile göğüs boşluğu açıldı. Eş zamanlı olarak safen ven bacaktan subkutan diseksiyon tekniği ile hazırlandı. Sol subklavian arter osteal total tıkalı olduğu için LİMA grefti hazırlanmadı. Asendan aorta ve bilateral subklavian arterler anastamoz için hazırlandı. Side klemp altında 14/7 Dacron Y greftin proximal anastamozu brachiocefalik arter yakın asendan aortaya yapıldı. Sonrasında subklavian arterlere distal anastamozlar gerçekleştirildi (Resim 1). Sistemik heparinizasyonu takiben aortik ve bikaval kanülasyon yapılarak kardiyopulmoner by-pass'a (CPB) girildi. Aortik kanül Y greftin hemen proximal kısmı lateraline konuldu. Vücut CPB'ta 32 c'ye kadar soğutuldu. Aorta'ya kross klemp konmasının ardından, antegrade ve retrograde soğuk K+'lu kan kardiyoplejisi tekniği ile kardiyak arrest sağlanarak safen ven ile distal bypasslara geçildi. LAD ve RCA main koroner arterlere distal anastamozlar yapıldı. Sonrasında sol atrium açıldı, mitral kapak hiç rezeke edilmeden 31 no St Jude biyolojik kapak anulusa implante edildi. Atriotomi kapatıldı. Sonrasında sağ safen greftin proximali antegrade iğne giriş yerine, LAD safen proximali de sağ safen ven proximalinin üzerine, asendan aortaya kross klemp altında anastamoz yapıldı.

Sistemdeki havaların tahliyesi ve kanama kontrölünün ardından hemodinami ve vücut ısılarının normale gelmesinden sonra CPB'a son verildi. Kanama kontrolünü takiben drenler yerleştirilerek, katlar anatomik olarak kapatıldı. Hasta KVC yoğun bakım ünitesine alındı. Operasyonda güvenli bir cerrahi için, serebral perfüzyonun devamı açısından öncelikle dacron greftle asendan aorta-bisubklavian bypass yapılmıştır. Sonrasında eş zamanlı olarak aortakoroner bypass ve mitral valav operasyonu gerçekleştirilmiştir.

Postop 1. gün vazopressör ilaç ihtiyacı olan hasta genel durumunun iyi olması üzerine 2. gün servise alındı. Servis takiplerinde genel durumu iyi seyreden ve herhangi bir komlikasyon gelişmeyen hastaya medikal tedavisi düzenlenerek ve önerilerde bulunularak poliklinik kontrölüne çağrılmak üzere postop 9. günde cerrahi şifa ile taburcu edildi.

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TARTIŞMA

TA genellikle genç kadınlarda erkeklere göre daha sıktır ve ortalama başlangıç yaşı Asya'da 25, Avrupa'da ise 41 olarak verilmektedir (2). TA'nin erkeklere göre kadınlarda yaklaşık 9 kat fazla görüldüğü bildirilmesine karşın, kadın ve erkeklerin eşit tutulduğunu belirtenler de vardır (8). Arterde darlık, tam tıkanma, anevrizma oluşumu, genişleme, bükülme ve fistül oluşumu şeklinde tezahür eden Takayasu arteritinin koroner arter tutulumuna ilk cerrahi müdahale, aortokoroner bypass tekniğinin ortaya konulmasından önce, 1961 yılında Inokuchi tarafından hastanın iki taraflı internal mammaria arterlerinin bağlanması suretiyle gerçekleştirilmiştir (9). Bu ilk müdahaleden günümüze kadar semptomatik koroner arter tutulumu sebebiyle ameliyat edilen Takayasu arteriti vakalarının sayısı 100'den azdır (10). Bu hastaların çoğunu japonlar teşkil etmiştir. Ayrıca bu hastaların yaklaşık üçte birinde koroner arter lezyonlarına ek olarak aort yetersizliği ve daha az oranda da mitral yetersizliği tesbit edilmiştir. TA'de en sık daralma, nadiren anevrizma ve dilatasyon şeklinde damar değişiklikleri gözlenir. Kerr ve ark. (1) en sık karotid arterlerin (%70), ikinci sıklıkta subklavian arterlerin (%45) daraldığını, femoral (%3.3) ve renal (%1.7) arterlerin ise çok az tutulduğunu belirtmişlerdir. Aynı araştırmacılar, üst ekstremitenin alt ekstremiteye göre daha sık tutulduğu ve özellikle klaudikasyonun erişkinlerde fazla olduğunu belirtmişlerdir. Açık kalp ameliyatı olacak hastalarda Takayasu arteritinin olması vasküler tutulum özelliklerine bağlı olarak; monitorizasyon, cerrahi manüplasyon ve greft seçimi, cerrahi teknik, postoperatif nörolojik sekel gelişimi açısından önem taşımaktadır. Asendan aortadaki tutulum açık kalp cerrahisinde kanülasyon ve proximal anastamoz gibi cerrahi manüplasyonlarda problem yaratabilmektedir. Erken dönemde aortadaki inflamasyona bağlı olarak safen ven oklüzyonu gelişebilir. Ancak çoğu zaman İTA kullanımı da mümkün olmamakta, dacron greft üzerine yapılan proximal anastamozlarda da erken oklüzyon bildirilmektedir.

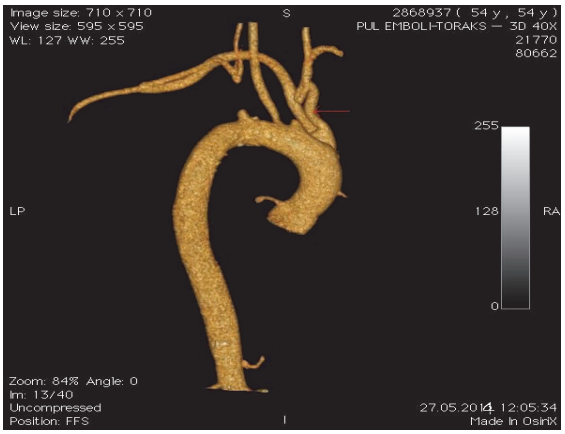
TA'nde kardiyak tutulum olasıdır; %70 kardiyomegali, %28 kalp yetmezliği ve %13,6 angina pectoris bildirilmiştir (11). Kalp yetmezliğinin ana nedeni ise aort kökü genişlemesine ikincil kalp yetmezliğidir. TA'nde en sık aort ve ana dalları etkilenmekte, aortta ise özellikle aortik ark tutulmaktadır (1,2,8). Olgumuzda aortik ark normal bulunmuş ve yalnızca innominate arter ile sol subklavian arterde total tıkanıklık saptanmıştır. Koroner arter hastalığı oranı TA'nde %6-16 olarak verilmektedir (1,2,11,12). TA'nde ana tedavi yöntemi yüksek doz kortikosteroid tedavisidir ve çoğu olguda yalnızca steroid remisyon için yeterlidir. Ancak yan etki durumunda veya ilaç dozunun yüksek tutulamayacağı olgularda immünsupresif tedavi eklenebilir (2,8,13). Bizim olgumuz remisyon döneminde olduğu için steroid tedavisi yeterli olmuştur.

Enflamatuar etki ameliyatın zamanlanması, cerrahi müdahalenin türü ve ameliyat sonrası uygulanacak tedavi konusunda birtakım tereddütler doğuruyorsa da, Takayasu arteritinin koroner arter tutulumunda cerrahi yaklaşım günümüzde etkinliğini ortaya koymuş bir yöntemdir (14,15). Vakaların çoğunda lezyonlar, koroner arterlerin ostium veya proximal bölümündedir (16). Damar darlığının ileri derecede olması, medikal tedaviye yanıt alınamaması veya ani tromboz durumlarında by pass gereklidir; greft operasyonu (ven veya yapay), ,transluminal anjioplasti veya endovasküler stent gibi yöntemlerle by pass uygulanmaktadır (1,2,17). TA'nde en başarılı yöntem otolog ven greftidir ve yapay greftlerin %36'sı tekrar tıkanmaktadır. Vaskülitlerde öncelikle akut faz yanıtlarının düşürülmesi ve remisyon sonrasında invaziv işlemlerin yapılması önerilmektedir (2,13,17). Aktif dönemde inflamasyon nedeniyle girişim yerinde anevrizma ve kronik dönemde darlık gelişme olasılığı vardır. Hasta aktif arterit döneminde olsaydı, steroid tedavisi başlanıp remisyona girmesi beklenip daha sonra operasyona alınırdı.

TA'nin koroner arter tutulumunun cerrahi tedavi sonuçları, steroidlerin ameliyat sonrası kullanıma girmesi ile iyileşme göstermiştir (15). TA'nde hipertansiyon, kalp yetmezliği, miyokard infarktüsü, inme, anevrizma rüptürü ve böbrek yetmezliği mortalite nedenleri olarak bilinmektedir (1,2,8,11,17). Buna karşın tedavi altındaki olguların 10 yıllık sağ kalım oranının oldukça yüksek (%80-90) olduğu belirtilmektedir (1,2,17). Bizim olgumuz yaklaşık 6 aydır izlem altındadır ve bu komplikasyonlardan hiçbirisi gelişmemiştir.

SONUÇ

Sonuç olarak, Takayasu arteritinde; aort ve ana dalları gibi vasküler tutulumlarla birlikte, koroner arter tıkanıklıkları ve kalp kapak hastalıkları eşlik edebilmektedir. Açık kalp cerrahisi adayı hastalarda klinik ve anatomik özelliklere göre uygulanacak farklı stratejiler açık kalp cerrahisinin güvenle yapılmasına izin verir. Remisyon dönemindeki Takayasu arteritli olgularda, serebral perfüzyonun devamı açısından açık kalp cerrahisiyle eş zamanlı vasküler prosedürlerin güvenle uygulanabileceğini düşünüyoruz. Ancak bu tedavi yönteminin güvenirliliği, etkinliği ve dayanıklılığının belirlenmesi için bu hastaların uzun dönem sonuçlarının yakın takip edilmesi gereklidir.



Resim 1. Takayasu arteritli olgunun CABGx2 ve MVR'a eş zamanlı uyguladığımız Asendan Aorta-Bisubklavian by pass Y greftin BT Angiorafideki görüntüsü.

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Spontaneous Ruptured Parasellar Dermoid Tumor: CT and MRI Findings

Spontan Rüptüre Parasellar Dermoid Tümör: BT ve MRG Bulguları

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Abstract

Dermoid tumors are benign, rare congenital intracranial lesions which arise from the ectoderm. These tumors are seen as non-enhancing, low-density masses that may include peripheral calcification on computed tomography. On magnetic resonance imaging, these tumors are observed hyperintense on T1-weighted images, depending on the lipid content while they are heterogeneous hypo-hyperintense on T2 weighted images. Lipid fraction of these tumors lose their intensity in the fat-suppressed T1 sequences. Spontaneous rupture of dermoid tumors occurs in a small percentage of patients. When they are ruptured, fat droplets spread throughout the subarachnoid space and ventricular system. These fat droplets in the subarachnoid space and ventricular system are often seen as hypodens on computed tomography and as hyperintense on T1 weighted images on magnetic resonance imaging. Also, fat-liquid leveling in the ventricular system have a diagnostic value on magnetic resonance imaging. In this study, we present the computed tomography and magnetic resonance imaging findings of a ruptured parasellar dermoid tumor.

Keywords: Dermoid; Ruptured; CT; MRI.

Öz

Dermoid tümörler, ektodermden köken alan, nadir görülen, intrakranial benign konjenital kitlelerdir. Bilgisayarlı tomografide yağ içerikli, kontrast tutulumu göstermeyen, periferik kalsifikasyon içerebilen, düşük dansitede kitle olarak izlenirler. Manyetik rezonans görüntülemede ise T1 ağırlıklı görüntülerde yağ içeriğine bağlı hiperintens, T2 ağırlıklı görüntülerde ise değişen sinyal intensitelerinde heterojen hipo-hiperintens sinyal özellikleri gösterirler. Bu tümörlerin lipid kısmı yağ baskılı sekanslarda T1 intensitelerini kaybederler. Dermoid tümörlerin spontan rüptürü hastaların çok küçük bir yüzdesinde görülür. Rüptüre olduklarında subaraknoid ve intraventriküler yayılım gösterirler. Dermoid tümör rüptürü sonucu subaraknoid boşlukta ve ventriküler sistemde bilgisayarlı tomografide hipodens, manyetik rezonans görüntülemede ise T1 ağırlıklı görüntülerde hiperintens yağ partiküllerinin görülmesi tipiktir. Ayrıca manyetik rezonans görüntülemede ventriküler sistemde yağ-sıvı seviyelenmesinin izlenmesi tanısaldır. Bu olgu ile, suprasellar yerleşimli rüptüre olmuş bir dermoid tümörün kranial bilgisayarlı tomografi ve manyetik rezonans görüntüleme bulgularının sunulması amaçlanmıştır.

Anahtar Kelimeler: Dermoid; Rüptüre; BT; MRG.

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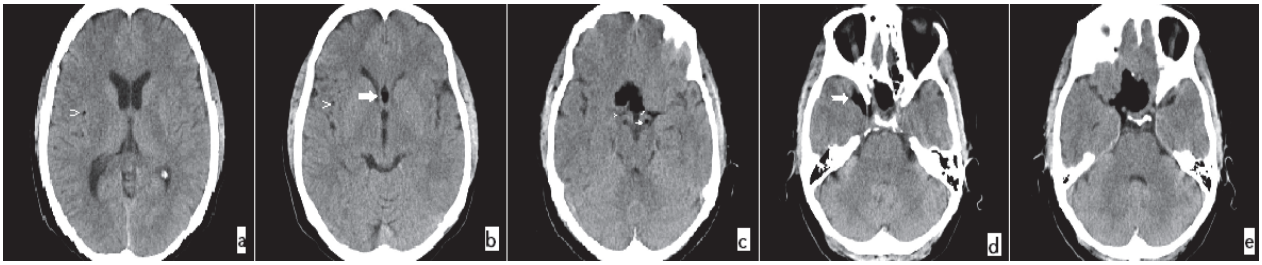
GİRİŞ

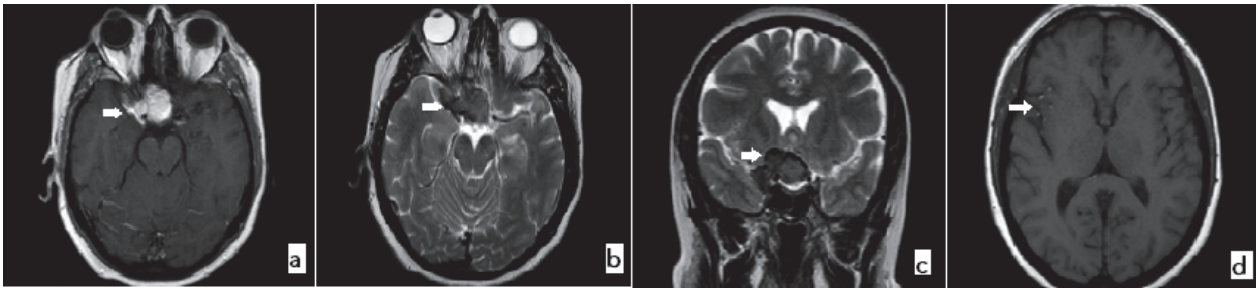
Dermoid tümörler (DT), nadir görülen intrakranial benign konjenital kitlelerdir. Tüm intrakranial lezyonların %1'den azını oluştururlar (1). Embriyolojik dönemde intrakranial bölge içerisinde kalan ektodermal hücrelerden köken alırlar. Deskuame epitel, sebase bez sekresyonları, yağ veya saç içebilirler ve yavaş büyürler (2). En sık yerleşim yerleri sellar, parasellar bölge ve frontonazal bölgedir. Daha az sıklıkla posterior fossa'da yerleşim gösterirler (3). Genellikle 3.-4. dekatlarda görülürler (4). Nadiren Goldenhar (okuloaurikülo-vertebral displazi) ve Klippel-Feil sendromları ile ilişkili olabilirler (2). Skuamöz hücreli karsinoma malign dejenerasyon nadir olmakla birlikte bildirilmiştir (2,4). DT'ün spontan rüptürü hastaların çok küçük bir yüzdesinde görülür. Rüptüre olduklarında subaraknoid ve intraventriküler yayılım gösterirler (5). Rüptür sonucunda kimyasal menenjit, nöbet, serebral iskemi ve hidrosefali gibi ciddi komplikasyonlar gelişebilir (2,4). Semptomlar tipik olarak, rüptür olduğunda değil, dağılmış içeriğin iritasyon etkisinin başlaması ile (3 ay -6.5 yıl arası) birlikte görülür (4). Baş ağrısı (%32) ve nöbet (%30) en sık semptomlardır (2). DT rüptürü sonucu subaraknoid boşlukta yağ partiküllerinin görülmesi ve yağ içeriğinin saptanması bilgisayarlı tomografi (BT) ve manyetik rezonans görüntülemede (MRG) tipik bulgular oluşturmaktadır. Bu olgu ile, suprasellar yerleşimli rüptüre olmuş bir DT'ün kranial BT ve MRG bulgularının sunulması amaçlanmıştır.

OLGU SUNUMU

Başının sağ tarafında, bir haftadır sürekli olan ve analjeziklerle rahatlamayan başağrısı şikayeti ile başvuran elli iki yaşındaki bayan hastanın ağrılarının on yıldır devam ettiği ancak şikayetinin son bir aydır frontalde ve ensede hemen hergün, özellikle ani postür değişikliklerinde arttığı öğrenildi. Hastanın travma veya major cerrahi hikayesinin olmadığı öğrenildi. Yapılan nörolojik muayenesinde sensörimotor defisit, meningeal irritasyon bulgusu veya intrakranial hipertansiyon bulgusu saptanmadı. Hastanın labaratuar bulguları normal sınırlar içindeydi. Kontrastsız kranial BT incelemesinde (Resim 1), parasellar bölgede, düzensiz sınırlı, septum pellusidum, bilateral orta serebral arter oluğu, interpedinküler sistern ve sağda temporal bölgeye uzanan, kalsifikasyon içeren, yağ dansitesinde (-45 —-52 HU dansitede) lezyon izlendi. Ayrıca sağ Silvian fissür ve sağ pariyetal bölgede hemisferik kortikal sulkuslarda, subaraknoid mesafeye dağılmış milimetrik yağ dansiteleri saptandı. Kranial MRG incelemesinde (Resim 2), lezyon T1 ağırlıklı (T1A) görüntülerde hiperintens, T2 ağırlıklı (T2A) görüntülerde hipointens sinyal özelliklerinde izlendi. T1A görüntülerde subaraknoid mesafeye dağılmış multipl hiperintens yağ damlacıkları izlendi. T1A kontrastlı görüntülerde kontrastlanma saptanmadı (Resim 3). Short tau inversion recovery (STIR) sekansında lezyonun baskılandığı ve hipointens sinyal özelliğinde olduğu görüldü (Resim 4). Lezyon rüptüre dermoid tümör ile uyumlu olarak değerlendirildi ve beyin cerrahisine refere edildi. Opere olan hastanın patolojisi de dermoid tümör olarak geldi.



Resim 1. Kranial BT incelemesinde, aksiyel kesitlerde, parasellar bölgede, septum pellusidum (b), bilateral orta serebral arter oluğu (c), interpedinküler sistern (c) ve sağda temporal bölgeye (d) uzanan, düzensiz sınırlı, yağ dansitesinde lezyon izleniyor. Ayrıca sağ pariyetal bölgede, subaraknoid mesafeye dağılmış milimetrik yağ dansiteleri (a, b) görülüyor.



Resim 2. Lezyonun aksiyel T1A görüntülerde (a) hiperintens, aksiyel (b) ve koronal (c) T2A görüntülerde hipointens sinyal özellikleri gösterdiği izleniyor. Aksiyel T1A kesitte (d) subaraknoid mesafeye dağılmış multipl hiperintens yağ damlacıkları görülüyor.

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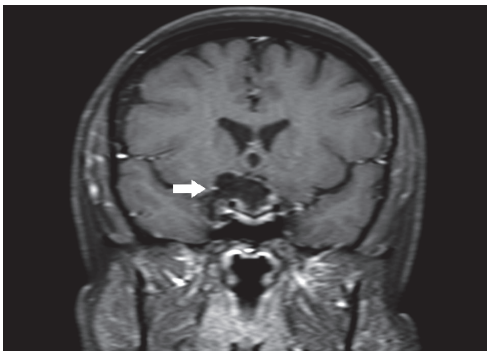
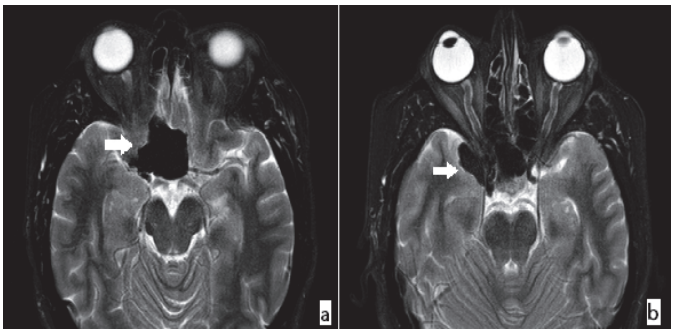


Resim 3. Koronal T1A kontrastlı imajda, lezyonda kontrastlanma izlenmiyor.



Resim 4. STIR sekansında (a, b), aksiyel görüntülerde lezyonun baskılandığı ve hipointens sinyal özelliğinde olduğu görülüyor.

