e-ISSN
2667-8675
Volume: 3 Issue: 3
December 2021

EJT

Eurasian Journal of Toxicology

www.dergipark.org.tr/ejtox

Case Reports

- **A Rare Cause of Acute Ischemic Stroke: Herbal Chocolate**
  Ayla Köksal, Cesareddin Dikmetaş, Serkan Doğan, Ahmet Erdur
- **Steven Johnson Syndrome Due to Allopurinol Use**
  Evrim Kar, Abdullah Algın, Hatice Şeyma Akça, Serdar Özdemir, Serkan Emre Eroğlu
- **Tianeptin (İlaç Kötüye) Kullanımına Bağlı Toksik Lökoensefalopati: Olgu Sunumu**
  İlknur Güçlü Altun, Harika Köşlük Gürler, Banu Özen Barut
- **Retained Foreign Body After Stingray Injury; A Case Report**
  Şeref Emre Atiş, Bora Çekmen, Öner Bozan

EPAT
Emergency Physicians Association of Turkey

EJT
Eurasian Journal of Toxicology

Siyavuşpaşa Mh. Mustafa Kemal Paşa Cd.
Oğuzhan Sok. No: 6 Daire: 4 / Bahçelievler / İstanbul
Telefon: 0553 199 95 59
info@puntodizgi.com
www.puntoajans.com

Editorial

Değerli Okuyucular,

Dergimizin, 2021 yılının son sayısı toksikoloji ile ilgilenen tüm okuyucularımıza katkı sağlayacak şekilde hazırlandı. İlgi çekici dört vaka sunumu dergimizin içeriğini oluşturuyor. Dergimize katkıda bulunan değerli yazarlara ve derginin hazırlanmasında emeği geçen tüm paydaşlarımıza, desteklerini esirgemeyen Acil Tıp Uzmanları Derneği (ATUDER) yönetim kuruluna ve başkanımız Prof. Dr. Başar Cander'e teşekkür ederiz.

Saygılarımızla.

Eurasian Journal of Toxicology Editörler Kurulu

Contents

Case Reports

1. A Rare Cause of Acute Ischemic Stroke: Herbal Chocolate 46
   Ayla Köksal, Cesareddin Dikmetaş, Serkan Doğan, Ahmet Erdur

2. Steven Johnson Syndrome Due to Allopurinol Use..... 49
   Evrim Kar, Abdullah Algın, Hatice Şeyma Akça, Serdar Özdemir, Serkan Emre Eroğlu

3. Tianeptin (İlaç Kötüye) Kullanımına Bağlı Toksik Lökoensefalopati: Olgu Sunumu 52
   İlknur Güçlü Altun, Harika Köşlük Gürler, Banu Özen Barut

4. Retained Foreign Body After Stingray Injury; A Case Report 56
   Şeref Emre Atiş, Bora Çekmen, Öner Bozan

Case Report
Eurasian Journal of Toxicology

A Rare Cause of Acute Ischemic Stroke: Herbal Chocolate

Ayla Köksal[1], Cesareddin Dikmetaş[1], Serkan Doğan[1], Ahmet Erdur[1]

[1]Department of Emergency Medicine, Istanbul Health Sciences University Kanuni Sultan Süleyman Training and Research Hospital

Abstract

The frequency of use of many food supplements sold under the name of herbal products has increased today. As a result of easy access to the whole society with tools such as television, radio and especially the internet, many such products sold uncontrolled and outside the control of physicians can cause serious health problems. Our case reports a 65-year-old male patient who was admitted to the emergency service with a headache and left arm numbness. In the detailed history taken, it was learned that he used a herbal product without the recommendation and control of the physician in order to increase sexual power. It was learned that he did not have any known disease, operation, and medicine used under the control of a physician. It is known that such herbal products cause serious neurological events. The use of these products should be questioned, especially in patients who are admitted to the emergency department with acute neurological complaints and have no apparent medical history.

Keywords: chocolate,herbal product,stroke.

Introduction

Today, the use of herbal products has increased all over the world. Many people can easily obtain these products from various stores that are not audited with tools that facilitate access and promotion to all segments of the society such as television, radio and especially the internet. In promotions made through all means, these products may cause a false perception that these products are natural and harmless. There is no detailed research on the actual ingredients, active metabolites and side effects of these products. Phytochemicals included in the composition of the products can affect especially the fibrinolytic system with its pharmacokinetic and pharmacodynamic mechanism. As a result, unwanted coagulation and bleeding disorders may occur in people who use it[1-3].

Sexual dysfunctions are among the most common problems worldwide. Many studies in the literature reveal that, regardless of gender, at least one out of every 3 people experience at least one sexual dysfunction in any period of their lives[4]. Reduced sexual desire, orgasm disorder and vaginismus in women, erectile dysfunction in men, premature ejaculation and lack of sexual desire are among the most common problems[5,6].