TARTIŞMA

İntrakraniyal DT, nadir görülen, epidermis ve dermisten köken alan, saç, ter ve yağ komponentleri içerebilen benign tümörlerdir. Embriyonik dönemde gelişmesine rağmen yavaş büyümesi nedeniyle erişkin döneme kadar bulgu vermeyebilir. Aynı nedenle semptom ya da bulgu vermeden oldukça büyük boyutlara ulaşabilir (6). Klinik bulgu lezyonun yerleşimine ve komşu parankime basısına bağlıdır. DT, travma sonrası, cerrahi sırasında veya spontan olarak rüptüre olabilir. Rüptüre olduğunda kist içeriği subaraknoid mesafeye yayılır. Rüptüre DT'de başağrısı (32%) ve nöbet (30%) en sık bulgular olmakla birlikte bulantı, kusma, görme bozuklukları, baş dönmesi, aseptik kimyasal menenjit, vazospazma bağlı geçici serebral iskemi, hemiparezi, olfaktör sanrılar, mental değişiklikler veya nadiren hızlı gelişen hidrosefali gibi klinik bulgular görülebilir (2). Bizim olgumuzda da bulgular geç yaşta ortaya çıkmış ve baş ağrısı şikayeti ile prezente olmuştur.

İntrakraniyal rüptüre DT, BT ve MRG'de tipik bir görünüm oluşturur. BT'de yağ içerikli, kontrast tutulumu göstermeyen, periferik kalsifikasyon içeren, düşük dansitede (0 ile -100 HU dansite arasında), kitle olarak olarak izlenir (2). DT çevresinde ödem izlenmez. Ventriküler sisteme rüptüre olursa BOS içinde ve ventriküler sistemde yağ-sıvı seviyelenmesi, hidrosefali izlenebilir. Rüptüre DT'de, subaraknoid aralıkta ve ventriküler sistemde hipodens yağ partiküllerinin izlenmesi tanısal BT bulgusudur (7,8). Bizim olgumuzda lezyon -45 — -52 HU dansitede ve kalsifikasyon içermekte idi. Çevresinde ödem mevcut değildi.

MRG'de ise DT, T1A görüntülerde yağ içeriğine bağlı hiperintens, T2A görüntülerde ise değişen sinyal intensitelerinde heterojen hipo-hiperintens izlenir. Kist, içindeki farklı komponentlere bağlı olarak heterojen izlenebilir. Bu tümörlerin lipid kısmı yağ baskılı sekanslarda T1 intensitelerini kaybederler (5). Bizim olgumuzda da lezyon T1A görüntülerde hiperintens, T2A görüntülerde hipointens sinyal özelliklerinde idi. Ayrıca lezyon STIR sekansında baskılandı.

DT, rüptüre olduğunda kolesterol kristalleri BOS'a geçer ve subaraknoid aralığa, özellikle de serebellopontin köşe, suprasellar ve prepontin sistern ve sagittal sinüs boyunca yayılır (2). Lipoid aseptik menenjit yağ yayılımına bağlı kolesterol kristallerinin neden olduğu meningeal iritasyon sonucu gelişir ve en sık komplikasyondur (2). Bu durumda subaraknoid mesafede ve ventriküler sistemde T1A görüntülerde hiperintens yağ partiküllerinin, ventriküler sistemde yağ-sıvı seviyelenmesinin izlenmesi tanısaldır (7,8). Yağ baskılı sekanslar lezyon içindeki yağ varlığını doğrulayabilir. DT, kontrast tutulumu göstermez. Rüptüre DT'ü bulunan hastada yaygın leptomeningeal kontrastlanma bulunması kimyasal menenjit lehine yorumlanabilir (2). Bizim olgumuzda da Silvian fissür ve pariyetal bölgede hemisferik kortikal sulkuslarda, subaraknoid mesafeye dağılmış milimetrik yağ dansiteleri izlenmekteydi. Lezyon kontrast tutulumu göstermemekteydi ve leptomeningeal kontrastlanma mevcut değildi.

Rüptüre DT tanısında, MRG ile rüptüre DT'ün subaraknoid mesafeye yayılımı, kitlenin kesin sınırları, kitle etkisi ve komşu serebral parankim, MRG anjiografi ile kitlenin vasküler yapılar ile komşuluğu ayrıntılı bir şekilde değerlendirilebilir. Bu nedenle BT ile rüptüre DT tanısı alan hastaların preoperatif MRG ile değerlendirilmesi önerilmiştir (4). Oldukça ciddi ve fatal bir durum olduğu düşünülen rüptüre DT'ün, MRG'nin yaygın kullanımı ile birlikte önceleri düşünüldüğünden daha sık izlendiği ve bazen asemptomatik ya da hafif semptomlarla da seyredebildiği belirlenmiştir (9). DT saptanan olgularda genel yaklaşım cerrahi olup, kisti kapsülü ile birlikte çıkarmak gerekmektedir. Ancak genellikle çevre yapılara yapışıklıklar nedeniyle ve rüptüre olduğunda subaraknoid aralığa yayılması nedeniyle total eksizyonu mümkün olmamaktadır (10).

Ayırıcı tanıda epidermoid, kraniofarinjiom, lipom ve teratom düşünülmelidir. Epidermoid kistler sıklıkla serebellopontin açı sisternasında ve parasellar alanda yerleşim gösteren, konjenital, benign tümörlerdir. BT'de epidermoid kistler BOS ile benzer hipodansitededir. Kemik erozyonu görülebilir. MRG'de T1 ağırlıklı sekanslarda BOS'a göre hafif hiperintens, daha az sıklıkla hiperintens (beyaz epidermoid) veya hipointens (siyah epidermoid) izlenirler. T2A görüntülerde BOS'a göre izointens veya hafif hiperintens izlenirler. Diffüzyon ağırlıklı sekanslarda tipik olarak diffüzyon kısıtlaması izlenir. Epidermoidler kontrast tutulumu göstermez. Kontrastlanması malign dejenerasyonu düşündürür (2).

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Kraniofarinjioma intrasellar ve suprasellar yerleşimli, genellikle 3. ventriküle uzanan, kafa tabanı erozyonuna neden olabilen, agresif orta hat kitlelerindendir. Çocukluk çağında görülen adamantinomatöz tipi BT ve MRG'de, solid ve kistik komponentleri olan heterojen kitle olarak izlenir. Nodüler kalsifikasyonlar içerebilir. Solid komponenti kontrast tutulumu gösterir. Rim tarzında kontrast tutulumu da gösterebilir. Kraniofarinjiomanın, erişkinlerde görülen papiller tipinde ise kistik komponent ve kalsifikasyon bulunmaz. MRG'de T1A ve T2A görüntülerde heterojen sinyal özellikleri gösterirler. Bu lezyonlar heterojen kontrast tutulumu gösterirken, dermoid tümörler minimal kontrast tutulumu gösterirler veya genelde kontrastlanmazlar (2).

İntrakranial lipomlar, sıklıkla korpus kallozum agenezisi ile birlikte bulunan, iyi sınırlı, matür, non-neoplastik, yağ dokusundan oluşan kitlelerdir. İnterhemisferik fissür, supratentorial alan, pineal bölge lipomun sık izlendiği lokalizasyonlar olup MRG'de düzgün sınırlı, T1 ağırlıklı sekanslarda hiperintens, T2 ağırlıklı sekanslarda hipointens, homojen olarak izlenir. DT'e göre daha homojendirler ve kapsüler kalsifikasyon nadiren görülür. Yağ baskılı sekanslarda baskılanır ve hipointens izlenirler. Kontrast tutulumu göstermezler. Kistik komponent içermezler (2).

Teratom, ektoderm, mezoderm ve endoderm'den köken alır. Buna bağlı kalsifikasyon, beyin omurilik sıvısı, yağ ve yumuşak doku içerebilir. Orta hatta, sıklıkla optik kiazma ile pineal gland lokalizasyonunda izlenir. Genellikle multikistik, multiloküledir. MRG'de belirgin heterojen sinyal özellikleri gösterir. Yumuşak doku komponentinin kontrastlanması tipiktir (2). Difüzyon ağırlıklı görüntülerde solid komponentde diffüzyon kısıtlaması izlenir (7).

Sonuç olarak; DT'ün spontan rüptürü oldukça nadirdir. İntrakranial DT ve rüptüre DT'ün BT ve MRG'de tama yakın doğrulukta tanı koydurucu görüntüleme özellikleri mevcuttur. Dermoid tümörlerin BT'de, tümörün predominant lipid içeriğine bağlı olarak tipik homojen hipodens görüntüleri vardır. MRG'de T1A görüntülerde hiperintens, T2A görüntülerde heterojen hipo-hiperintens sinyal özellikleri gösterirler. Bu tümörlerin lipid kısmı yağ baskılı sekanslarda T1 intensitelerini kaybederler. Subaraknoid mesafe ve ventriküllerde BT'de hipodens, MRG'de T1A sekanslarda hiperintens izlenen alanlar da rüptüre bağlı lipit damlacıklarını temsil eder. DT tedavisi cerrahidir, ancak çevre yapılara yapışıklıklar ve rüptüre olduğunda subaraknoid mesafeye ve ventriküler sisteme yayılması nedeniyle total eksizyonu genellikle mümkün olmamaktadır (12).

35. Ulusal Radyoloji Kongresi, 1-16 Kasım 2014, Antalya (poster bildiri)

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The Long-Term Results of the Combination of Dermofat Graft and Platelet Rich Plasma in a Patient with Hemifacial Atrophy: A Case Report

Hemifasiyal Atrofide Trombositten Zengin Plazma ve Dermofat Greft Kombinasyonunun Uzun Dönem Sonucu: Olgu Sunumu

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Abstract
There are many surgical techniques for repairing the contour deformities of hemi-facial atrophy. In this report, we aim to present the long-term results of a patient whom we treated with a combination of fat graft and platelet rich plasma, which is known to enhance the viability of the dermofat graft. A 30-year-old male patient was admitted with the complaint of his left hemi-facial atrophy. The anamnesis revealed that the hemi-facial atrophy had not been progressing for the last 5 years. We discussed the various treatment choices with the patient and decided to perform a combination of fat graft and the platelet rich plasma, simultaneously. We achieved aesthetically satisfying results. The platelet rich plasma contains growth factors and cytokines and by these contents it decreases the adverse effects in terms of the formation of the absorption and the fat cysts, and it improves the viability of the fat graft by enhancing neovascularization. Compared to free flap procedures, which are time consuming and risky as well as they cause morbidity for donors, the platelet rich plasma combined with fat grafts may be an alternative application for its advantages such as its easy application and reproducible procedure.
Keywords: Facial Hemiatrophy; Fat Cells; Tissue Grafts; Platelet-Rich Plasma.

Öz
Hemifasiyal atrofi de kontur bozukluklarının düzeltilmesi için birçok cerrahi yöntem kullanılmaktadır. Dermofat greftin yaşayabilirliğini arttırdığı bilinen trombositten zengin plazma ile yağ greftini kombine ettiğimiz bir hastmızdaki uzun dönem sonuçlarını paylaşmak istiyoruz. Hastamız 30 yaşında erkek hasta yüzünün sol yarısında erime şikâyeti ile geldi. Son 5 yıldır yüzdeki erime şikâyetinin ilerlemediğini öğrendik. Diğer tedavi seçeneklerini hasta ile paylaşarak yağ grefti ile eş zamanlı trombositten zengin plazma uygulamaya karar verdik. Estetik açıdan tatmin edici sonuçlar aldık. Trombositten zengin plazma içerdiği büyüme faktörleri ve sitokinler sayesinde yağ greftlerinde ortaya çıkan absorbsiyon ve yağ kistleri oluşumu gibi olumsuz etkileri azaltarak, neovaskülarizasyonu arttırarak yaşayabilen yağ doku miktarını arttırmaktadır. Uzun süren, riskli, donor alanda morbiditeye neden olan serbest flep uygulamalarına kıyasla daha kolay ve tekrarlanabilen bir prosedür olduğundan trombositten zengin plazma ile kombine yağ greftlerinin alternatif olabileceği kanaatindeyiz.
Anahtar Kelimeler: Fasial Hemiatrofi; Yağ Hücreleri; Doku Greftleri; Trombositten Zengin Plazma.

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GİRİŞ

Parry-Romberg sendromu (PRS) veya Romberg sendromu genellikle yüzün bir tarafındaki deri, subkutan yağ, kas, kıkırdak ve kemik dokunun progresif atrofisi olarak tanımlanmıştır. Daha sonra bu sendromun kazanılmış bir hastalık olduğu ve progresif hemifasiyal atrofi olarak isimlendirilmesi gerektiği belirtilmiştir. Karakteristik olarak atrofi yıllar içinde yavaşça gelişerek durağan hale gelmektedir. Bu sendrom daha çok bayanlarda ve özellikle yüzün sol tarafında görülmektedir (1). Hastalığın etiyolojisi tam olarak bilinmemekle birlikte heredite, viral enfeksiyonlar, travma, endokrin bozukluklar, otoimmmün hastalıklar, sempatik sistem bozukluklar, trigeminal nörit, bağ doku hastalıkları özelliklede skleroderma etiyolojide suçlanmaktadır (1).

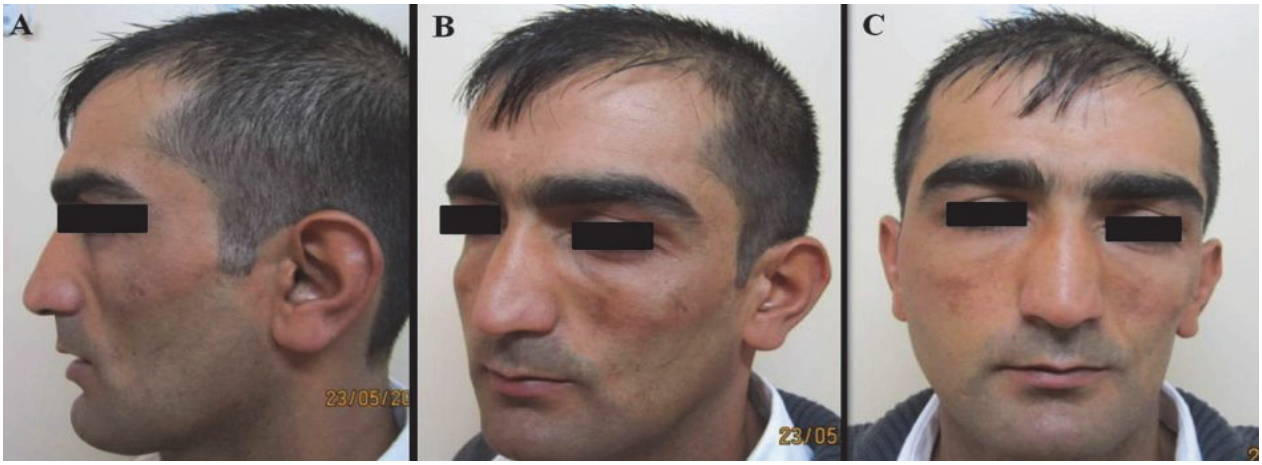
Yüzdeki bu kontur deformitesinin giderilmesi plastik cerrahide çözüm bekleyen konulardan biridir. Tedavi için önerilen yöntemlerin çoğunluğu yumuşak doku rekonstrüksiyonu içindir. Kontur deformitelerinin düzeltilmesinde dermofat greft birçok hastada kullanılmakta ve genel olarak konulan greftin zamanla absorbe olduğunu bildirilmektedir. Trombositlerin alfa granüllerinde bulunan birçok büyüme faktörü ve sitokinin yağ greftlerinin yaşayabilirliğini arttırabileceği ve bu konunun araştırılması gerektiği belirtilmiştir (2). Biz bu çalışmada dermofat greftin vaskülarizasyonunu arttırmak için trombositten zengin plazma (TZP) kullanarak dermofat greftin yaşayabilirliğini arttırmayı amaçladığımız ve postoperatif 3 yıllık sonuçları bulunan bir hastamızın bulgularını paylaşmak istiyoruz.

OLGU SUNUMU

30 yaşında erkek hasta yüzünün sol yarısında 11 yaşında başlayan ve 25 yaşına kadar devam eden bir erime şikayeti ile başvurdu. Hasta başvuru esnasında durağan dönemde olduğu hastalığın artık ilerlemediği öğrenildi. Yapılan sorgulamada ailesinde bu şekilde hiç akrabasının olmadığı öğrenildi. Hastada eşlik eden herhangi bir sistemik hastalığı yoktu.

Yapılan muayenede her iki yanakta hiperpigmentasyonların olduğu, sol yüz yarısında özellikle subkutan dokunun atrofiye olduğu belirlendi (Resim 1). Yüz kemiklerindeki etkilenme düzeyinin belirlenmesi için çekilen üç boyutlu tomografide kemik yapıların minimal düzeyde etkilendiği ve müdahale gerekmediği düşünüldü (Resim 2). Hastaya yapılabilecek diğer operasyonların faydaları, başarı düzeyleri ve komplikasyonları hakkında bilgilendirme sonrasında dermofat greftle birlikte tombositten zengin plazma uygulamasına karar verilerek onam formu alındı. Standart pozisyonlarda fotoğrafları çekildi.

Hasta genel anestezi ile operasyona alındı. Yüzdeki yumuşak doku eksikliği haritalanarak defektin bulunduğu alan belirlendi. Defekt haritası sağ inguinal bölgede kıl içermeyen alana çizildi. Donor alanın kapatımının kolaylaştırılması için eliptik insizyon yapıldı. Sol yüz bölgesi preauriküler bölge, sol göz kapağı altından subsiliyer ve sol nazolabial sulkustan açılarak yüzeyel muskuloaponevrotik sistem (superficial musculoaponeurotic system: SMAS) altında bir boşluk oluşturuldu. Hastanın sağ inguinal bölgeden kıl içermeyecek şekilde cilt deepitelize edilerek dermofat greft hazırlandı. Dermofat greft yağ nekrozu olma potansiyeli nedeniyle planlanan volümden %50 daha fazla alındı. Hastadan alınan 30cc kan 5000 devirde 3 dk santrifüj edilerek kan hücresel komponenetleriyle plazma kısmı ayrıştırıldı. Trombositten zengin plazma elde etme süreci hasta operasyona alındığında operasyon başlamadan kan alınarak operasyon süresindeki uzama engellendi. Elde edilen TZP, kalsiyum klorür ile karıştırılarak trombositlerin degranüle olması ve büyüme faktörlerini salgılaması sağlandı (3). Büyüme faktörü içeren plazma dermofat greftin altına ve etrafına ve içine enjekte edildi. Greft donor alanı primer olarak kapatıldı.



Resim 1. Hastanın başvuru esnasında çekilen fotoğrafları
A: Sol lateralden görüntü
B: Sol oblik pozisyonda görüntü
C: Önden görüntü

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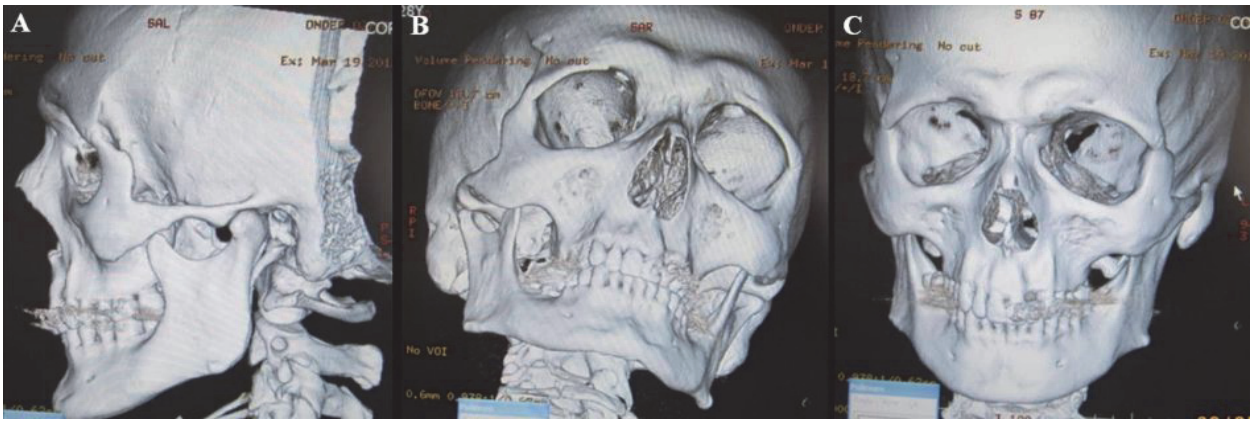
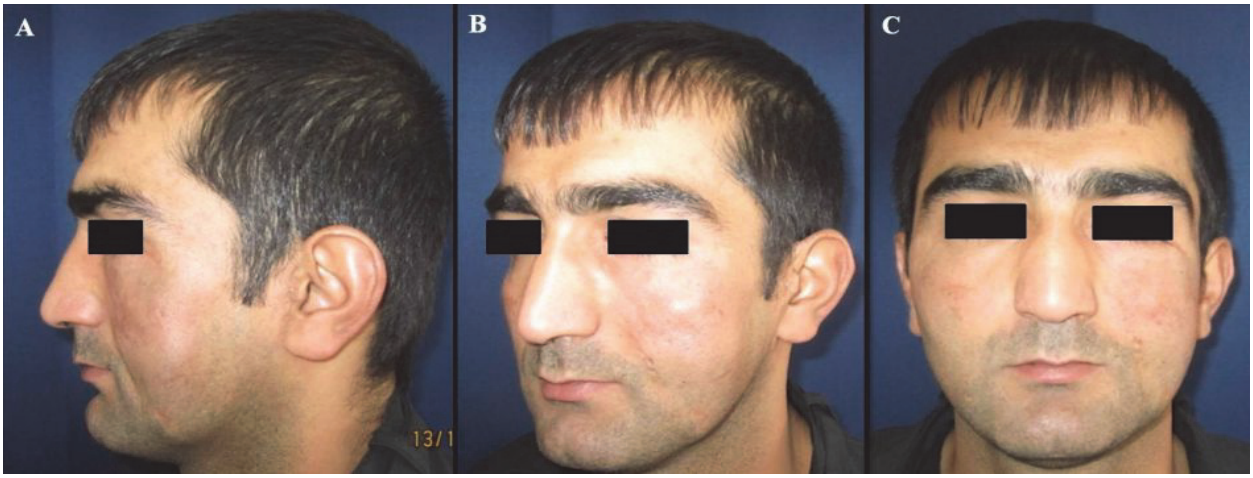


Resim 2. Hastanın başvuru esnasında çekilen üçboyutlu tomografisi
A: Sol lateralden görüntü
B: Sol infero-oblik pozisyonda görüntü
C: Önden görüntü

SONUÇ

Hastada postoperatif hematom, seroma ve enfeksiyon gelişmedi ve postoperatif 2. gün taburcu edildi. Hastaya taburcu edilirken yeni damarlanmaların oluşma sürecini bloke etmemesi için yüz mimiklerini 10 gün boyunca kullanmaması tavsiye edildi. Yüzdeki dikişler 5. günde, inguinal bölgedeki dikişler ise 10. günde alındı. Hasta postoperatif 3., 6., 12., 24. ve 36. aylarda kontrole çağrılarak preoperatif çekilen pozisyonlarda fotoğraflandı (Resim 3). Hastaya takip eden periyotta başka herhangi bir cerrahi uygulanmadı. Hastanın yüz görünümü simetrik, estetik olarak tatmin ediciydi ve hasta sonuçtan memnundu.



Resim 3. Hastanın operasyon sonrası 36. ayında çekilen fotoğrafları
A: Sol lateralden görüntü **B:** Sol oblik pozisyonda görüntü **C:** Önden görüntü

TARTIŞMA

Hemifasiyal atrofi progresif, kendikendini sınırlayan, yüzün bir tarafını tutan kraniofasiyal bir asimetridir (4). Yüzdeki asimetrinin düzeltilmesi için literatürde silikon enjeksiyonu, yüz protezleri, otojen yağ greftleri ve değişik free fleplerin kullanıldığı ve değişik başarı oranları bildirilmiştir (5-7).

Silikon ve protez gibi vücuda yabancı materyallerin kullanılmasında enjeksiyonu sonrası erken dönemde enfeksiyon ve alerjik reaksiyon, geç dönemde ise granülom, pseudokist oluşumu gibi immünolojik reaksiyonlar bildirilmiştir (8).

Serbest fleplerle rekonstrüksiyonda birçok serbest flep tanımlanmıştır. Serbest flep seçeneklerinden hastaya uygun olanı yapılmakta ancak üzerinde fikir birliği sağlanmış bir serbest flep seçeneği henüz oluşmamıştır. Ayrıca serbest fleplerin uygulanmasının belirli bir öğrenme süreci gerektirmesi, operasyon sürelerinin uzun olması, donor alandaki skar ve fonsiyonel deformiteler ve revizyon operasyonlarının gerekmesi gibi bazı dezavantajları (9) nedeniyle tercihler otolog yağ greftlerinin kullanılmasına yönelmiştir.

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Liposakşının teknik olarak standardize edilmesinden sonra yağ enjeksiyonu birçok doku defektinin onarımında kullanılmıştır (10). Yağ greftlerinin rezorbsiyonunu azaltıcı birçok çalışma yapılmıştır (2). Otolog yağ grefti uygulanması kolay, bol bulunabilmesi, düşük maliyeti allojenik materyallere kıyasla allerji potansiyelinin düşük olması, operasyon süresinin ve postoperatif komplikasyonların serbest fleplere nazaran daha az olması, ayrıca yağ doku kökenli kök hücre kaynağı olması nedeniyle basit bir çözüm sağlamakta son zamanlarda önerilmektedir (11).

Yağ dokusunun kendisinde bulunan kök hücrelerin ve trombositlerin alfa granüllerinde bulunan büyüme faktörleri ve sitokinler nedeniyle hücre proliferasyonu, kemotaksis, anjiogenezis, hücre diferansiasyonu, ekstrasellüler matriks sentezinin arttırılması gibi etkileri nedeniyle de otolog yağ greftlerinin yaşayabilirliğini arttırma potansiyelleri vardır (12). Trombositlerin alfa granüllerinde bulunan büyüme faktörleri degranüle olduktan sonra sitoplazmik sinyal proteinleri üzerine etki ederek trozin kinaz (platelet-derived growth factor [PDGF], fibroblast growth factor [FGF], insulin-like growth factor [IGF], vascular endothelial growth factor [VEGF], epidermal growth factor [EGF]) veya serin tirozin kinazı (transforming growth factor [TGF]-beta, bone morphogenetic protein [BMP]) aktive ederek çekirdekteki bazı genlerin ekspresyonunu arttırarak etki etmektedirler (13). Sonuç olarak sadece hedef hücrelere değil aynı zamanda diğer birçok hücreye etki etmiş olmaktadırlar. TZP içeriğindeki anjiojenik materyaller (VEGF, PDGF-BB, ve FGF) anjiogenezisin ve de novo adipogenezisin başlatılması için önemlidir (14). TZP' nin diğer önemli etkilerinden biride inflamasyonu ve ödemi azaltıcı etkisidir. Bu etkilerini siklooksijenaz-1-2 ve membran prostaglandin E sentaz enzimlerinin etkisini azaltarak gösterdikleri invitro ve invivo olarak gösterilmiştir (15). Özellikle siklo oksijenaz-2 'nin doku inflamasyonun majör markırı olduğu bilinmektedir.

Bizde bu çalışmada yağ greftinin yaşayabilirliği ve vaskülarizasyonunu arttırmak için hastadan aldığımız kandan elde ettiğimiz TZP'yi kullandık. Estetik açıdan tatmin edici sonuçlar aldık. Yağ dokusundan elde edilen kök hücrelere tombosit kaynaklı büyüme faktörlerinin hücresel düzeydeki etkilerinin nasıl olduğu bilimemektedir.

Bu hastadaki çok geç dönem sonuçların bilinmemesi ve hücresel düzeyde kök hücrelerin büyüme faktörlerine verdiği yanıtların net olmaması yeni çalışmalara ihtiyaç olduğunu göstermektedir. Hastada yağ greftinin volümetrik ölçüm imkânlarının olmaması nedeniyle rezorbe olan miktar bilinmemektedir. Ayrıca hastaya intraoperatif olarak tek seferde otolog yağ grefti konulmuş ve tek sefere mahsus olmak üzere TZP uygulanmış olması çalışmanın kısıtlı yönlerini oluşturmaktadır. Tekrarlayan dozlarda uygulamadaki sonuçlarının bilinmesi için yeni çalışmalara ihtiyaç vardır.

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A Possible Guillain-Barre Syndrome Associated with Diabetic Ketoacidosis: A Case Report and Literature Review

Diyabetik Ketoasidozla İlişkili Olası Bir Guillain-Barré Sendromu: Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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Abstract
Guillain-Barre Syndrome (GBS) is an acute inflammatory polyradiculoneuropathy. Diabetic ketoacidosis (DKA) is a serious, life-threatening complication of Type 1 diabetes mellitus (DM). In the pathogenesis of Guillain-Barre Syndrome and DKA, autoimmunity plays a role. A thirty-five year old male patient, who had been followed up in endocrinology service with a diagnosis of diabetic ketoacidosis (DKA), complained of weakness in the arms and legs on the seventh day of hospitalization. The patient had no diseases except for diabetes mellitus type 1. The patient was diagnosed with Guillain Barre Syndrome (GBS) on the basis of neurological examination, cerebrospinal fluid results and electrophysiological findings. Clinical improvement was observed as a result of intravenous immunoglobulin therapy. Diabetic ketoacidosis induced GBS was considered for the patient. There is no study that points to diabetes mellitus or DKA as risk factors for GBS. Case reports of Guillain Barre Syndrome associated with diabetic ketoacidosis are rare in the literature.
Keywords: Diabetic Ketoacidosis; Guillain Barre Syndrome; Treatment.

Öz
Guillain Barre Sendromu (GBS) akut inflamatuvar bir poliradikülonöropatidir. Diyabetik ketoasidozis (DKA) ciddi, hayatı tehdit edici tip 1 diyabetes mellitusun (DM) komplikasyonudur. Guillain Barre sendromu ve diyabetik ketoasidozus patogenezinde otoimmunite rol alır. Otuzbeş yaşında erkek hasta diyabetik ketoasidoz tanısıyla endokrinoloji servisinde izlenmekte iken yatışının 7. gününde kol ve bacaklarında güçsüzlük yakınması gelişti. Tip 1 diyabetes mellitus dışında bilinen bir hastalığı yoktu. Nörolojik muayene, beyin omurilik sıvısı ve elektrofizyolojik bulgular ile Guillain-Barré Sendromu tanısı konuldu. İntravenöz immunglobulin tedavisi ile klinikte düzelme izlendi. Olgumuz da DKA'un tetiklediği GBS düşünülmüştür. Guillain Barre sendromu risk faktörü olarak diyabetes mellitus veya DKA'u işaret eden bir çalışma yoktur. Literatürde çok az sayıda olgumuza benzer vaka sunumları vardır.
Anahtar Kelimeler: Diyabetik Ketoasidoz; Guillain Barre Sendromu; Tedavi.

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INTRODUCTION

Guillain-Barre Syndrome (GBS) is an acute inflammatory polyradiculoneuropathy usually characterised by progressive, ascending, symmetrical power loss and areflexia (1). Clinical signs usually occur 2-4 weeks after non-specific infection (2). Diabetic ketoacidosis (DKA) is a serious, life-threatening complication of diabetes mellitus (DM) that is especially common in children with Type 1 diabetes. It manifests itself due to drastic reduction of insulin and increased secretion of anti-insulin hormones like glucagon, adrenaline, cortisol, and growth hormone. Besides, intercurrent infections, emotional stress, and other similar factors lead to increased insulin requirements (3, 4). In the pathogenesis of Guillain-Barre Syndrome and DKA, autoimmunity plays a role. This paper presents the case of a patient who developed GBS during diabetic ketoacidosis treatment.

CASE REPORT

A thirty-five-year-old male patient was admitted to the emergency room with complaints of continued weakness, vomiting, joint pain, and intermittent fever that had been going on for five days. It was learnt that the patient had started an antibiotic treatment at an outside facility with no change in the symptoms. The laboratory examination results were was follows: serum glucose 394 mg/dL; blood urea nitrogen: 17 mg/dL; creatinine 0.9 mg/dL; alanine aminotransferase 35 IU/L; aspartate aminotransferase 47 IU/L; sodium 135 mmol/L; potassium 3.9 mmol/L; white blood cell count 13,000/mm3; and positive (+++) glucose and ketone in complete urinalysis. The patient was taken to the endocrinology service for monitoring with a diagnosis of diabetic ketoacidosis. On the 7the day, he developed weakness in the distal of his lower extremity which spread to the upper limbs. within 2-3 days. The patient did not have any known diseases except for Type 1 DM which was diagnosed 25 years ago. We learnt that the patient had been using insulin for diabetes mellitus for the last 10 years. The medical history of the patient also revealed that he had neuropathic pain prior to hospitalisation. The patient did not have recent upper or lower respiratory tract infection or diarrhoea. Neurological examination revealed a muscle strength of 3/5 in the lower extremities and a muscle strength of 4/5 in the upper extremities. There was no facial diplegia. Deep tendon reflexes were lost and the patient had glove and stocking hypesthesia (with no revealing sense defects). The protein level in the cerebrospinal fluid (CSF) was 141 mg/dL with no pleocytosis. There was no electrolyte imbalance in the blood examination; the haemoglobin A1C level (10.8%) was high. The laboratory tests requested for the diagnosis of potential infections and CSF results were normal. With a treatment targeted at diabetic ketoacidosis, the blood sugar levels of the patient were brought down to normal levels within the first three days. The electroneuromyography (ENMG) on the sixth day of the onset of clinical picture showed mixed type polyneuropathic involvement that basically affected sensory nerves (there was no observed transmission blocks; there was delayed motor distal latency in the upper extremity; conduction velocity was slow; and F responses were delayed). The needle EMG revealed increase win motor unit potential amplitude; the frequency was diluted with polyphase (Table 1).

Having evaluated the clinical, CSF and electrophysiological findings all together, we considered the possibility of GBS after the differential diagnosis. The treatment consisted of intravenous immunoglobulin (IVIG) (0.4 g/kg/day) administration for 5 days. The examination on the 20th showed a muscle strength of 4+/5 in the upper and lower extremities. With improved clinical status in the follow-ups, the patient has been followed by neurology and endocrinology clinics for 12 months.

Table 1. Nerve conduction studies (Day 6)

	Stimulated area	Amplitude Motor:mV, Sensorial: μV	Latency ms	Speed m/s	F frequency ms
Median (R)	Wrist	NR (>20)	NR (<3,4)	NR (>50)	
Ulnar (R)	Wrist	NR (>18)	NR (<3,0)	NR (>50)	
Sural (R)	Calf	NR (>5)	NR (<4,5)	NR (>40)	
Median (R)	Wrist	9,4 (>5)	5,80 (<4,1)	35 (>50)	
	Elbow	7,1	12,90		
Ulnar (R)	Wrist	9,9 (>7)	4,85 (<3,1)	31 (>50)	36 (<32)
	Sub-ulnar	8,2	11,1		
Peroneal (R)	Wrist	1,2 (>3)	7,55 (<5,1)	33 (>40)	59 (<50)
	Lower knee	0,9	13,2		
Tibial (R)	Wrist	2,3 (>6)	9,40 (<5,5)	29 (>40)	68 (<51)
	Knee	1,8	17,5		
Median (L)	Wrist	NR (>20)	NR (<3,4)	NR (>50)	
Ulnar (L)	Wrist	NR (>18)	NR (<3,0)	NR (>50)	
Sural (L)	Calf	NR (>5)	NR (<4,5)	NR (>40)	
Median (L)	Wrist	8,5 (>5)	6,10 (<4,1)	37 (>50)	
	Elbow	8,1	14,1		
Ulnar (L)	Wrist	9,5 (>7)	5,15 (<3,1)	38 (>50)	37 (<32)
	Sub-ulnar	7,7	9,8		
Peroneal (L)	Wrist	2,2 (>3)	6,40 (<5,1)	35 (>40)	57 (<50)
	Lower knee	1,4	11,3		
Tibial (L)	Wrist	1,9 (>6)	9,40 (<5,5)	34 (>40)	67 (<51)
	Knee	1,3	18,8		

APB: Abductor Pollisis Brevis; **ADM:** Abductor Digiti Minimi; **EDB:** Extensor Digitorum Brevis; **AH:** Abductor Hallusis; **R:** Right; **L:** Left; **NR:** No response.

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DISCUSSION

Diabetic ketoacidosis is the most important cause of morbidity and mortality in type 1 diabetes. In DKA patients, blood glucose is around 200 mg/dL and serum osmolality is over 320 mmol/l while blood pH is acidic. Insulin deficiency results in unavailability of glucose which leads to hyperglycaemia and hyperosmolarity; these pictures further lead to essential dehydration and electrolyte loss (3, 4). Guillain-Barré syndrome is an autoimmune disease that develops as a result of production of antibodies by peripheral nerves against antigenic proteins due to T cell activation. Antibodies target myelin though, in some cases, axons may also be the target of immune-mediated damage. Antibody production is triggered by infectious agents, surgical procedures, birth, and immunization (5). Although infections cause the onset of GBS in 3/4 of cases, other rare causes in the literature are malignancy (such as Hodgkin's lymphoma), systemic lupus erythematosus, sepsis, multiple organ failure, disseminated intravascular coagulation (DIC), and other systemic diseases (6-10). A small number of acute polyneuropathy cases have also been reported as a complication of diabetic ketoacidosis (11).

Our patient, who had Type 1 DM, complained of neuropathic pain before hospitalisation. The intravenous immunoglobulin treatment fixed his complaints of weakness though he still had ongoing neuropathic pain. We thought that neuropathic pain and glove and stocking hypesthesia could be induced by diabetes.

Although there is no study that points to diabetes mellitus or DKA as risk factors for GBS, there are studies reporting DKA-induced GBS (12-14) as it was the case in our patient.

In recent years, it has been reported that GBS may follow a course similar to those of critical illnesses (such as DIC and sepsis). The mechanism of GBS developing in patients with diabetic ketoacidosis is not yet fully known. Among the hypotheses, there are the T-cell response developing against the antigens on nerve surface and release of inflammatory mediators leading to humoral immune response due to complement activation on the surface of nerves. Although the most common cause of GBS is infectious causes, critical illness such as DKA may also result in initiation of immune responses. Despite the reports suggesting this atypical course of GBS, there is need to investigate its pathophysiology and need for more extensive studies on more patients.

The fact that there are no studies in the literature showing any antibodies that can be related to both GBS and diabetes at the same time and that some cases lack the infection-related causes weakens the hypothesis of autoimmunity pathogenesis (12, 14). The presence of diarrhea in Fujiwara et al.'s report (13) and the presence of Guillain-Barre syndrome suggested by sural nerve biopsy results in Rouanet-Larrivier et al.'s study (14) strengthen the relationship between these two diseases.

Diabetic polyradicular plexopathy, insulin neuropathy, and chronic inflammatory demyelinating polyneuropathy (CIDP) should be considered in differential diagnosis as well.Insulin neuropathy is an intensive, acute, painful neuropathy seen into the 3rd-4th weeks of insulin therapy (16). Since our case has had a history of insulin intake for many years, we did not consider this condition. Diabetic polyradicular plexopathy is a painful neuropathy especially seen in type 2 diabetic patients with unilateral or asymmetric involvement. Power loss is usually to the proximal lower extremities; upper extremity involvement is rare. There is extreme weight loss in its clinical picture (17). Clinical findings of our case were not compatible with this picture either. CIDP is a chronic and progressive condition with relapses. A two-month or longer progression story is required for the diagnosis. It is 11 times more common with diabetes mellitus compared to the general population. Motor symptoms are affected in the foreground and it is a more severe polyneuropathy. Increased CSF protein and absence of cell (albuminocytologic dissociation) are typical for GBS and CIDP. Protein increase starts especially from the second day onwards and reaches its height in the 3rd-4th weeks. We detected increased protein level in our patient in the first week. Prior to hospitalization, our patient did not have additional symptoms other than neuropathic pain; the clinical picture of our patient had started seven days ago and had been acute. Due to his mono-phase clinical picture (compatible with GBS) and ENMG findings, we did not consider CIDP or an onset of CIDP in our patient (18).

CSF pleocytosis and a mixed type of polyneuropathy can be seen in the course of DM. However, we believe that our patient had GBS because of the high level of (141 mg/dL) CSF protein, acute loss of strength in the lower and upper extremities, which is uncommon in the course of traditional DM, and the rapid response received after the IVIG treatment.

Evaluating the 5 cases in the literature (12-15), we see that the condition is more common in women between 25-64. These cases also reveal that antibodies can target the axon or myelin and that GBS initiates within the first two weeks after the onset of DKA (Table 2).

In cases developing diabetic ketoacidosis, patients should be evaluated carefully for GBS if there are clinical symptoms such as muscle strength loss, autonomic findings, and pain along with a previously known diabetic polyneuropathy.

In the pathogenesis of diabetic ketoacidosis and GBS, autoimmune mechanisms are known to play a role and both conditions are triggered by infections. As far as our case is concerned, we think that diabetic ketoacidosis could have lead to the autoimmune response caused by the onset of GBS pathogenesis.

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Table 2. Demographic and clinical characteristics of our patients and the cases found in the literature.

Case	Sex/Age	Onset of clinical symptoms	ENG	BOS Protein	Study
1	F/44	6 days	Demyelinating	High	Rouanet-Larniviere et al. 1994
2	F/25	14 days	Axonal	High	Rouanet-Larniviere et al. 1995
3	F/37	6 days	Demyelinating	High	Fujiwara et al. 1996
4	F/44	2 days	Not known	High	Novielo et al. 2008
5	F/64	4 days	Demyelinating	High	Kanemasa et al. 2011
6	M/35	7 days	Mixed	High	**Our patient**

S: Sex; **A:** Age; **F:** Female; **M:** Male; **ENG:** Electroneurography

CONCLUSION

During the treatment of diabetic ketoacidosis patients with pain in the back, arms or legs along with muscle weakness and autonomic symptoms, GBS should be considered. In such cases, treatment should begin as soon as possible after further examinations. Especially patients developing diabetic neuropathy should be examined more carefully.

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A Rare Cause of Haematuria: Angiomyolipoma

Nadir Bir Hematüri Sebebi: Anjiyomiyolipom

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Abstract

Haematuria, basically means seeing red blood cells in urine, is one of the causes of emergency service admissions and it has a wide range of etiology from urinary tract infection to malignancy. Renal angiomyolipoma, which is common in tuberous sclerosis patients, is one of these etiologies. These masses often manifest themselves with haematuria and can cause significant morbidity. In this paper, we present the case of a twenty-four-year-old female patient who complained of haematuria and left flank pain. She had been followed for tuberous sclerosis for eleven years and we diagnosed her as postpartum spontaneous renal angiomyolipoma rupture accurately, after performing abdominal ultrasonography and computed tomography. Then she recovered fully and discharged after stopping bleeding by transarterial embolization method.

Keywords: Haematuria; Angiomyolipoma; Pregnancy; Emergency.

Öz

En basit tanımıyla idrarda kan hücresi görülmesi demek olan hematüri, basit idrar yolu enfeksiyonundan maligniteye kadar çok geniş etiyolojisi olan bir acil servis başvuru nedenidir. Özellikle, tüberoz skleroz tanılı hastalarda görülen renal anjiyomiyolipom ise bu sebeplerden biridir. Çoğunlukla hematüri ile ortaya çıkan bu kitleler önemli derecede morbiditeye sebep olabilirler. Çalışmamızda acil servisimize hematüri ve sol yan ağrısı şikayetleriyle başvuran ve aynı zamanda on bir yıldır tüberoz skleroz tanısı ile takip edilen yirmi dört yaşındaki bayan hastada, postpartum dönemde görülen spontan renal anjiyomiyolipom rüptürü vakası sunulmuştur. Hastaya ultrasonografi ve bilgisayarlı tomografi vasıtasıyla hızlıca doğru tanı konuldu. Sonrasında ise transarteryel embolizasyon işlemi ile kanama durduralarak hasta başarıyla tedavi edildi.

Anahtar Kelimeler: Hematüri; Anjiyomiyolipom; Gebelik, Acil.

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INTRODUCTION

Hematuria refers to the presence of RBCs in urine detected through microscopic examination. The most common causes for hematuria are urinary tract infections, kidney stones, traumas, nephropathies, prostate cancer, renal cell cancers, bladder induced cancers, benign prostatic hypertrophy, angiomyolipoma (AML), oncocytoma, and surgical complications (1). As can be seen, hematuria has a wide etiology from urinary tract infections to cancer (2).

In this study, we present the case of a tuberous sclerosis (TS) patient who was admitted to our emergency department with hematuria and was diagnosed with renal AML rupture. What makes our patient an extraordinary case is the manifestation of hematuria after birth, which is a rare entity in the literature.

CASE REPORT

A twenty-four-year-old female patient presented in our emergency department with hematuria that had started five hours ago and left flank pain. With no history of trauma or use of anticoagulants or similar drugs, the patient related that the complaints began spontaneously and suddenly. The patient had been followed for TS for 11 years and had given birth by vaginal delivery three months ago. On physical examination, the patient's general condition was moderate with fever at 36,5^{0}C, blood pressure around 90/70mmHg, and heart rate at 95/min. The abdominal examination revealed costovertebral angle tenderness on the left with no rebound or defense. The initial laboratory tests at the emergency room were as follows: haemoglobin: 8,3 g/dL; hematocrit: 25,1%; international normalised ratio (INR): 1,2; creatinine: 1,13 mg/dL; urea 21 mg/dl; and with densely present erythrocytes in the urinalysis. The other laboratory tests were normal. The abdominal ultrasonography (USG) performed in the emergency department showed hyperechoic masses in both kidneys. The computed tomography (CT) revealed many cortical lesions as dense as fat with vague limits in both kidneys (angiomyolipomas). We also observed bleeding in the pelvicaliceal system of the left kidney (Figure 1). With the results of the existing imaging modalities and clinical picture, we diagnosed the patient with TS-related renal AML rupture.

We first monitored the patient for hemodynamics in the emergency room. We followed the course of hematuria after inserting a urinary catheter and started erythrocyte suspension (ES). The patient was referred to the urology department where she was admitted to the urology service for hospital stay. Although she was given ES in the urology service, the haemoglobin values continued to fall. With no planned surgical intervention, the patient was referred to the radiology department. In the bilateral renal angiography performed on the same day by the radiology department, we identified a bleeding locus in the left kidney. This was stopped by administrating transarterial embolization (TAE). In time, the patient was followed in the urology department with decreasing hematuria and improving haemoglobin values. After a five-day-follow-up in the hospital and due to the improvement of the patient's general condition, the patient was discharged and recommended to take AML tests at short intervals.

DISCUSSION

AMLs are benign tumour formations composed of smooth muscles, blood vessels, and fat tissues. Its prevalence is approximately 0.3% while its incidence rate among renal masses is 3% (3). AML has two types; the first and most common type is the isolated AML with an incidence rate of 80% while the other is the TS-related AML. Isolated AML is generally asymptomatic, large, and solitary and occurs later in life. TS-related AML is bilateral, small, and multiple; it is seen at earlier ages and surfaces with bleeding (4). Affected patients often present with hematuria and flank pain while 20% of cases may develop retroperitoneal haemorrhage that might lead to hemorrhagic shock. It is often thought that those greater than 4 cm in size have serious risk of bleeding. Another complication of AML is abdominal pain and blocked urine flow caused by the mass (5).

AML is usually incidentally detected in CT or magnetic resonance imaging (MRI) taken during other investigations (6). The USG view shows dense haemorrhage and hyperechoic masses. Since it is capable of showing the fat tissue within the mass, CT is the gold standard for diagnosis. If CT is contraindicated and the lesions are small and mixed, MRI can be helpful (4). In our case, the initial abdominal ultrasonography showed macroscopic hematuria with renal masses that could not be fully evaluated; yet, the following CT enabled us to diagnose the patient with bilateral and multiple AML. Besides, the fact that the patient had been followed for TS for 11 years supported our diagnosis. Because, the incidence of sporadical renal AML is 1-2% whereas this rate is around 50-75% in TS patients (6).

The increase in intra-abdominal pressure and renal blood flow during pregnancy increases the possibility of spontaneous rupture of renal AML development (7). In addition, oestrogen and progesterone receptors that are known to be present in the muscle tissues at high rates also cause AML's growth and rupture with the increasing stimulating effect of these hormones during pregnancy (3). In our study, our patient had a history of vaginal delivery 3 months ago. Despite our detailed questioning, we failed to

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determine any related history of trauma and drug use and we concluded that the cause of spontaneous AML rupture was the hormonal and physiological changes during the pregnancy and postpartum periods. The literature survey conducted in 2012 showed 26 AML rupture cases during pregnancy while there was only one AML rupture case in the postpartum period (7). Therefore, having developed after the delivery, our patient is a rare case.

Management of AML patients have been much discussed in the literature. The asymptomatic AMLs smaller than 4 cm should be periodically checked and followed every 6 months with ultrasound and CT. It is indicated that bilateral and multiple AMLs with a potential to increase in size over time when they are accompanied by TS should be monitored more closely. But the symptomising bilateral lesions must be intervened with arterial embolization or partial nephrectomy. Patients with retroperitoneal bleeding and deteriorating hemodynamics may need radical nephrectomy (3, 6). In our case, we were able to stop the bleeding in the left kidney by applying a successful TAE process.

CONCLUSION

Consequently, practitioners should keep in mind AML as a rare cause of hematuria in patients presenting at the emergency department. Such patients should be monitored closely and receive a swift diagnosis through abdominal CT. In addition, the TS patients with renal AML should be followed at frequent intervals due to the risk of growth during pregnancy.

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Surgical Resection of a Giant Aortocoronary Saphenous Vein Graft Aneurysm without Performing Cardiopulmonary Bypass

Dev Aortokoroner Safen Ven Greft Anevrizmasının Kardiyopulmoner Bypass Kullanmadan Cerrahi Rezeksiyonu

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Abstract
Aneurysms of saphenous vein grafts are infrequent complications of coronary bypass surgery. Although these aneurysms are usually asymptomatic, they may lead to sudden death by rupture or compression of cardiac chambers and vascular structures. A sixty-three year old male patient, who had undergone coronary bypass surgery eighteen years ago, was admitted with chest pain. The patient also had a history of renal transplantation. Coronary angiography revealed an aneurysm of the saphenous vein graft to the right coronary artery and occlusion of native right coronary artery. Computed tomography demonstrated a giant (130x100x100 mm) saphenous vein graft psudoaneurysm compressing the right atrium and ventricule. The aneurysm was approached through a median sternotomy and resected without the use of cardiopulmonary bypass (CPB). Saphenous vein graft aneurysms can potentially reach large dimensions. In such cases, surgery is the choice of treatment. Surgical resection can be performed without CPB when coronary revascularizaton is not needed.
Keywords: Saphenous Vein; Graft; Coronary Artery Bypass; Aneurysm.

Öz
Safen ven greftlerinin anevrizmaları koroner bypass cerrahisinin sık görülmeyen komplikasyonlarıdır. Bu anevrizmalar genellikle asemptomatik olmakla birlikte rüptür ile ani ölüme neden olabilmekte veya kardiyak boşluklar ve vasküler yapılara bası uygulayabilmektedirler. On sekiz yıl önce koroner bypass cerrahisi uygulanmış olan altmış üç yaşındaki erkek hasta göğüs ağrısı ile başvurdu. Hastada ayrıca geçirilmiş renal transplantasyon öyküsü bulunmaktaydı. Koroner anjiyografide sağ koroner artere ait safen ven greftinde anevrizma bulunduğu ve nativ sağ koroner arterin tıkalı olduğu görüldü. Bilgisayarlı tomografide safen ven greftinin dev yalancı anevrizmasının (130x100x100 mm) sağ atriyum ve ventriküle bası uyguladığı saptandı. Hastaya cerrahi tedavi uygulandı. Anevrizma, median sternotomi yaklaşımıyla ve kardiyopulmoner bypass (KPB) kullanılmadan rezeke edildi. Safen ven grefti anevrizmaları büyük boyutlara ulaşabilme potansiyeline sahiptir. Bu tip olgularda cerrahi tedavi öncelikli seçenektir. Koroner revaskülarizasyonun gerekli olmadığı olgularda cerrahi rezeksiyon KPB kullanılmadan yapılabilir.
Anahtar Kelimeler: Safen Ven; Greft; Koroner Arter Bypass; Anevrizma.

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GİRİŞ

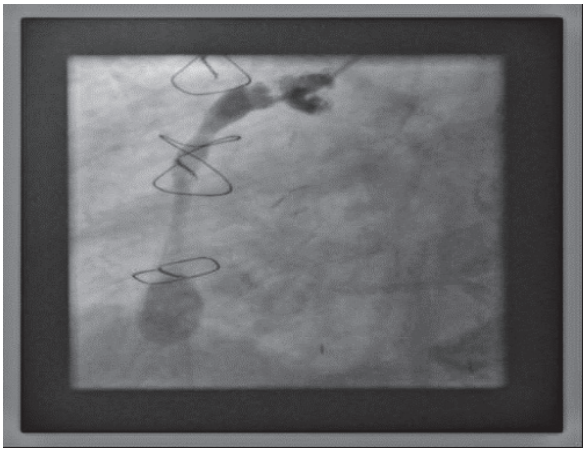
Safen ven, koroner arter bypass cerrahisinde ilk olarak 1968 yılında Favaloro tarafından kullanılmıştır ve günümüzde de bu ameliyatlar için en sık tercih edilen greftler arasında yer almaktadır (1). Aortokoroner bypass grefti olarak kullanılan safen ven ile ilgili başlıca sorun aterosklerozun neden olduğu darlık ya da oklüzyon ile kendini gösteren greft yetmezliğidir ve postoperatif dönemde iskemik semptomların tekrar ortaya çıkmasının başlıca nedenidir.

Safen ven grefti (SVG) anevrizmaları ise nadir olarak görülen komplikasyonlardır. Bu anevrizmalar damarın histolojik olarak her üç tabakasını birden içeren gerçek anevrizmalar ve kanın damar duvarının dışında kalan bağ dokusu ile sınırlanmış olduğu yalancı anevrizmalar şeklinde sınıflandırılmaktadır. Hem gerçek hem de yalancı anevrizmalar genişleyerek çapı 10 cm.'yi aşan "dev" boyutlara ulaşabilme potansiyeline sahiptirler ve ölümcül komplikasyonlara yol açabilmeleri nedeniyle büyük önem taşımaktadırlar (2).

Bu olgu sunumunda sağ koroner artere ait safen ven greftinde oluşan dev anevrizmanın cerrahi tedavisi sunulmakta ve literatür bilgileri ışığında benzer olgulardaki tedavi yaklaşımları tartışılmaktadır.

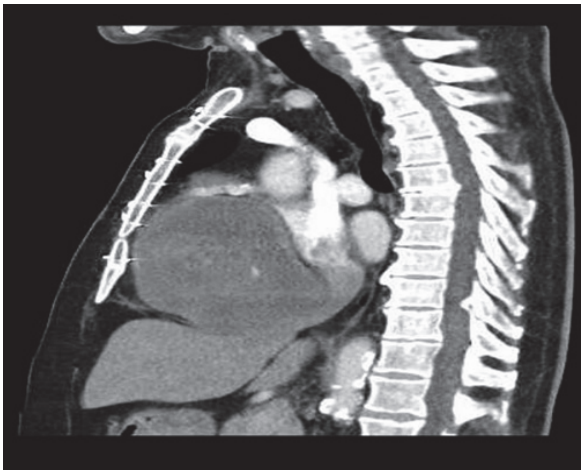
OLGU SUNUMU

On sekiz yıl önce koroner baypas cerrahisi ve bir yıl sonra da renal transplant uygulanmış olan 63 yaşındaki erkek hasta göğüs ağrısı ile başvurdu. Koroner anjiyografide sol ön inen arterin tıkalı ve sol internal torasik arter greftinin açık olduğu görüldü. Sağ koroner arter proksimal bölgede tamamen tıkalı olup, sağ koroner artere ait safen ven greftinde anevrizma bulunduğu gözlemlendi (Resim 1).



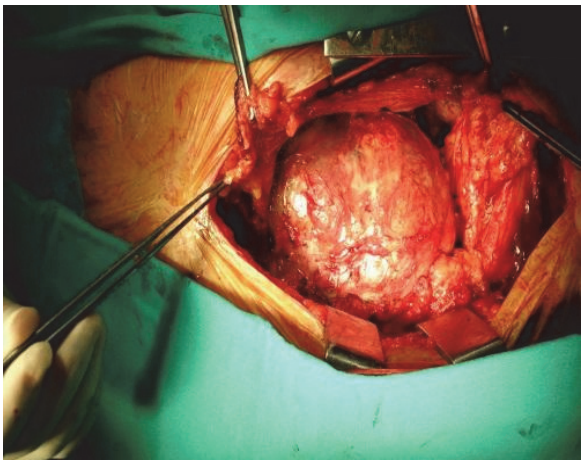
Resim 1. Sağ koroner safen ven grefti anevrizmasının anjiyografik görünümü.

Anevrizmatik greftin anatomisinin daha iyi tanımlanabilmesi için 0.5 mm kesit kalınlığında bilgisayarlı tomografi tetkiki yapıldı. Sağ koroner arter bypass grefti ile ilişkili ve kalbin anterior tarafında yerleşimli, sağ atriyum ve ventrikülü bası altında bırakan 130x100x100 mm boyutlarında tromboze yalancı anevrizma saptandı (Resim 2).



Resim 2. Bilgisayarlı tomografide mediastende yer kaplayan dev anevrizmanın görünümü.

Hastadaki safen ven grefti anevrizmasının sağ kalbe bası uygulaması ve rüptür ihtimalinin yüksek olması göz önüne alınarak cerrahi müdahaleye karar verildi. Olguda renal transplant bulunması nedeniyle kardiyopulmoner bypass (KPB) ile olumsuz etkiler oluşabileceği düşünüldü ve cerrahinin KPB kullanmadan yapılmasına karar verildi. Median sternotomi yapılmadan önce KPB'a girilmesine ihtiyaç duyulabileceği düşünelerek femoral arter eksplore edildi. Strenotomi yapıldı ve ön mediasteni dolduran dev anevrizma kesesinin sağ atriyum ve ventriküle bası yapmış olduğu görüldü (Resim 3)



Resim 3. Sternotomi sonrası anevrizmanın görünümü.

Anevrizma çevre dokulardan serbestleştirildi. Greftin proksimal anastomoza yakın kısmında anevrizma çapının yaklaşık 2 cm civarında olduğu tespit edildi. Greft bu bölümde askıya alındı ve klempe edildi. Anevrizma kesesi açıldığında distal nativ koroner arter tarafının tromboze olduğu ve geri dolum olmadığı gözlemlendi (Resim 4).

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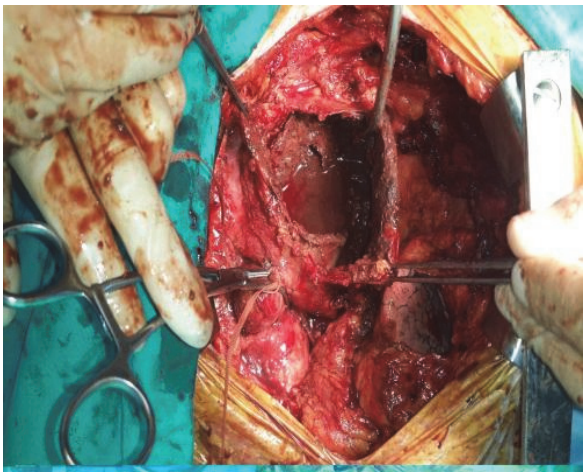

Resim 4. Anevrizma kesesinin açıldıktan sonraki görünümü.

Anevrizmanın sağ ventrikül ve atriyum tarafında ileri derecede yapışık olan serbest duvarı hariç tümüyle rezeke edildi. Klempin proksimalinde akım bulunması nedeniyle greft aorta en yakın olduğu bölümde ligatüre edildi ve proksimal anastomoz bölgesi pledjitli 3-0 polipropilen sütür ile tamir edildi. Kanama olasılığına karşı anevrizmadan geriye kalan güdüğe 4-0 polipropilen sütür ile transfiksiyon dikişleri koyularak ameliyat sonlandırıldı. Postoperatif dönem sorunsuz seyretti ve hasta 7. günde taburcu edildi.

TARTIŞMA

Koroner arter bypass cerrahisinde kullanılan safen ven greftlerinde anevrizma oluşumu ilk olarak 1975 yılında Riahi ve arkadaşları tarafından bildirilmiştir (3). Safen ven grefti (SVG) anevrizmalarının çoğu asemptomatik seyirli olmakla beraber klinikteki ilk yansımaları rüptüre bağlı ani ölüm şeklinde olabilmektedir. Bu nedenle bu sıradışı komplikasyonun görülme sıklığı kesin olarak bilinmemekte ancak %1'in altında olduğu tahmin edilmektedir (4). Safen ven greftlerinin yalancı anevrizmaları genellikle sakküler yapıda olup postoperatif 4-12 ay sonra ortaya çıkmakta ve sıklıkla anastomoz bölgelerinde yer almaktadır. Cerrahi sonrası erken dönemde görülen yalancı anevrizmaların oluşumundan sütür hattındaki gerilim ya da hatalı cerrahi teknik kullanılması nedeniyle anastomozda dehisans olması ve postoperatif dönemde gelişen enfeksiyon sorumlu tutulmaktadır (1). Genellikle greftin gövdesinde ve fusiform yapıda ortaya çıkan gerçek anevrizmalar ise tipik olarak postoperatif 5. yıldan sonra görülmektedir (5). Geç dönemde ortaya çıkan gerçek anevrizmaların oluşumunda ven grefti aterosklerozunun, endotel fonksiyon bozukluğunun ve yan dallar ile kapakçıklarının olduğu bölgelerde dairesel düz kas tabakasının bulunmamasına bağlı ven duvarındaki zayıflığın rol oynadığı düşünülmektedir (2).

Ven grefti endotelinde yapısal ya da fonksiyonel bozukluğa yol açan bir takım etkenler anevrizma oluşumuna zemin hazırlamaktadır. Greftin hazırlanması sırasında damar duvarının hasarlanması, variköz damarların kullanılması, steroid tedavisi, hiperlipidemi, sigara kullanımı ve hipertansiyon anevrizma riskini artırmaktadır. Ayrıca endoskopik safen ven çıkartılması ile ilişkili artan travmanın da anevrizma gelişimine yol açabileceği düşünülmektedir (6).

SVG anevrizması bulunan hastalar genellikle asemptomatik olup, anevrizma ile ilişkili olmayan başvuruları sırasında yapılan incelemelerde rastlantısal olarak tanı almaktadırlar. Bu tip olgularda sıklıkla tanıya yönlendiren bulgu akciğer grafisinde dikkati çeken hiler veya mediastinal kitle görünümüdür (1). Semptomatik olgular ise çoğunlukla kardiyak kökenli yakınmalar ile başvurmaktadırlar. En sık karşılaşılan semptom göğüs ağrısıdır. Göğüs ağrısı nativ koroner arter hastalığının ilerlemesi, ven greftinin oklüzyonu, intraluminal trombüsten kaynaklanan distal embolizasyon veya büyük anevrizmanın oluşturduğu bası etkisi ile ilişkili olabilir. Geçirilmiş koroner bypass cerrahisi, göğüs ağrısı ve mediastinal kitle triadı SVG anevrizması varlığından şüphelendirmelidir (7). Göğüs ağrısı dışında en sık karşılaşılan semptom nefes darlığıdır ancak olguların çoğunda birden fazla semptom bir arada bulunabilir (2). Kanamaya ya da anevrizma ile komşu bronş yapıları arasında fistül oluşmasına bağlı olarak hemotoraks ya da hemoptizi görülebilir. Ayrıca anevrizmanın sağ atriyum başta olmak üzere kalp boşluklarına fistülizasyonu kalp yetmezliğine, bası uygulayan kitle etkisi de süperiyor vena kava sendromuna yol açabilmektedir. Anevrizmanın rüptürü durumunda oluşan kardiyak tamponad ise ani hemodinamik bozulma veya şok tablosu ile seyretmektedir (4). SVG anevrizmalarının tedavisi ile ilgili tecrübelerin esas olarak olgu sunumları ve küçük vaka serilerine dayanması nedeniyle yerleşmiş tedavi algoritmaları bulunmamaktadır. Ancak semptomatik olgulara ve çapı 2 cm.'den büyük anevrizmalara müdahale edilmesi önerilmektedir (1). Bununla birlikte komplikasyonların üçte birinin çapı 2 cm ve daha küçük olan anevrizmalarda ortaya çıktığı düşünüldüğünde bu anevrizmalar için güvenli takip yapılabilecek bir çap sınırın belirlenmesi güç görünmektedir. Bu nedenle asemptomatik olup anevrizma çapı 1 cm.'den büyük olan veya greft akımı azalmış olgularda da erken cerrahi tedavi önerenler mevcuttur (7). Anevrizma çapı 1 cm.'den küçük ve yeterli greft akımı olanlarda klinik izlem yaklaşımı benimsenebilir. (2).

Cerrahi müdahale SVG anevrizmalarının tedavisinde ön plandadır. Çoğunlukla median sternotomi yaklaşımı kullanılmakta ancak anevrizmanın kalbin anterior tarafında yerleştiği olgularda sağ torakotomi de tercih edilebilmektedir. Miyokardiyumun önemli bir bölgesinin tehdit altında olduğu ve nativ koroner arterde revaskülarizasyonun gerekli olduğu durumlarda genellikle anevrizma rezeksiyonu veya ligasyonu ile birlikte yeni bir greft ile bypass yapılmaktadır. Anevrizma içindeki aterosklerotik debris materyalinden kaynaklanan embolik olaylardan kaçınmak için ameliyat esnasında dikkatli olunmalıdır. Bu tip komplikasyonların engellenmesi için aortun klemplenerek kalbin arrest edilmesinden ve hastalıklı greftin ligasyonundan önce anevrizmanın manipüle edilmesinden kaçınılmalıdır. Retrograd kardiyopleji kullanımı nativ koroner arterden debris materyalinin uzaklaştırılmasını sağlayabilir. Başka

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bir faydalı strateji de müdahalenin kardiyopulmoner bypass kullanmadan yapılmasıdır (8). Cerrahinin yüksek risk taşıdığı ya da anevrizmanın rüptüre olduğu durumlarda perkütan girişimsel yöntemler tercih edilebilir. Bu yöntemler endovasküler coil ile embolizasyonu ve kaplı stent ya da vasküler oklüzyon tıkaçları ile anevrizmanın kapatılmasını içermektedir (9).

Sunduğumuz olguda, hastanın organ transplantasyonu sonrası steroid tedavisi kullanmış olmasının anevrizma oluşumuna ve ileri derecede genişlemesine yol açmış olabileceğini düşünüyoruz. Nativ sağ koroner arterde doluş olmaması nedeniyle revaskülarizasyon ihtiyacı bulunmadığından perkütan girişimsel yöntemler ile müdahale edilmesi düşünülebilirdi. Ancak anevrizmanın dev boyutlarda olması endovasküler yöntemler açısından zorluk yaratmaktaydı. Ayrıca anevrizmanın sağ kalbe ait yapılara bası uygulaması cerrahi tedaviyi tercih etmemizde rol oynadı. Hastanın renal transplantasyon geçirmiş olduğu göz önüne alınarak postoperatif böbrek fonksiyonlarının daha iyi korunması açısından cerrahi tamiri KPB kullanılmadan gerçekleştirdik (10).

SONUÇ

Safen ven greft anevrizmasına sahip hastalar sıklıkla göğüs ağrısı ile kliniğe başvurmaktadırlar. Anevrizmanın büyük boyutlara ulaşması halinde asemptomatik olsa bile rüptür riski taşıması nedeni ile müdahale edilmesini gerekli kılmaktadır. Bu tip olgularda öncelikli tedavi seçeneği cerrahi rezeksiyondur. Koroner revaskülarizasyona ihtiyaç bulunmaması halinde rezeksiyonun KPB kullanılmadan yapılması cerrahinin olumsuz etkilerden kaçınılması için avantaj sağlayabileceğini düşünmekteyiz.

13. Türk Kalp ve Damar Cerrahisi Kongresinde poster bildiri olarak sunulmuş ve özet kitabında yayınlanmıştır.

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A Case of Sudden Death due to Lighter Refill Gas Inhalation

Çakmak Gazı İnhalasyonuna Bağlı Ani Gelişen Ölüm Olgusu

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Abstract
A component of lighters refill tubes, butane is a colourless and flammable substance with gasoline-like or natural gas odour. The abuse of easily accessible lighter gas butane is increasing among children and adolescants and this abuse causes euphoric effects. Inhalants are the most commonly used drug after alcohol and tobacco among adolescents. In the literature, it is reported that butane inhalation directly affects central nervous system, respiratory and cardiovascular systems. To prevent this increasing trend, we believe that society, especially youth, should be educated through precautionary educational activities, sales of lighter refill tubes should be monitored and be made age-restricted, and lighter refill tubes should have warning signs that everyone would understand and attract attention. We present a case of the sudden death of a seventeen-year-old male due to inhaling butane containing lighter refill gas with friends along with the autopsy findings and the results of toxicology and histopathology investigations.
Keywords: Butane; Lighter Refill Gas; Sudden Death; Autopsy.

Öz
Renksiz, yanıcı özellikte ve doğal gaza benzer kokusu bulunan bütan gazı çakmak dolumunda kullanılan gazın bileşimde bulunmaktadır. Kolay ulaşılması nedeniyle çakmak gazı solunması çocuklarda ve gençlerde giderek yaygınlaşan keyif verici amaç için kullanılmaktadır. Adölesanlarda sigara ve alkolden sonra en sık kötüye kullanılan madde olduğu belirtilmektedir. Literatürde bütan gazı inhalasyonu sonrası santral sinir sistemi, solunum ve kardiyovasküler sistemin etkilendiği olgular bildirilmektedir. Bu artış eğilimini önlemek için, toplum, özellikle gençlerin, eğitim etkinlikleri yoluyla eğitilmeleri gerektiğine inanıyoruz. Ayrıca çakmak dolum tüpü satışları izlenmeli ve yaş kısıtlaması yapılmalı, hafif dolum tüplerinin üzerine herkesin anlayacağı ve dikkatini çekeceği uyarı işaretleri konulmasının yararlı olacağı kanaatindeyiz. Çalışmada; iki arkadaşıyla birlikte bütan içerikli çakmak gazı solunması sonrası ani ölüm meydana gelen 16 yaşındaki erkek olgu otopsi bulguları, toksikolojik ve histopatolojik inceleme sonuçları ile sunulmaktadır.
Anahtar Kelimeler: Bütan; Çakmak Gazı; Ani Ölüm; Otopsi.

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INTRODUCTION

Substance abuse is a major public health problem affecting the health of individuals and society. It is also the cause of serious burden to economy through loss of labor force, increase in illegal actions, and health problems. Research has shown that substance use is increasing all over the world and that it especially affects young population (1).

According to the 2012 data of the United Nations Office on Drugs and Crime (UNODC), 5% of the world population aged 15-64 use illicit drugs. UNODC's research in six cities in Turkey conducted among participants aged 15-64 has shown that cannabis use (by 4.3%) and inhalant use (by 4.2%) are the most common drugs abused "at least once in a lifetime" (2-3).

Volatile substance use is the most commonly abused substance after alcohol and cigarettes because they are easy to reach and use as they are also cheap showing rapid effect; they are also commonly used in group activities as a source of joy as an alternative to alcohol (1, 4). Inhalant use is most commonly observed in 13-15 years of age while it peaks between the ages of 11 and 17 (4). In Turkey, the most commonly abused volatile substances are toluene (paint thinner), chlorinated hydrocarbons, and lighter refill gas (5). The contents of lighter refill gas generally include a high proportion of butane in aliphatic hydrocarbon structure and a small portion of isobutane and propane (1, 6).

Butane, CH3(CH2)2CH3 (also known as n-butane, butyl hydride, or methylethyl-methane), is a colourless, flammable gas with a smell similar to that of natural gas (7, 8). Following its intake, it creates a euphoric effect, disinhibition, visual and auditory hallucinations along with flying or floating sensation (1, 9). Because it is applied by spraying the lighter refill gas directly into the mouth, it is difficult to set the dose, which in turn can lead to sudden cardiac death (1, 9). Butane replaces oxygen and creates asphyxiating effects that leads to unconscious dangerous behaviour and eventually to traumas, vagal inhibition, respiratory depression, and sudden sniffing death syndrome (8, 10). Caused by ventricular arrhythmia due to large amount of catecholamine release, sudden sniffing death syndrome accounts for 50% of volatile substance related deaths (8).

In this study, we present the autopsy findings of a 16-year-old male, who died due to sudden sniffing death syndrome after inhaling butane from a lighter refill can with two of his friends, discuss the results of toxicological and histopathological examination in the light of the literature, and draw attention to the increasing prevalence of the problem of use of volatile substances and the risk of sudden death.

CASE REPORT

It is related that a 16-year-old male patient suddenly collapsed during gas inhalation from the butane containing lighter refill tube with two friends upon which his friends had called 112 emergency services. He was taken to hospital by the emergency service staff but was lost in the hospital despite all interventions. Crime scene investigation carried out by police officers confirms the abuse of butane containing lighter refill tubes which were also used by his two friends. We were unable to reach the patient's medical file about the incident.

The autopsy conducted 5 hours after the death of the person revealed that he was 185 cm tall, weighed 70-75 kg, and had a tattoo on his left forearm that read "Good Day To Die..♡" (Figure 1). The patient had two circular-shaped panther figures on the left arm, bloody fluid coming out through the nostrils, ecchymosed graze areas around the left scapula and left lumbar region, defibrillator spoon scars, and pin traces on the inside of both elbows and on the left wrist.

Figure 1. The tattoo on the arm of the lost patient.

When the headroom was opened up, we discovered petechiae areas under the scalp; there were oedema and hyperaemia in the brain, cerebellum, and the brain stem (Figure 2). The brain weight was 1434 grams. The chest examination showed broken ribs on the midclavicular line on the 1st-3rd ribs due to revitalisation process, sub-epicardial petechial bleeding areas in the heart, and hyperaemia around the myocardial areas. Both lungs were swollen with bright oedemas and petechial haemorrhage. The right lung weighed 846 grams while the left lung was about 1050 grams. The sections of the lungs had congestion and the bronchi and bronchioles showed signs of bloody foamy liquid (Figure 3). The stomach contained 100ml of dark brown-black liquid. The liver and right kidney revealed areas with hyperaemia.

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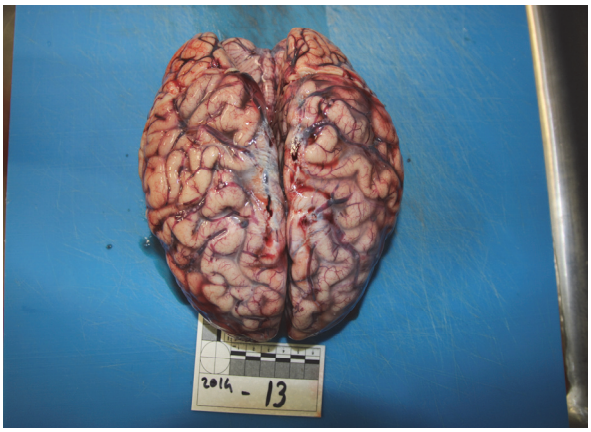

Figure 2. Oedematous view of the brain with hyperaemia.

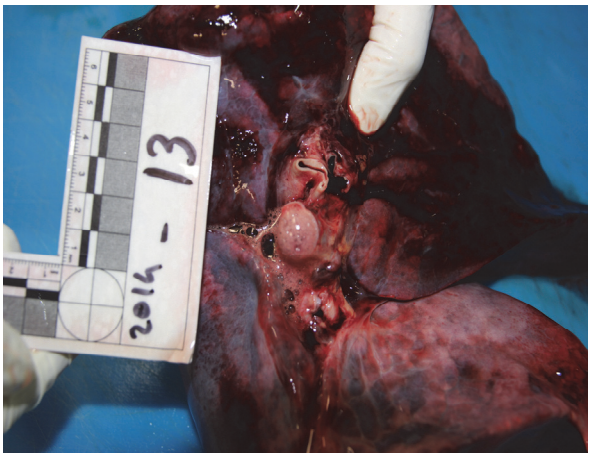

Figure 3. The swollen view of the lungs with oedemas

The samples obtained from the heart, brain, kidney, liver, lungs, and pancreas were sent to the pathology laboratory in 10% formaldehydes for histopathological evaluation. The tissue samples were stained with hematoxylin-eosin (HE) and evaluated with a light microscope following routine tests. The microscopic examination showed oedema and fresh intra-alveolar haemorrhage in the lung, autolysis in the pancreas, and extravasated red blood cells in the parenchymal fat tissues. The examination of other body samples showed signs of congestion.

We collected samples from the liver, kidney, stomach contents, brain and fat tissue, intraocular fluid, bile, and blood as well as the entire right lung obtained from the right bronchial side in a closed environment, nasal swabs, and nasopharyngeal swab and sent these samples to the chemistry lab at Institute of Forensic Medicine, Malatya Headquarters where the autopsy was carried out for systematic toxicological evaluation. The samples were maintained in the refrigerators of the chemistry lab in accordance with the procedures until necessary investigations were carrie out. Studying the samples with Gas Chromatography Mass Spectrometry (GC/MS) device, we found butane, one of the lighter refill gas components, in the blood samples and lung samples with blood. We did not observe alcohol or other toxic substances in the analysis of the samples. According to the autopsy findings and histopathological results of the samples, we did not find any evidence of natural disease or a trauma that could have caused his death. We assumed that the death of the person was due to the toxic effect and respiratory complications caused by directly inhaling lighter refill gas (butane).

DISCUSSION

With its low molecular weight, lipophilic nature, and aliphatic hydrocarbon structure, butane creates sedative effects in the central nervous system by taking the place of oxygen and leads to death through asphyxiating effects. It is stated that majority of the deaths caused by butane inhalation are due to direct toxic effect, aspiration, asphyxia, and cardiac arrhythmia (11). There are studies on the concentration of butane affecting the brain, spleen, kidney, adipose tissues, lung, and blood distribution. Especially in the cadavers that are in the decomposing process, butane is at detectable levels when its concentration is reduced in adipose tissues (10). Butane is known to boil at -0.5 degree C in room temperature and under normal atmospheric pressure. If blood samples are kept at room temperature or at 40 degrees C, gas concentration tends to decrease. Studies have shown that butane gas concentration is reduced by 10% within 2 weeks if samples are stored at -300 degrees C (11). Therefore, if an examination is not going to be conducted soon, samples are recommended to be stored at -300 degrees C.

Direct toxic effect (51%), asphyxia caused by use of plastic bags (21%), gastric content aspiration (18%), and traumatic (drowning, traffic accidents, hanging etc.) reasons are among the common causes of volatile component inhalation related deaths (12).

Because our patient died in the hospital during cardiopulmonary resuscitation, the reason of death has been evaluated in the light of the autopsy and scene investigation findings. The autopsy has reported pulmonary oedema, bloody frothy fluid in the bronchi and bronchioles, cerebral oedema, and congestion and petechial haemorrhages in the internal organs. Blood samples and lung samples of blood showed signs of butane, one of the lighter gas components. These findings are consistent with asphyxiating changes associated with butane inhalation in the literature. It is indicated that pathognomonic morphological changes have not yet been identified in deaths caused by butane inhalation (8). Therefore, a detailed crime scene investigation of the materials that would confirm inhalation of volatile gases along with swiftly conducted toxicological examination of cadavers will help achieve conclusive diagnosis. At length, in the light of the autopsy findings and results of toxicological and histopathological examinations, we believe that the death of the person was caused by asphyxia due to butane-induced direct toxic effect and respiratory depression.

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CONCLUSION

The low prices and accessibility of volatile substances that lead to addiction by sniffing or inhaling and negatively affect the physical and psychological development of younger population increase the abuse of these substances by children and young people. To prevent this increasing trend, we believe that society, especially youth, should be educated through precautionary educational activities, sales of lighter refill tubes should be monitored and be made age-restricted, and lighter refill tubes should have warning signs that everyone would understand and attract attention. Besides, addition of malodorous substances into lighter refill tubes will also be beneficial in reducing their abuse.

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A Case with Idiopathic Bilateral Multifocal Retinal Pigment Epithelium Detachment

Bilateral İdyopatik Multifokal Retina Pigment Epitel Dekolmanlı Bir Olgu

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Abstract

A 47-year-old woman presented with near sight issues with 10/10 best corrected visual acuity in both eyes. The intraoculer pressure was 14mmhg in right eye and 16mmhg in left eye. The slit-lamp examination showed a normal anterior chamber. The dilated fundus examination showed that there were cystic, hypopigmented, and swollen lessions in the both fovea. The patient did not have metamorphopsia. At the same time in serological tests performed on the patient did not develop any pathology. With no present systemic problem, the patient was diagnosed with idiopathic retina pigment epitel detachment at the end of examination with fluorecein anjiography and optical chorence tomography.

Keywords: Idiopathic Retina Pigment Epitel Detachment; Fluorecein Anjiography; Optical Cohorence Tomography.

Öz

Göz polikliniğine yakını görememe şikayeti ile başvuran 47 yaşındaki bayan hastanın yapılan oftalmolojik muayenesinde en iyi düzeltilmiş görme keskinliği sağ gözde: 10/10, sol gözde 10/10' idi. Hastanın göz içi basınçları sırasıyla sağ:14 mmhg, sol: 16 mmhg 'idi. Biyomikroskobik muayenede her iki göz ön segment muayeneleri doğal görünümdeydi. Hastanın dilate fundus muayenesinde her iki foveada kistik ve yüzeyden hafif kabarık hipopigmente değişiklikler olduğu gözlendi. Hastanın metamorfopsi şikayeti yoktu. Aynı zamanda hastanın yapılan serolojik testlerinde herhangi bir patoloji saptanmadı. Sistemik herhangi bir problemi olmayan hastaya yapılan flöresein anjiografi (FA) ve optik kohorens tomografi (OCT) tetkikleri sonucunda, İdyopatik retina pigment epitel dekolmanı tanısı konuldu.

Anahtar Kelimeler: İdyopatik Retina Pigment Epitel Dekolmanı; Floresein Anjiografi; Optik Kohorens Tomografi.

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INTRODUCTION

Serous pigment epithelial detachment (PED) can be seen without any significant clinical or angiographic choroidal neovascularization. Developing without any systemic or ophthalmic causes at young ages (<50 years), PEDs is considered to be a variant of central serous chorioretinopathy (CSC) (1). According to another view, serous PEDs occur as a result of increased choroidal permeability secondary to choroidal ischemia (2, 3).

In this report, we aim to present the case of a patient who was admitted to our ophthalmology clinic with complaints of near sight and no systemic diseases, and diagnosed with idiopathic serous PED.

CASE REPORT

A forty-seven-year-old female patient was admitted to the clinic with near sightedness. The complete ophthalmic examination with Snellen visual acuity chart showed the best corrected acuity of 10/10 in both eyes and an intraocular pressure of 14 mmHg in the right eye and 16 mmHg in the left eye. The anterior segments of both eyes were normal in the biomicroscopic examination. The dilated funds examination revealed cystic, hypo-pigmented lesions with protuberant surface in the fovea in both eyes (Figure 1). The patient did not have any metamorphopsia complaints. We evaluated the patient for systemic and serological components and applied immunological tests. The test results showed that the patient had negative anti TORCH and normal ASO and CRP. With no detected systemic diseases, the patient was scheduled for FA and OCT.

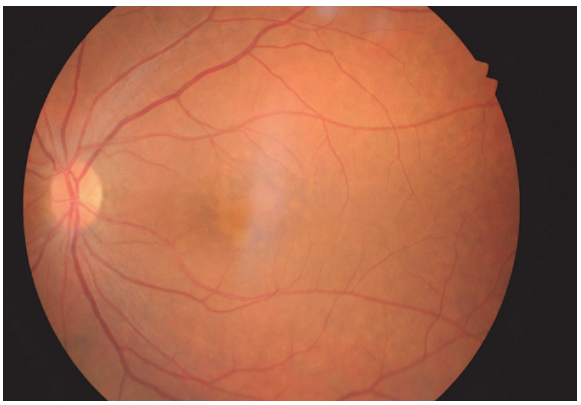

Figure 1. Hypo-pigmented, lobulated lesion in the fovea of the left eye.

The flouorescein angiography of the patient showed hyper-flouresceined foci that had started in the early period and increased in the later period (Figures 2a, 2b).

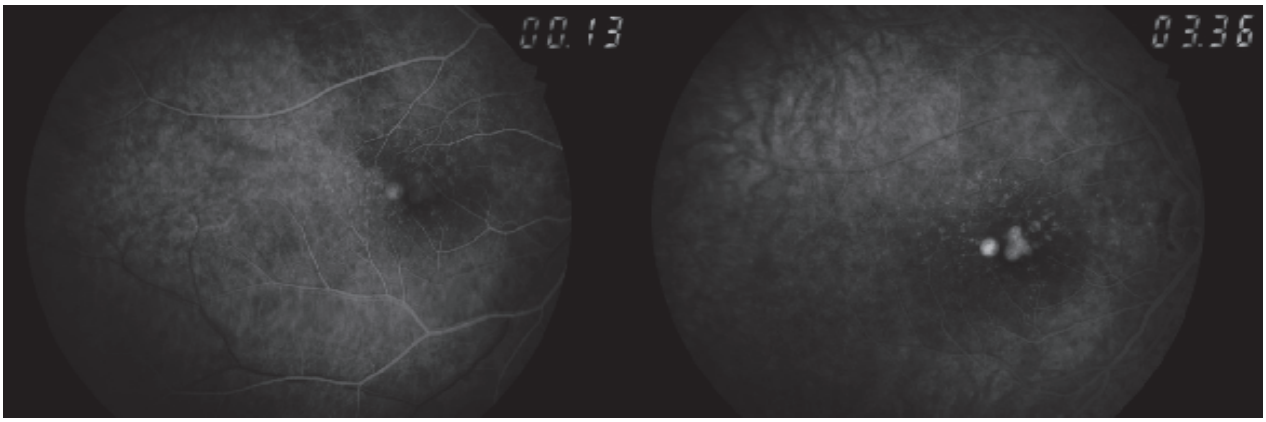

Figure 2a. Early and late FA findings of the right eye.

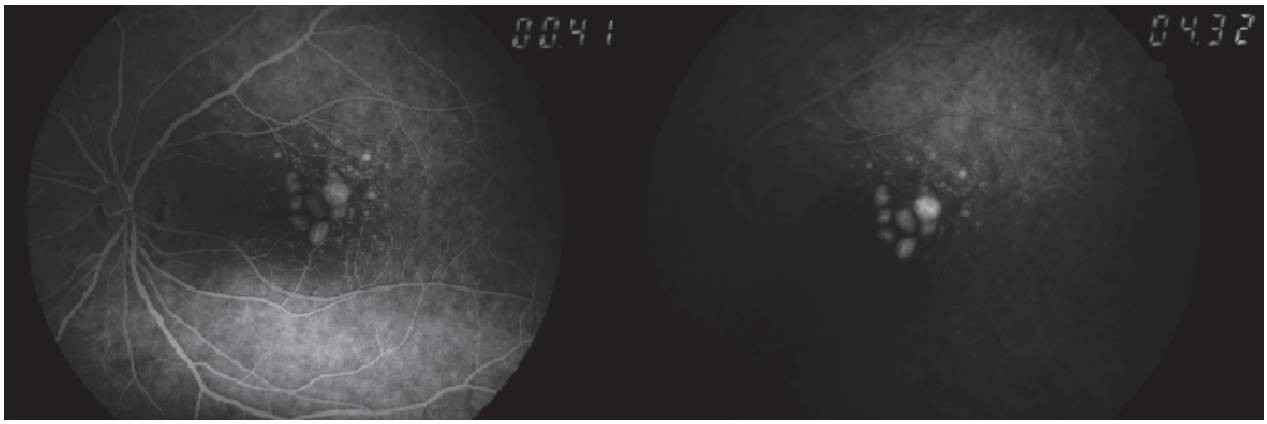

Figure 2b. Early and late FA findings of the left eye.

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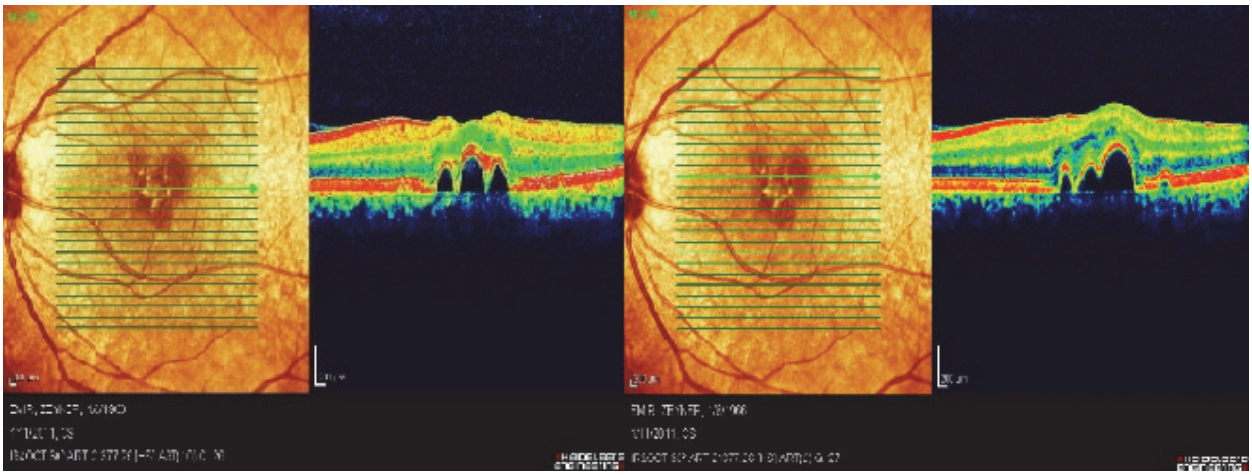
The OCT sections of the patient showed neighbouring serous PED areas in both fovea (Figures 3a, 3b).



Figures 3a and 3b. OCT results of the patient.

DISCUSSIONS

Serous detachment of the retinal pigment epithelium can be seen in healthy individuals as well (1). This case is either because of a variant of CSC (2) or of an increase in permeability in the choriocapillary layer (3, 4).

The PED was observed bilaterally in our case; considering the age of the patient and because there were no systemic diseases, we diagnosed our patient with idiopathic PED. This picture was thought to be a sequelae of a previous CSC. Close to the large PED areas in the OCT, there were smaller PED areas which made us think that the patient must have had CSC before (Figure 3b).

Nobel et al. have detected serous PEDs in the posterior retina pole in 5 middle-aged patients and diagnosed the patients with idiopathic PED when they failed to detect certain underlying causes (5).

In their case study of a patient with suspected neurosyphilis, Anan and Mushin have identified multifocal serous PED areas and concluded that this was related to permeability increase in the choriocapillary layer (6). In our case, we did not detect any serologic findings including syphilis.

Multifocal PED areas can be in certain numbers in various cases. The largest number of PED areas related to this is found in Japanese patients. In a seven-case series, researchers have identified more than 100 PED areas (7, 8). In our case, the number of PED areas was no more than 3 and these areas were connected to each other (Figures 3a-3b).

In this paper, our aim was to present the case of a disease-free young female patient with bilateral idiopathic multifocal PED which was identified by chance during routine outpatient visits.

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Bilateral Peripheral Facial Paralysis in a Pregnant Patient Admitted to Emergency Service: A case of Guillain-Barre Syndrome

Acil Servise Başvuran Gebede Bilateral Periferik Fasiyal Paralizi: Guillain Barre Sendromu

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Abstract
Unilateral facial paralysis is frequently seen in emergency services but bilateral facial paralysis (BFP) is rare. The most common causes of bilateral facial paralysis are Gullian Barre syndrome, lyme disease, Bell paralysis, skull fracture, moebius, multiple sclerosis, and infectious mononucleosis. Gullian Barre Syndrome is a demyelinating polyneuropathy which is associated with acute infection. The majority of cases present with symmetric muscle weakness and areflexia. Gullian Barre Syndrome can be diagnosed by clinical findings together with lumbar puncture and/or electrodiagnostic results. It is a rare disease in pregnancy. Plasma exchange or gamma globulin treatment is the preferred treatment. In this report, we present the case of a 20-week pregnant woman who presented with bilateral facial paralysis and was eventually diagnosed with Gullian Barre syndrome.
Keywords: Gullian Barre Syndrome; Pregnant; Bilateral Facial Nervous Paralysis.

Özet
Acil Serviste tek taraflı periferik fasiyal sinir paralizisi sık görülmektedir, fakat bilateral fasiyal sinir paralizisi (BFP) nadir görülür. Bilateral fasiyal sinir paralizisinin en yaygın nedenleri; Guillain Barre sendromu, lyme hastalığı, Bell paralizisi, kafatası fraktürü, moebius, multipl skleroz, enfeksiyoz mononükleozdur. Guillain Barre sendromu akut enfeksiyonla ilişkili demiyelizan bir polinöropatidir. Hastaların büyük çoğunluğu simetrik kas güçsüzlüğü ve arefleksi ile başvururlar. Klinik bulgular, lumbal ponksiyon ve/veya elektrotanısal testler ile desteklenerek Guillain Barre sendromu tanısı konur. Gebelikte nadir görülen bir hastalıktır. Tedavide gama globulin ya da plasma exchange uygulanır. Bu yazıda, bilateral periferik fasiyal sinir paralizi ile başvuran ve Guillain Barre tanısı konulan, 20 haftalık gebe vakası sunulmuştur.
Anahtar Kelimeler: Guillain Barre Sendorumu; Gebe; Bilateral fasiyal sinir paralizisi.

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INTRODUCTION

Guillain-Barre syndrome is an acute inflammatory demyelinating nerve disease with an incidence rate of 1-2 in 100,000 in the population. It is more common in men than females by 1,5-2 times (1). Retrospective studies have shown that it has increased incidence within the first 4 weeks of the the postpartum period although it has a similar incidence rate in the general population and pregnant women (2).

Cases with GBS usually show symptoms around 1-3 weeks after gastrointestinal tract or respiratory tract infections. Lower limbs are usually more affected than upper extremities. The disease usually begins with numbness in both lower extremities and progresses with growing loss of strength in the following hours and days later (3).

CASE REPORT

A 30-year-old 5-month pregnant patient was admitted to the emergency department with complaints of weakness and inability to close both eyelids in the last 2 days. We learnt that the patient had had diarrhea for a few days about one month ago. Two weeks before her admission, she had suffered from the onset of back pain and numbness in both hands and feet. She had body-wide weakness and could not walk the stairs. She consulted another physicians for her inability to close both eyelids two days ago and was referred to our hospital with normal audiometric test results for BFP etiology. On admission, she did not have any infection-related complaints.

In neurologic examination, she was conscious, oriented, and cooperative. She had isochoric pupils with a light reflex of + / + and corneal reflex of + / +, respectively. Both upper extremity had a muscle strength of 5/5 while both lower limbs had a distal muscle strength of 4/5 and a proximal muscle strength of 4/5. Deep tendon reflexes in the upper extremities were normoactive; these reflexes were hypoactive in the lower extremities. Sensory and cerebellar examinations were normal. The patient had ataxic gait. Apart from this, other system examination results were normal.The complete blood count, C-reactive protein, liver and kidney function tests were within the normal range except for a 14000/mm3 value of white blood cell count in the urinalysis.

The patient was suggested to undergo a diagnostic lumbar puncture for central nervous system infection but the patient refrained from this application. The electroneuromyography (ENMG) showed extension along the distal latency as observed in the bilateral median and ulnar nerves in both upper extremities and in the tibial and peroneal nerves in the right lower extremity and decrease in the amplitude of the combined floor action potential. The motor conduction velocity of the patient was normal. Sensory conduction velocity and amplitude of sensory nerve action potentials were normal in the bilateral median and ulnar nerves in both upper extremities and the sural nerves in the right lower extremity. We detected prolongation in the F latency of the nerves in both upper limbs and the right lower extremity. The ENMG conducted also revealed signs of motor polyneuropathy accompanied by axonal degeneration. The patient was given 25 g/day intravenous immunoglobulin (IVIG) therapy. She was discharged after a five-day follow-up period due to the decline of her symptoms.

DISCUSSION

0,3-2% of facial paralysis cases have bilateral facial nerve paralysis (4). Viral infections, hyper-coagulability, hypertension, and immunosuppression factors are among the causes of facial paralysis during pregnancy (5). Guillain-Barre syndrome is an acute autoimmune-induced polyneuropathy often rooted in a bacterial or viral infection. The earliest and most common symptom is tingling sensation. The most important finding of the syndrome is usually symmetrical power loss developing in the early stages. Cranial nerve involvement is less common at the beginning but bilateral facial nerve paralysis (25-55%) and oculomotor palsy (5-13%) usually accompany the symptoms (6). 40% of the patients have a history of respiratory tract infection while 20% of the patients share a history of gastroenteritis about a month before the onset of the symptoms (7). The most common infectious agents are campylobacter jejuni by 26% and cytomegalovirus by 13%. Our patient, too, had had diarrhoea about 1 month ago and numbness in both hands and feet as well as back pain 2 weeks after the diarrhea. These were followed by loss of strength inability to walk the stairs, and, for the last 2 days, inability to close both eyelids.

Early diagnosis is very important for the treatment. IVIG and plasmapheresis are among the treatment methods used in GBS. IVIG and plasmapheresis administration have been shown to be equally effective in the prevention of progress of neurological symptoms (8). With its easy applicability, IVIG comes to the forefront as the better option. Affecting all components of the immune system, IVIG provides Fc receptor blockade, inhibition of complement activation, suppression of cytokines, adhesion molecules and chemokines, T cell activation and differentiation, and regulation of effector functions (9).

Bilateral facial nerve paralysis is very rare. An accurate and detailed patient history, complete physical examination, and laboratory investigations are required in order to elucidate the etiologies. In conclusion, GBS should be kept in mind while evaluating patients presenting with bilateral facial nerve paralysis.

This case was presented at the 11th National Emergency Medicine Congress in Antalya (Turkey) on 16-19 April 2015.

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Remission of Obsessive-Compulsive Symptoms in Hypomanic Period in a Patient with Comorbid Bipolar Affective Disorder and Obsessive Compulsive Disorder: A Case Report

Bipolar Affektif Bozukluk ve Obsesif Kompulsif Bozukluk Eştanılı Bir Olguda Hipomanik Dönemlerde Obsesif-Kompulsif Belirtilerin Düzelmesi: Bir Olgu Sunumu

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Abstract

Given the prevalence rates of obsessive compulsive disorder and the bipolar affective disorders in the general population, one would expect the co-occurrence of these syndromes to be rare. Yet, findings have revealed extremely high rates of comorbidity in obsessive compulsive disorder with both depressive disorders (50%) and bipolar disorder (10%) and shown that obsessive compulsive disorder is the most common anxiety disorder in patients with bipolar disorder. This situation makes it difficult to recognize the changing clinical disease and prognosis while response to treatment can also be adversely affected. Clarifying the phenomenological features of obsessive compulsive disorder-bipolar affective disorder comorbidity has important etiological and treatment implications. In this article, we discuss the pathophysiological importance of the improvement of obsessive compulsive symptoms during hypomanic episodes in a bipolar disorder patient, who had comorbid obsessive-compulsive disorder.

Keywords: Bipolar Affective Disorders; Obsessive Compulsive Disorders; Comorbidity.

Öz

Bipolar affektif bozukluk ve obsesif kompulsif bozukluğun genel nüfustaki yaygınlık oranları göz önüne alındığında iki sendromun birlikteliğinin nadir olması beklenebilir. Ancak çalışmalar obsesif kompulsif bozukluğun hem depresif bozuklukla (%50) hem de bipolar affektif bozuklukla (%10) birlikteliğinin yüksek oranlarda görüldüğünü ortaya koymuştur. Bipolar bozuklukta en sık görülen anksiyete bozukluğunun obsesif kompulsif bozukluk olduğu gösterilmiştir. Bu durum, hastalığın kliniğini değiştirerek tanınmasını güçleştirmekte, prognozu ve tedaviye yanıtı olumsuz olarak etkileyebilmektedir. Obsesif kompulsif bozukluk ve bipolar affektif bozukluk birlikteliğinin fenomenolojik özelliklerinin netleştirilmesi etyolojisini aydınlatma ve tedavi yaklaşımı açısından önemlidir. Biz de bu yazıda bipolar affektif bozukluk ve obsesif kompulsif bozukluk eş tanılı bir olguda hipomanik dönemlerde obsesif kompulsif belirtilerinin düzelmesinin fizyopatolojik önemini tartıştık.

Anahtar Kelimeler: Bipolar Affektif Bozukluk; Obsesif Kompulsif Bozukluk; Eş Tanı.

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INTRODUCTION

Studies show that Bipolar Affective Disorder (BAD) and anxiety disorders usually manifest themselves simultaneously (1). Although it has been suggested that this association was coincidental (2), large-scale epidemiological studies have demonstrated that this is more than a coincidence (3, 4). It has even been suggested that these two may be related pathophysiologically.The common biological mechanisms involved in their etiologies and the overlapping neurotransmitter and neuromodulator systems are signs of the reliability of this model as reports show. There are also some studies that assess generalized anxiety, panic, social phobias, obsessions, and compulsions as pathological symptoms of bipolar disorder (1).

The majority of these patients receive comorbid multiple anxiety disorder diagnosis. It has been shown that the most common anxiety disorder is obsessive-compulsive disorder (OCD) (2). This changes the clinical picture of the patient and makes the disease difficult to recognise while also adversely affecting the prognosis and response to treatment (5). It has been suggested that OCD comorbidity increases the risk of suicide in bipolar patients and influences the quality of life negatively (6).

Recent epidemiological and clinical studies point to a high incidence of association between BAD and OCD; however, the number of studies concerning socio-demographic and clinical characteristics of this association is limited. Moreover, comorbidity of these two disorders make diagnosis and treatment difficult. With the aim to contribute to this topic, we aim to present the case of a patient with comorbid BAD and OCD by studying the mechanisms underlying the improvement of OCD during hypomanic episodes.

CASE REPORT

A 23-year-old male student, E.D, was brought to our clinic with complaints of talking too much along with excessive mobility and spending. His medical history showed that the complaints had started 15 days ago accompanied by decreased sleep at night. Despite sleeping less, he had constantly been on the move and taken up the habit of purchasing expensive items that he did not need and storing them in his drawer. The initial mental state examination revealed that he was conscious, cooperative, and had full orientation with accelerated association. His mood was euphoric and did not have insight into his disease. At the start of his hospital stay, his Young Mania Rating Scale score was 20.

The psychiatric history of the patient revealed that his first complaints started as compulsive behaviours such as constantly watching his back in high school. He related that he felt he was being tracked by his family and friends and he had obsessive thoughts about religion. The patient had been followed for OCD for the last 2 year and he had not used any drugs in the last 2 months. About 1 year ago, he spent his time indoors for about 1 month during which he was obsessed with fate concept, read many books on the subject, and gave much thought on people's life goals. During this period, his condition was accompanied by OCD and depression. He defined a depressive mood in which he did not enjoy anything in that period. He stated that he thought he lost his energy although he did not attempt or think about suicide. We learnt that his obsessions continued to increase during this depressive time. At the time, he had started using fluoxetine, benzodiazepine, and clomipramine but discontinued using these drugs due to the side effects. However, we also learnt that, following the depressive episode a year ago, the patient had experienced a similar hypomanic period during which he was hyperactive, talked a lot, and spent too much money. This was repeated once again after 6 months. The patient informed us that these obsessions and compulsions disappeared during his hypomanic periods. After the medical history, mental status examination, and interview with the family, the patient was diagnosed with bipolar affective disorder type 2 accompanied by pre-diagnosed hypomanic episodes and hospitalised.

Throughout his time at the hospital, we observed that the patient was still in his period of hypomania though without any signs of OCD. We started to give the patient valproic acid 1000 mg/day and risperidone 3 mg/day. At the end of three weeks, his mobility and talking decreased. He could sleep in regular sleep patterns although, immediately after this, he developed obsessions and compulsions once again. We started anafranil 75 mg/day and discharged the patient for outpatient follow up and treatment. In his follow-ups, we observed that the predominant symptoms were of OCD when BAD-2 was in remission.

DISCUSSION

In this case report, we present the case of a 23-year-old male patient with comorbid BAB type 2 and OCD. It is stated that patients with bipolar affective disorder have higher risk to develop at least one more anxiety disorder. It has been reported that the most common anxiety disorders is OCD (1). In the past, OCD was associated with major depressions but recently it is thought that there is a strong link between OCD and BAD (2). A study has shown that 16% of the followed OCD outpatients patients had comorbid BAD and 67% of these patients had BAD 2 (7). In our case, although BAB and OCD co-existed, OCS symptoms were denser in depressive episodes whereas obsessive-compulsive symptoms were more notable during hypomanic episodes and this makes our patient a noteworthy case.

Studies on the pathophysiology of co-existing BAD and OCD are limited. Striatal hyperactivity is thought to be a common biological basis for both (8). It is known that both diseases are caused by the changes in the serotonergic, dopaminergic, GABAergic, and glutamatergic neurotransmissions (9). The fact that drugs that block serotonin reuptake bring about good results for OCD has turned the attention to OCD-serotonin

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hypothesis (10). It is known that serotonin alone is inadequate to explain the etiology of the disease. The change in balance between serotonin and other neurotransmitters or receptor changes may be more effective in explaining its etiology (11). But the high rates of hypomania and mania associated with the use of antidepressants in all anxiety disorders prevent the serotonin reuptake inhibitors in the treatment of comorbid conditions (12). The presence of OCD in patients with basal ganglia damage in which dopamine neurones are dominant has attracted attention to the idea that dopamine may play a role in OCD. Another sign that supports this idea is that dopaminergic agents can lead to the formation of symptoms and that SSRIs improve when they are added antidopaminergic agents. Antidopaminergic treatment alone is not effective. Anxiety and egodystonicity seen in OCD are not present with the symptoms that develop with dopaminergic agents only. This suggests that serotonergic dysfunction is necessary for egodystonicity (13). Norepinephrine and serotonin are more commonly mentioned in the studies analysing the biochemical etiology of bipolar disorder. The effect of dopamine has also been theoretically recognised. Data show that dopamine, serotonin, and norepinephrine levels decrease in depression while they tend to increase during manic episodes (14). These neurotransmitters, which increase during manic episodes, are the ones that decrease in OCD and may be responsible for the etiology of OCD. Therefore, the data presented above about our case may explain the biological factors concerning the onset of manic episodes which took place when the patient was not followed as well as the remission of OCD. It can be taught that neurochemical factors such as dopamine, serotonin, and norepinephrine, which are responsible for the pathophysiology of manic episodes, may be correcting the symptoms of OCD. However, as each neurotransmitter is not sufficient alone to explain the etiology, the interaction and imbalance between the two diseases suggests that the coexistence of these two disorders change the clinical course for patients.

As a result, in order to follow the prevalence of OCD in bipolar disorder patients, associating factors, and clinical processes of these disorders, more follow-up studies are required. In this article, we have aimed to draw attention to the pathophysiological importance of the disappearance of OCD symptoms during manic episodes. In this regard, further research will provide progress in the description of the pathophysiology and treatment of both diseases.

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Hemolytic Uremic Syndrome as a Cause of Adult Acute Renal Failure

Erişkin Akut Böbrek Yetmezliğinin Bir Sebebi Olarak Hemolitik Üremik Sendrom

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Abstract

Thrombotic microangiopathy is a microvascular occlusive disorder characterized by microangiopathic hemolytic anemia, thrombocytopenia, and variable signs of organ injury due to platelet thrombosis in the microcirculation. Regarding to the severe of brain or renal lesions, two clinical entities (pathologically similar but clinically different) are described: thrombotic thrombocytopenic purpura and hemolytic uremic syndrome. Thrombotic thrombocytopenic purpura usually affect adults, and is characterized by severe neurologic involvement in most cases, and variable renal involvement. Hemolytic uremic syndrome occurs in young children, and is characterized by acute renal failure, and absent or minimal neurologic abnormalities. In this case report, the clinical features, diagnosis, pathophysiology, and treatment of an adult with acute renal failure due to the thrombotic microangiopathy with hemolytic uremic syndrome are discussed.

Keywords: Acute Renal Failure, Thrombotic Thrombocytopenia; Hemolytic-Uremic Syndrome, İntensive Care.

Öz

Trombotik mikroanjiopati, mikroanjiopatik hemolitik anemi, trombositopeni ve çeşitli organ tutulumları ile karekterize mikrovasküler bir hastalıktır. Trombotik mikroanjiopati'de beyin veya böbrek tutulumunun ciddiyetine göre; patolojik olarak benzer, ancak klinik olarak farklı iki klinik tablo tarif edilmiş olup; bunlar trombotik trombositopenik purpura ve hemolitik üremik sendrom olarak adlandırılmıştır. Trombotik trombositopenik purpura daha çok erişkinlerde görülmektedir, nörolojik bulgular ön plandadır ve böbrek tutulumu hafiftir. Buna karşın hemolitik üremik sendrom, daha çok çocukluk çağında görülür, akut böbrek yetmezliği belirleyici özellik olup, nörolojik bulgular hafif veya yoktur. Bu olgu sunumunda erişkin akut böbrek yetmezliği gelişen trombotik mikroanjiopatiye bağlı hemolitik üremik sendromun klinik bulguları, tanısı, patofizyolojisi ve tedavisi tartışılmıştır.

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INTRODUCTION

The common findings of thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS) are microangiopathic hemolytic anemia, intravascular thrombus/fibrin formation, organ dysfunction, and thrombocytopenia (1-3). TTP is one of the most common causes of acute renal failure in infants and children (4). It is rare in adults. HUS may also rarely occur following glomerular pathology. The underlying pathology is thrombotic microangiopathy accompanied by microvascular occlusive disorder of often capillaries or less frequently of arteries (3). Thrombotic thrombocytopenia purpora, which shares similar clinical features and pathologies, often causes cerebral ischemic lesions due to platelet aggregation but platelet-fibrin thrombus usually affect the kidneys in HUS (5, 6). However, TTP-HUS continue to be a life-threatening disease despite of the early treatment strategies. In this case report, the clinical features, diagnosis, pathophysiology, and treatment of an adult with acute renal failure due to the thrombotic microangiopathy (MA) with hemolytic uremic syndrome are discussed.

CASE REPORT

Table 1 presents laboratory findings of a 22-year-old female patient at emergency department admission and after treatment who was diagnosed with HUS and presented with abdominal pain, nausea, vomiting, diarrhea, confusion, anuria, hypotension and shock in our emergency department. She had been hospitalized 3 days ago due to diarrhea and had been discharged with antibiotic therapy. On the initial examination the patient was unconscious, intubated, hypotensive, and tachycardiac in the emergency department. The patient was transported to intensive care for taking care and treatment. We connected the patient to mechanical ventilator in spontaneous assisted breathing mode and performed full monitoring (ECG, temperature and oxygen saturation tests, and arterial monitoring). We also obtained all the cultures and pre-diagnosed the patient with sepsis. Within the first hour, we administered a broad-spectrum antibiotic therapy. The thorax tomography revealed haemathorax in right lung and the right chest tube was placed. As the patient had a hypotensive course, we started to administer dopamine infusion. The patient was then taken to the hemodialysis after hemodialysis catheter was placed. After the first ten days, the patient still could not be detached from the mechanical ventilation upon which we applied percutaneous tracheostomy with Griggs method. The parenteral nutrition that had started on hospitalisation was further supported with enteral nutrition on the second day. Then the parenteral nutrition was replaced by a 31-day enteral nutrition. The patient received eight sessions of hemodialysis and had to discontinue the session due to acute renal failure after plasmapheresis three times. The patient stayed in intensive care for 49 days and was transferred to the infectious disease department.

Table 1. The laboratory findings at emergency department admission and after the treatment.

	Before	After
Leucocytes (/mm^3)	13700	4300
Hemoglobin (gr/dL)	10,6	7,1
Haematocrit (%)	30	20
Platelet (/mm^3)	24000	106
CRP (gr/dL)	6,18	10,4
Glucose	100	95
LDH (U/L)	1760	670
Lipase U/L	16	17
Amylase U/L,	34	33
ALP U/L	46	
Urea (mg/dl)	40	59
Creatinin (mg/dl)	5,76	4,93
AST (U/L)	131	15
ALT (U/L)	131	12
GGT(U/L)	8	6
Albumin	2,8	2,5
Sodium (mEq/lt)	133	134
Potassium (mEq/lt)	2,8	3,6
Phosphor (mg/dL)	7,2	5
Total biluribin (mg/dL)	0,8	0,9
Direct biluribin (mg/dL)	0,4	0,5
PTT	13,6	10
aPTT sec (24-36)	34,4	25
Ptz	65%	60%
Fibrinogen mg/dL	302	200
D-Dimer mikrogFEU/mL	4,4	1
INR	1,09	0,9
Anti HBsAg IU/mL (micro)	19,5	
AntiHAVIgG	Positive	
Anti-HCV	Negative	
pH	7,36	7,36
pCO2 mmHg	32	36
pO2 mmHg	230	100
Saturasyon %	99	98
BE	-6,5	2,3

DISCUSSION

HUS is characterised by thrombocytopenia, acute deterioration in renal function, microangiopathic anaemia, and endothelial dysfunction. HUS is rare and serious disease with a variety of etiologies among adults. HUS is also one of the rare causes of acute renal failure in adults (7, 8). The chronic renal failure rate after HUS is between 40-60% (8-10). Our patient was diagnosed with HUS due to the presence of acute renal failure, thrombocytopenia, and microangiopathic haemolytic anaemia triad. Because of the presence of fever, diarrhea, hypotension, leukocytosis, and inotropic need, we diagnosed the patient with HUS-related sepsis. There was no underlying chronic diseases. Studies in human kidney have shown that cytotoxin often binds with renal tubular cells close to the glomeruli and that the cytokines produced by such cells may play a role in the pathogenesis of HUS (2).

Central nervous system and neurological dysfunction are common pictures in HUS (11-13). The severity of acute illness has been found to be associated with the first need of dialysis and symptoms of central nervous system (7, 11). Our patient had clouded consciousness and

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convulsions. Microthrombus in HUS patients constitute the most damage in the kidneys (2). In our case, too, there was acute renal failure. Our patient received 8 sessions of hemodialysis and underwent plasmapheresis three times. We administered fresh frozen plasma and regular antibiotic therapy. The patient eventually recovered from renal insufficiency. The literature also reports the case of a patient who developed HUS-related renal failure in the postpartum period and recovered with TDP, plasmapheresis, and hemodialysis (6,7).

In a cohort study, plasmapheresis administration has provided high response and survival rates (6). However, the literature also reports the case of a patient who, after undergoing plasmapheresis for 28 times, could not recover from renal failure and had to need renal raplacement therapy (14). Another study reports the case of a HUS patient accompanied by a secondary disease with increased mortality and recurrence (15,16).

As a result, HUS is a rare yet major cause of kidney failure in adults. Still, a convenient and fast fluid electrolyte therapy, antibiotics, and dialysis and plasmapheresis for patients with renal failure may reduce mortality.

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Intravascular Branul Fracture

İntravasküler Branül Fraktürü

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Abstract

The peripheral vascular catheter is usually used in intensive care patients to perform medical treatment and invasive blood pressure monitoring. However, during or after this procedure, some complications can develop. One of the complications is intravascular branule fractures. The delay of the treatment process can increase the incidence and severity of complications. Radiography and ultrasonography may be useful for early diagnosis. The reliability of ultrasonography in acute cases is quite high but it can be inadequate in delayed cases or when broken components have moved to a more proximal position. Besides these complications also cause legal actions taken against physicians and health care professionals. In this case, we aim to present the case of a branule fracture in which broken part of a branule remained within the vessel until our peripheral vascular intervention.
Keyword: Peripheral Catheterization; Complications; Embolism.

Özet

Yoğun bakıma yatırılan hastalara medikal tedavilerin yapılabilmesi ve invazif kan basıncı monitorizasyonu için periferik damarlardan genellikle periferik branül yerleştirilir. Ancak bu işlemler sırasında veya sonrasında bazı komplikasyonlar gelişebilir. Bu komplikasyonlardan biri intravasküler branül fraktürleridir. Bu gibi durumlarda erken tanı konulabilmesi için radyografi ve ultrasonografi kullanılabilir. Acil durumlarda ultrasonografinin güvenirliği oldukça yüksekdir. Fakat gecikmiş vakalarda ultrasonografi yetersiz olabilir veya kırılan branül parçası daha proksimale hareket edebilir. Tedavi sürecinin gecikmesi komplikasyonların sıklığını ve önemini arttırabilmektedir. Yine bu komplikasyonlar hekimlerin ve sağlık personellerinin hukuki olarak da suçlanmasına sebep olabilecektir. Bu vakada periferik vasküler girişim sonrası damar içinde kırılan ve damar içinde kalan vakayı sunmayı amaçladık.
Anahtar Kelimeler: Periferal Kateterizasyon; Komplikasyon; Emboli.

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INTRODUCTION

For the medical treatment and invasive blood pressure monitoring, patients admitted to intensive care are often applied branule placement through peripheral veins. However, complications may develop during or after the insertion process. In this report, we aim to present the case of a broken branule within the blood vessel during a peripheral vascular intervention.

CASE REPORT

The 20G 32mm branule inserted to the left wrist of a 31-year-old female patient at the Turgut Ozal Medical Center Maternity ICU in order to treat the cephalic vein came off while removing from the neck at the distal of the injection port 3 days after its insertion. To prevent embolisation, we applied tourniquet with gauze bandage to the proximal portion of the branule's broken end (Figure 1).

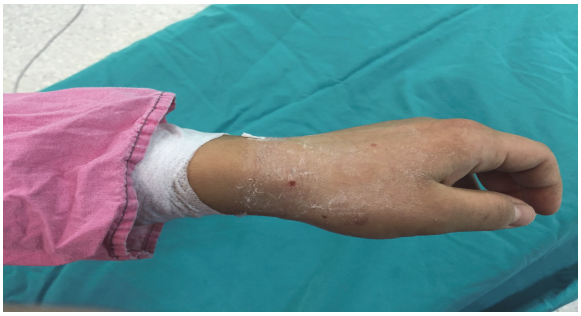

Figure 1. Tourniquet application to prevent embolisation in the proximal portion of the branule's broken end.

The diagnosis was established by clinical examination and ultrasonography. While asking the patient to sign the surgical consent form, we informed the patient that direct radiography or ultrasonography may be insufficient due to the radiopaque structure of catheters especially in late diagnosis or in cases when the remaining piece moves up towards a more proximal position. Then, we opened the cephalic vein under local anaesthesia and detected the broken part of the branule. We removed the broken part and applied primary repair (Figure 2). The patient was discharged without any problems.

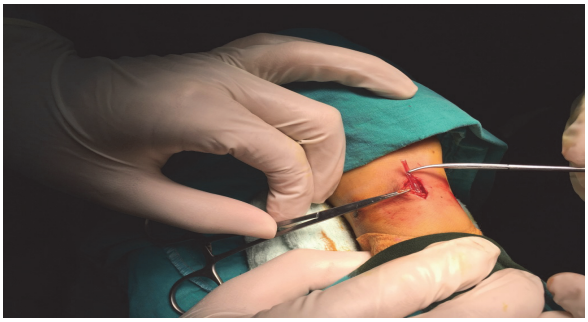

Figure 2. Removing the broken part of the branule from the vein.

DISCUSSION

Peripheral venous branules are commonly applied for the treatment and follow-up of inpatients in hospitals (1). Peripheral venous branules are used to apply blood, liquid, nutritional agents, and drugs into the peripheral circulation as well as to monitor invasive blood pressure. As in many invasive procedures, the increase in the use of branules comes with complications during and after the application. These complications include local complications such as vascular insufficiency, bleeding, skin and subcutaneous lesions, phlebitis, hematoma, and branule embolisms as well as systemic complications such as sepsis and air embolisms (2). In addition, branule fracture and, thus, the presence of a foreign object within the veins bring about additional surgical procedures to the patient, extend the duration of the treatment, and increases the risk of new complications. Moreover, these complications can lead to legal indictment of physicians and medical staff.

A study on the American Anesthesiology Society database has shown that 2% of lawsuits against physicians were due to peripheral vascular catheterisation with common complications such as crusting on the the skin (28%), swelling/infection (17%), nerve damage (17%) , fasciotomy scars (16%), and air embolism (8%) (3). The incidence of broken venous branules with remains within the vein is reported to be 0.1%.

A study conducted among 11 paediatric patients with a control group has shown that the size of branule, its location, or the type of administered liquid are not influential factors on intravascular branule fractures though the length of time branule remained attached, leak around the area where branule is inserted, and branule blockage are found to be factors leading to this situation (4). In one of the studies on the complications, the risk of pulmonary embolism developing form vein thrombosis due to peripheral branule is reported as 12% (5). The clinical signs of branule embolisation are malfunctioning branule (56%), arrhythmia (13%), lung symptoms (4.7%), and septic syndromes (1.8%). But this can be asymptomatic in 24.2% of the cases; the mortality rate is 1.8% in such cases (6). It has also been shown that applying tourniquet to the region where the branule fractures has occurred reduces the risk of embolism (7). Branule-related infections, another major complication associated with branule use, constitute 7% of nosocomial infections in the literature. Besides, if the remains of the intravenous catheter stay within the vessel for more than 48 hours, this raises the risk of contamination to 52% (8-9).

Intravenous branule parts can lead to pulmonary arterial embolism through vena cava, right atrium, and right ventricle. Although they are very rare, the most serious complications can be listed as follows: myocardial perforation or necrosis due to the embolisation of the right ventricle and pulmonary artery, tricuspid or pulmonary valve defects, endocarditis, pulmonary abscesses, arrhythmia, and sudden death. The risk of

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bacterial contamination in cases when intravenous catheter components remain within vessels for more than 48 hours is 52% (10).

For the effectiveness of treatment, early diagnosis is important in cases with suspected peripheral catheter fracture. Radiography and ultrasonography may be useful for early diagnosis. The reliability of ultrasonography in acute cases is quite high but it can be inadequate in delayed cases or when broken components have moved to a more proximal position. In cases when it is not for certain that broken pieces are still in the vessels, radiological examination could be misleading with false positive results. For this reason, it is important to inform patients prior to surgery.

Today, as a result of the increase in the use of intravascular branules, the incidence of complications with mortality and morbidity rates has also likewise increased. For this reason, health service staff who apply these procedures should be trained while practitioners should also intervene accurately and quickly in case of such complications. Training health personnel is important not only because it may affect the continuity of treatment but also it will prevent legal processes related to serious complications caused by branule fractures.

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Role of Cytokines during Pregnancy

Gebelik Sürecinde Sitokinlerin Rolü

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Abstract

The maternal immune system plays an important role in the establishment of a successful pregnancy. Pregnancy is a unique immunological challenge during which maternal immune system has to tolerate the fetal alloantigen while preserving the ability to fight infections and enviromental pathogens. In mammalian pregnancy this balance is also regulated by the complex cooperation between cytokines. Cytokines are immunoregulatory molecules that are crucial for normal reproductive functions, including implantation, placentation and trophoblast invasion. It is widely proposed that, during pregnancy, Th2 immune response is neccessary for successful pregnancy, whereas a Th1 response is detrimental to fetus. In addition to this, it has been suggested that Th1/Th2 activity balance displays a strong shift towards Th2 activity during the physiological pregnancy. Studies concerning Th1/Th2 balance in physiological and pathological pregnancy have shown that Th1/Th2 cooperation is needed for a successful pregnancy. This review focuses on the potential roles of cytokines during pregnancy and will contribute to the understanding of the roles and mechanisms behind the cytokines that effect physiological and several pathological conditions of pregnancy.

Keywords: Pregnancy; Cytokines; Th1/Th2 Cytokines.

Öz

Maternal immun sistem başarılı bir gebeliğin kurulmasında önemli rol oynamaktadır. Gebelik, maternal immun sistemin fetal alloantijenlerini tolere ederken aynı zamanda infeksiyonlar ve çevresel patojenlerle de savaşma yeteneğini koruduğu eşsiz immünolojik bir başarı sürecidir. Memelilerde gebelik sırasında bu denge sitokinler arasındaki işbirliği ile sağlanır. Sitokinler, implantasyon, plasentasyon, trofoblast invazyonu gibi normal üreme fonksiyonlarının gerçekleşebilmesi için gerekli olan immun düzenleyici moleküllerdir. Genel bir kanı olarak Th2 immun cevabın başarılı bir gebelik için gerekli olduğu ancak Th1 cevabın fetüs için zararlı olduğu önerilmiştir. Buna ek olarak fizyolojik bir gebelikte Th1/Th2 aktivitesinde dengenin Th2 yönünde olduğu ortaya konulmuştur. Th1/Th2 ilgili yapılan çalışmalar başarılı bir gebelik için Th1/Th2 ortaklığının gerekli olduğunu göstermiştir. Bu derleme, sitokinlerin gebelik sırasındaki potansiyel rolleri üzerine odaklanmıştır ve hem fizyolojik hem de çeşitli gebelik patolojilerinde sitokinlerin rolü ve mekanizmalarının anlaşılmasına katkı sağlayacaktır.

Anahtar Kelimeler: Gebelik; Sitokin; Th1/Th2 Sitokinler.

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Maternal immun sistemin, gebeliğin oluşumunda önemli roller üstlendiği bilinmektedir. Gebelik sırasında immun düzenleyici olarak görev yapan sitokinler, immun cevabın belirlenmesinden sorumludur. Bu süreçte kritik roller üstlenen sitokinler gebeliğin sağlıklı bir şekilde gerçekleşebilmesi için büyük öneme sahiptir (1).

Sitokinler, immun sistem hormonları olarak da tanımlanabilen, immun sistemin düzenlenmesinde önemli rolleri olan, pleotropik moleküllerdir (2). Bu moleküller, bir uyaranın etkisi ile immun ve nonimmun hücrelerden sentezlenirler ve kendilerine özgü hedef hücre reseptörlerine bağlanarak genellikle birden fazla mekanizmayı etkilerler (3).

Düşük moleküler ağırlıklı proteinler olan sitokinler; siklik korpus luteumun korunması, fetal adezyon ve invazyon, implantasyon, fetal ve plasental büyüme ve farklılaşma ve bazı immunmodülatör mekanizmaların düzenlenmesine katılırlar. Hücreler arası iletişimin sağlanmasında görev alan sitokinler, sadece embriyo tarafından değil aynı zamanda, periferal kan lenfositleri (PBL), makrofajlar, oviduktal ve endometriyal hücreler tarafından da salgılanırlar (3). Bu derlemede gebelik sürecinde kritik öneme sahip olan sitokinlerin rolleri açıklanmaya çalışılmıştır.

Sitokinlerin Genel Özellikleri:

Fetusun anne tarafından reddedilmesinin önlenebilmesi için düzenlenmiş bir çevre gereklidir. Bu çevre öncelikle maternal-fetal aralıkta ve uterus dokusunda meydana gelmelidir. Klasik olarak saf CD4 T hücreleri sitokinlerin esas üreticileridir (4). Sitokin üreten lenfosit CD4 hücreleri antijenlere karşı immun cevabın verilmesinde, B hücreleri tarafından gerçekleştirilen antikor üretiminin düzenlenmesinde ve sitotoksik T hücrelerinin işlevinde önemli roller üstlenirler (5, 6). Bu populasyon içinde yer alan sitokinler esas görevlerine göre örneğin, pro- ve anti-inflamatuar veya farklı yardımcı T hücreleri (Th) ile ilişkili olan Th1, Th2, Th17 ve düzenleyici (Treg) hücreler olarak guruplandırılabilirler (4). Th1 esas olarak interlökinleri (IL), IL-1, IL-2, IL-12, IL-15, IL-18, interferon-gamma (IFN-γ) ve tümör nekroz faktör-α (TNF- α) üretirken Th2 hücreleri IL-4, IL-5, IL-6, IL-13 ve granulosit-makrofaj koloni stimüle edici faktörü (GM-CSF) üretir (7). Th17 hücreleri ise IL-17A ve IL-17E'nin kaynağıdır (1). Treg hücrelerinin salgıladıkları sitokinlere de örnek olarak IL-10 ve transforming growth factor β (TGF-β) verebiliriz (4).

Hücresel bağışıklık büyük ölçüde Th1 hücrelerinin aktivitesine bağlı iken bunun aksine Th2 hücreleri esas olarak sıvısal cevabın düzenlenmesiyle ilişkilidir. Makrofajlar ve "naturel killer" (NK) hücreler doğal bağışıklığın esas bileşenleridir. Bu hücreler uygun sitokinleri üreterek T CD4 lenfositlerinin fonksiyon görecekleri yerlere gitmelerinde etkili olurlar. Bu hareketin Th1 aktivitesi yönünde olabilmesi için IFN-γ ve IL-12'ye ihtiyaç duyulurken Th2 aktivitesi için IL-4'ün ortamda bulunması gerekmektedir (8).

Treg lenfositlerinin gebelikte oynadıkları önemli roller ilk kez 2004 yılında farede gösterilmiştir. Treg hücreleri en erken çiftleşme sonrası uterusu drene eden lenf nodüllerinde tespit edildiği bildirilmiştir (9). IL-10 ve TGF-β'nın immun baskılama sırasında arttığı ve gebelik sürecinde önemli roller oynadığı bilinmektedir (10).

Yardımcı T hücrelerinin alt grubu olan Th17 hücreleri proinflamatuar olan IL-17A üretir ve bunlar inflamasyon ve akut transplant rejeksiyonun başlatılmasında önemli roller üstlenirler. Son yapılan çalışmalarda, normal hamile kadınlarla idiopatik tekrarlı düşük yapan hamileler karşılaştırıldığında periferal kan ve desiduada Th17 hücrelerinde artış olduğu gözlemlenmiştir (11).

Gebelik Sırasında Sitokinlerin Aktivasyonu:

İnsanlarda endometriyum, menstrual siklusun proliferatif ve sekretör fazı boyunca çok çeşitli sitokinleri üretir. Bu sitokinlerin gebeliğin kurulumu sırasında uterus çevresinin düzenlenmesi, gelişen konseptusun implantasyonu için uterusun hazırlanması ve fonksiyonel plasenta oluşumu gibi önemli roller oynadıkları gözlemlenmiştir (4).

Gebelik sırasında, Th1 ve Th2 sitokin kaynakları, desidual epitelyum ve stroma, sito- ve sinsityotrofoblast, koryon, amnion ve Haufbauer hücreleridir. Bu dokulardan köken alan sitokinler, fetal allografta karşı maternal toleransın başlatılmasında, infektif faktörlere karşı meydana gelen lokal bağışıklığın düzenlenmesinde ve trofoblast invazyonu esnasında plasental hormonal üretim ile doku yenilenmesinde görev alırlar (7).

Th ilişkili sitokinler ayrıca trofoblast hücreleri, stromal hücreler, epitelyal hücreler, maternal T lenfositleri, makrofajlar, NK hücreleri ve diğer maternal lökositler tarafından da üretilir (12). Bu durum fetal-plasental birimin gelişimi ve sürdürülmesinin bu sitokinlere bağlı olduğunu göstermektedir. Bu sitokinlerin maternal-fetal aralıktaki varlıkları implantasyon, plasental gelişim, sitotrofoblast proliferasyonu, anjiyogenezis, ekstravillöz trofoblast hücre invazyonu, spiral arterlerin yeniden yapılandırılması, hücre büyümesi ve apoptosis gibi süreçleri düzenleyerek uygun çevrenin sağlanmasına etki etmektedir (4).

Yapılan in vitro deneyler, Th1 sitokinlerinin (IL-1, TNFα) endometriyal desidualizasyonu negatif olarak etkilediğini göstermektedir. Çoklu implantasyon başarısızlığı yaşayan kadınlarda düşük konsantrasyonlarda serum leukemia inhibiting factor (LIF), IL-4, IL-6 ve IL-10 görülmüştür (13). İmplantasyon sırasında embriyo, kendi başına aktif olarak (TGF-β ve prostaglandin PGE_2 aracılığı ile) çoğunlukla Th1 (IL-2, TNF-α) sekresyonunu azaltarak, Th2 (GM-CSF) sitokinlerinin üretimini ise artırarak desidua ile olan etkileşimini düzenler. Dahası embriyonun otokrin yolla Th2 sitokinleri (IL-10), TGF-β salgılayabildiği, trofoblastların invaziv özelliklerini baskılayabildikleri ve parakrin yolla da maternal dokulardan proinflamatuar Th1 sitokinlerinin (TNF-α, IFN-γ) üretimini durdurabildikleri bildirilmiştir (14, 15).

Th1 sitokinlerinden IL-2, IL-12, TNF-α ve IFN-γ artışı durumunda da trofoblast gelişimi reddedilir ve bu da fetal kayıplara neden olur. Ayrıca Th0 hücrelerinden Th1'in farklılaşması ve NK hücrelerinin ekspresyonu, maternal desiduada da bol bulunan Th2 sitokinleri ile

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inhibe edilir. Gebe uterusunda baskın olarak bulunan Th2 shiftleri önemli ölçüde gebeliğin sürdürülmesi ile ilişkilidir (6).

Treg hücreleri tarafından üretilen IL-10 ve reseptörlerinin normal koşullar altında erken gebelik sırasında endometriyum ve desiduada bulunması gerekmektedir. Bu sitokin desidual hücrelerin proliferasyonuna ve TNF-α'nın sekresyonuna sebep olmaktadır (16). Kadınlarda erken gebelik sırasında IL-10'un seviyesinde belirgin bir artış olduğu üçüncü trimester sırasında doğum başlamasından hemen önce ise yüksek olarak kaldığı bildirilmiştir (17). IL-10 orijinal olarak Th2 sitokinlerinden biri olduğu düşünülse de, tam olarak Th2 hücreleri tarafından salgılanmaz. Ayrıca materno-plasental aralıkta bulunan IL-10 düzenleyici T hücreleri tarafından üretilir (18). IL-10 yalnız Th1 immunitesi tarafından baskılanmaz, ayrıca bazı inflamatuar aracıları da içine alarak Th2 immunitesini baskılar. Bu nedenle anti-inflamatuar sitokin olarak sınıflandırılması daha doğrudur (19). Diğer bir anti-inflamatuar sitokin olan TGF-β implantasyon sırasında maternal immun toleransın sağlanmasında ve çeşitli vasküler endotelyal büyüme faktörü (VEGF), matriks metallopeptidaz-9 (MMP-9), insülin benzeri büyüme faktör bağlayıcı protein-1 (IGFBP-1) ve LIF gibi implantasyonla ilişkili moleküllerin düzenlenmesinde rol alır (20, 21). Ayrıca TGF-β knockout farelerde erken embriyonik ve doğum sonrası ölümlerin meydana geldiği rapor edilmiştir (22). Gebelik sırasında maternal dokularda gerekli olan immun baskılamanın IL-10, tumor growth factor-β ve proinflamatuar TH1 sitokinlerinden IFN-γ ve TNF-α'nın eşzamanlı olarak baskılanması ile gerçekleştiği bildirilmiştir (23).

Jenkins C ve ark. (2000) tarafından yapılan bir çalışmada ise geçmişinde tekrarlı düşük hikayesi olan ve sonradan başarılı bir gebelik geçiren kadınlardan alınan serumlarda, IL-10 değerinin sonradan düşük yaşayan kadınlara oranla önemli ölçüde yüksek olduğu görülmüştür (24). Gebe olmayan ve tekrarlı düşük hikayesi olan kadınlar ile sağlıklı kadınların endometriyal T-yardımcı hücrelerine bakıldığında, tekrarlı düşük hikayesi olan kadınlarda öncelikli olarak Th1 sitokinleri üretilirken, sağlıklı kadınlarda Th2 hücrelerinin daha fazla oranda üretildiği görülmüştür (25, 26).

Th2 sitokinleri (IL-4, IL-6, IL-13), IL-10 ve TGF-β gibi sitokinler, Th2' nin daha da geliştirilmesi için uygun bir ortam yaratılmasını sağlarlar. IL-1β, TNF-α'nın aynı zamanda da IL-8 ve prostaglandinlerin pro-inflamatuar etkilerini sınırlarlar. Buna ek olarak insanlarda sitotrofoblastların Th2 lenfositlerinin farklılaşmasına katkıda bulunan IL-4'ü ürettikleri tespit edilmiştir (3). Makrigiannakis ve ark. (2001), trofoblastlar ve plasental desidua tarafından üretilen kortikotropin-releasing hormonunun (CRH), aktive olmuş T hücrelerini öldürerek erken gebeliğin ve insanlarda implantasyonun sürdürülmesini teşvik ettiğini kaydetmişlerdir (27).

IL-6 yaralanmalar ve enfeksiyon sonucunda akut-faz cevapların verilmesinde önemli bir aracıdır (4). IL-6 menstrual siklus boyunca insan endometriyumunda ve erken gebelik sırasında desidua da bulunur (28). Ayrıca ekstra villöz trofoblast hücrelerinin IL-6'yı eksprese ettiği ve bu sitokinin MMP'leri up-regüle ederek trofoblast invazyonuna etkileyebileceği rapor edilmiştir (29).

IL-8 ve şimdilerde bilinen adıyla CXCL8, pro-inflamatuar çok fonksiyonlu CXC kemokin olarak sınıflandırılır. İnsanlarda erken gebelik döneminde desidua da bulunan NK hücreleri CXCL8'in üretildiği esas yerlerdir. Ayrıca CXCL8'in trofoblast invazyonunu uyardığı in vitro modellerde gösterilmiştir (30).

IL-1 ve IL-18, embriyonik-endometriyal iletişimde gerçekleşen invazyon, neoanjiyogenezis ve implantasyonda önemli bir faktördür (31). IL-1β, IL-6 ve TNF-α gibi diğer sitokinler ovaryum siklusunun düzenlenmesinde gereklidir ve ovaryum folikülünün büyüme ve gelişmesinde önemli rol oynarlar (32). Tümör nekroz faktörü-alfa (TNF-α) artı IFN-γ gibi Th1 sitokinlerin artan üretimi, IL-10 ile karşılaştırıldığında bunların infertilite ve tekrarlı spontan düşüklerle bağlantılı olduğu görülmüştür (33).

Th1 hücreleri tarafından üretilen TNF-α sitokini, baskın olarak monositler/ makrofajlar tarafından salgılanırlar. TNF-α, lipid metabolizmasında, koagulasyonda, insülin direncinde ve endotel üzerinde etkili olan multifonksiyonel proinflamatuar bir sitokindir (34). TNF-α, hücrelerdeki apoptotik değişiklikleri indükleyerek trofoblastların büyümesini baskılar (35). Yapılan çalışmalarda tekrarlı spontan düşüklerde ve üreme yetmezliklerinin olduğu olgularda, serumda TNF-α düzeyinin yüksek olduğu saptanmıştır (34). Ayrıca Th1 sitokin bağımlı infertilite görülen hastalara anti TNF-α ilaçları verilerek bu hastaların tedavisine yeni bir yaklaşım getirilmiştir (36).

Feto-maternal aralıkta bulunan IL-1 ise trofoblastik hücreler ve desidualize olmuş stromal hücreler tarafından üretilir. IL-1 reseptörü hem endometriyal epitelyum hücrelerinde hem de trofoblastlar da bulunur (37). IL-1 blastosistten gelen ve endometrium üzerine etki eden ilk sinyallerden biridir. IL-1 prostoglandin E_2'nin endometriyal sekresyonunu, LIF ve integrin β_3 alt biriminin ekspresyonunu artırır (16).

Farelerde IL-1 reseptör antagonisti implantasyon öncesinde verildiğinde implante olmuş embriyoların sayısında ciddi bir azalma olmuştur. Bu da IL-1'in embriyo implantasyonundaki önemini göstermiştir. IL-1, trofoblastlardaki MMP-9 aktivasyonunu ve endometriyal stroma hücrelerinin ekspresyonunu uyarır. Böylece feto-maternal aralıkta yer alan sitokinlerden IL-6, MMP-2 ve MMP-9 aktivitesini uyararak trofoblast invazyonunu indüklerken, IL-10, MMP-9 ve trofoblast invazyonunu baskılar (37).

Th1 sitokinlerden olan IFN-γ in vitro kültürde trofoblastların büyümesini inhibe eder (38). Mahdi'nin (2011) yaptığı çalışmada infertil kadınların oluşturduğu grup fertillerle karşılaştırıldığında, infertil olanlarda IFN-γ seviyesinde bir artış görülmüştür (35). IFN-γ veya IFN-γ reseptörü çıkarılan başka bir çalışmada, farelerin normal üreme fonksiyonlarını devam ettirerek döl verdiği

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görülmüş ve IFN-γ'nın fetal yaşam için hayati olmadığı saptanmıştır (39).

Uterustaki NK hücrelerinden salgılanan IFN-γ'nin, implantasyon alanındaki konsantrasyonunun desidual hücre canlılığının sürdürülmesinde maternal arter duvarının değiştirilmesinde ve aşırı artan trofoblast büyümesi ve invazyonunun inhibisyonunda gerekli olduğu bildirilmiştir (35). Mahdi (2011) kendi yaptığı çalışmalarla diğer çalışmaları karşılaştırdığında, IFN-γ konusundaki çelişkilerin hasta seçimine, vücut-kütle indeksine, etnik kökene ya da az sayıda hastayla çalışılmış olmasından kaynaklanabileceğini söylemiştir (35).

Menstrual siklusun luteal fazında endometriyal hücrelerde Th2 sitokinlerinin (IL-4, IL-6) mRNA ekspresyonları Th1 sitokinleri (IL-2, IL-12, IFN-γ) ile karşılaştırıldığında arttığı gözlemlenmiştir (40). IL-4, endometriyumdan infiltre edilen lenfositler tarafından salgılanır ve endometriyal dokulardan (LIF) 'ün üretimini uyarır (41). Peri-implantasyon süreci için önemli sitokinlerden olan IL-4, TGF-β ile birlikte trofoblast invazyon sürecini (41) ve endometriyal desidualizasyonu kolaylaştırır (42), desidual lenfositler ve trofoblastlar arasındaki etkileşimi düzenler ve trofoblastik villiler içindeki anjiyogenezisi (IL-6 ile birlikte) kontrol ederler (43).

Ayrıca IFN-γ in vitro kültür ortamlarında trofoblast hücrelerinin büyümesini baskıladığı, sitotoksik T hücrelerinin ise IL-2 tarafından aktive edilerek trofoblastlarda apoptosisi ve fetal kayıpları indüklediği gösterilmiştir. (39).

İnsanlarda gebeliğin sürdürülmesi için önemli diğer bir faktörün de platelet-activating factor (PAF) olduğu düşünülmektedir. Preimplantasyon embriyoları ve desidual hücreler önemli ölçüde PAF salgılarlar. Nasu ve ark. (1999) kültür ortamında normal endometriyal stromal hücrelerdeki sitokin konsantrasyonunu ölçmüşler ve desidual dokulardan PAF salgılanmasını ve embriyo gelişiminin endometriyal stromal hücrelerden sitokin sentezini uyardığını ön görmüşlerdir. Bu lokal sitokin konsantrasyonundaki artışı da gebeliğin erken dönemlerinde gebeliğin sürdürülebilmesi için hayati önem arz ettiğini düşündürmüştür (44).

İnsanlarda gebelik sırasında gebeliğin anne tarafından tanınmasının fertilize olmuş ovum tarafından gönderilen sinyaller aracılığı ile gerçekleştiği ve bunun da intrauterin Th2 hücrelerinin baskın olmasına yol açtığı düşünülmektedir (45). Ayrıca gebelik sırasında Th1/Th2 dengesinin Th2 yönünde baskın duruma geldiği erken gebelikte ise periferal kanda Th1/Th2 oranının değişmediği gözlenmiştir (46). Hem Th1 hem de Th2 sitokinleri maternal desiduada, feto-maternal aralıkta üretilir. Ancak kesin olan bir şey var ki erken gebelikte özellikle implantasyon alanında desiduada Th2 baskındır (47). Eğer Th1 sitokinleri baskın olursa bu durum embriyo gelişimini ve plasental büyümeyi olumsuz yönde etkiler (48). Sonuç olarak Th1 ve Th2 arasındaki dengenin, implantasyon ve gebeliği de içine alan normal üreme fonksiyonlarının gerçekleşebilmesinde kritik bir önemi vardır (23). Th1/Th2 immun cevabın düşük indeksli olması ise fizyolojik bir gebeliğin gerçekleşmesine yardımcı olur (49).

Th1/Th2'nin ikili karşıtlığının keşfinden sonra Wegmann ve ark. (1993) gebelik sırasında Th2 cevabı etkili iken Th1 cevabın gebelik için zararlı olduğunu öne sürülmüşlerdir (50). Gebelik sırasında multipl skleroz, romatoit artirit gibi Th1 ilişkili otoimmun hastalıkların görülmesi bu düşüncenin desteklenmesine neden olmuştur (4). Ancak Th1 sitokinlerin gebeliğin devamı için esansiyal olduğu gösterildiğinde Th1'ler hakkındaki bu düşüncenin basit olduğu görülmüştür. Örneğin IFN-γ'nın başarılı bir gebelik ve bu gebeliğin başarılı şekilde sonlanması ve spiral arterlerin yeniden yapılanması için gerekli olduğu bildirilmiştir (51). Dahası Th2 knockout (IL-4, IL-5, IL-9 ve IL-13) farelerde normal üreme sonuçlarının olduğu gösterilmiştir (52).

Th1/Th2 paradigmasını desteklemeyen ancak tekrarlı düşüklerde etiyolojik faktörlerinde etkili olduğunu gösteren çalışmalar da bulunmaktadır. Örneğin Bates MD ve ark.'nın (2002) yaptıkları çalışmada tekrarlı düşük görülen kadınlarda IFN-γ üretimi düşük iken IL-10 ve IL-4 üretiminin yüksek olduğu bildirilmiştir. Ayrıca bu çalışmada geçmişinde tekrarlı düşük hikayesi olan ve tekrar düşük yapan kadınlar ile başarılı gebelik geçirenler arasında önemli bir fark olmadığı ve tekrarlı düşük yapan kadınlarda TNF-α değerlerinin önemli ölçüde düşük olduğu da saptanmıştır (53).

Sonuç olarak, memelilerde gebelik immun tolerans ve baskılama arasında bir denge gerektiren eşsiz immünolojik bir süreçtir. Erken dönemde gebeliğin sürdürülebilmesi fetal dokular ile maternal desidua arasındaki etkileşime bağlıdır. Bu etkileşimin başarılı bir şekilde gerçekleşebilmesi için spesifik lökosit popülasyonuna ve uygun sitokin ekspresyonuna gereksinim vardır. Bu derleme ile gebelik sırasında Th2 ve Th1 aktivitesinin belirli bir dengede olması gerektiği ancak bu sayede uygun immünolojik reaksiyonların meydana gelebileceği ve başarılı bir gebeliğin gerçekleşebileceği anlatılmıştır. Ayrıca pre-eklemsi, tekrarlı gebelik kaybı, tekrarlı düşük gibi gebelik patolojilerinde yer alan sitokinlere de açıklık getirilmeye çalışılmıştır.

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Clivus Fracture After Minor Head Trauma

Minör Kafa Travması Sonrası Görülen Klivus Fraktürü

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Dear Editor,

Clivus is a deep-seated complex formation that provides mechanical support for the brain stem and vascular structures therein (1). Often occurring in high-energy traumas like traffic accidents or falling down from high places, clivus fracture is rare (2) with an incidence rate of 0.55% (3). Because of its anatomical proximity to the vertebrobasilar system, brain stem, and cranial nerves, it can lead to severe neurological deficits and early mortality (4).

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A 6-year-old male patient was admitted to the emergency room of our hospital with complaints of neck pain and limitation of motion. We learnt from the medical history taken from his family that he had fallen over after had been pushed by his brother while playing in the evening and within an hour, he had developed restricted movement and pain in the neck. In the first examination in the emergency department, GCS was 15 and the patient was conscious with no neurological deficits. The patient was given a Philadelphia collar. The computed tomography and cervical imaging applied in the emergency room revealed transverse fracture of the clivus (Figure 1, 2). Then we administered cranial and cervical MRIs.

Having observed no pathologies in the spinal channel, the parencyma, or the vascular formations the patient was discharged with a neck collar and was followed.

The incidence rate of the clivus fracture is %0.33 according to Ochalski et al.'s study on pediatric head trauma patients (5); %0.36 in Menkü et. al's study (4); and %0.55 according to Corradino et al.'s study (1).

Clivus fractures are divided into three groups according to the imaging method: transverse (37.5%), longitudinal (37.5%), and oblique (29.4%) (1). They are most frequently observed due to frontal, axial, or occipital loading following high-energy traumas such as traffic accidents and falling (6). Longitudinal fracture of the clivus is often after high-energy pulses to the occipital region and has a high mortality rate of 67-80% (1, 4). It is thought that transverse fractures are generally caused by axial loading. Another mechanism put forward in the formation of oblique and transverse fractures is progressing posterolateral force advancing along the petrous bone and anterolateral impact force advancing along the sphenoid wing. Transverse fractures usually occur in the sphenoccipital synchondrosis (1, 7).

Due to the location of the clivus neighbouring critical areas, traumatic clivus fractures may result in complications such as cranial nerve palsy, vertebrobasilar system injury, endocrine insufficiency, rhinorrhea, and infections (8). Occlusions in the vertebrobasilar system, traumatic aneurysms, entrapment and constriction in the broken line can be seen in more lethal longitudinal fractures of the clivus (1, 3). In transverse fractures, 6th and 7th cranial nerve palsies and anterior circulation injuries may occur (1).

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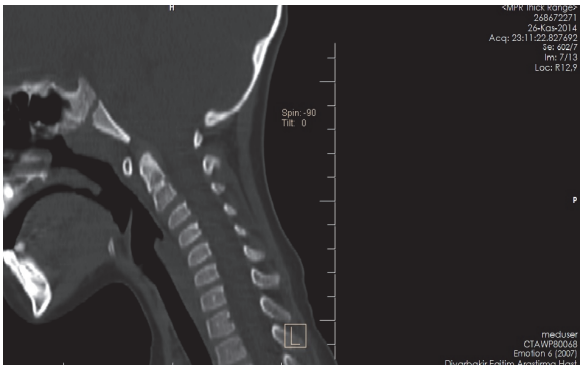

Figure 1. The transverse clivus fracture line along the craniocervical line; CT sagittal section.

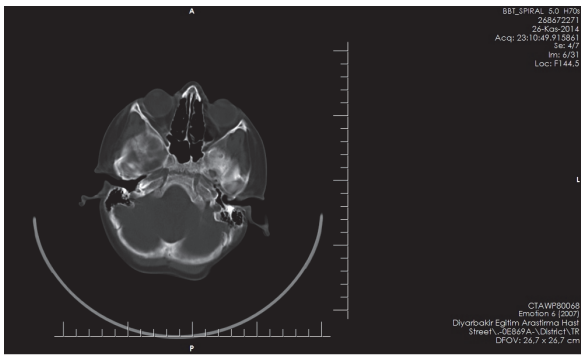

Figure 2. The transverse clivus fracture line axial section; CT image

In the literature, there are reports of clivus fractures following severe head traumas accompanied by vascular and cranial nerve injury due to the settlement of the clivus. However, in our patient's case, the transverse clivus fracture was observed one hour after a mild head trauma causing limitation of neck motion.

Keeping in mind that this could lead to serious complications, our patient underwent high-resolution CT followed by a three-dimensional CT scan and, due to the risk of brain stem injury and vascular injury, the patient was further evaluated with MRI and MR angiography. With no neurological deficits, the patient developed transverse clivus fracture after a minor trauma as the fracture line was probably caused by incompletion of the fusion between the exoccipital bone and the basioccipital bone.

As a result, it should be kept in mind that clivus fracture may take place without neurological deficits even after mild head traumas. Practitioners should consider clivus fractures and skull base fractures in patients with post-traumatic pain and limitation of motion in the neck and head; in such cases, skull base and clivus fractures should be evaluated with high-resolution bone window tomography and multiplanar reconstruction methods. Because of its anatomical location, crucial neighbourhood, and possible complications, potential vascular injuries and brain stem injuries that may involve the clivus should be investigated with cranial CT, cranial MRI, and cranial MR angiography.

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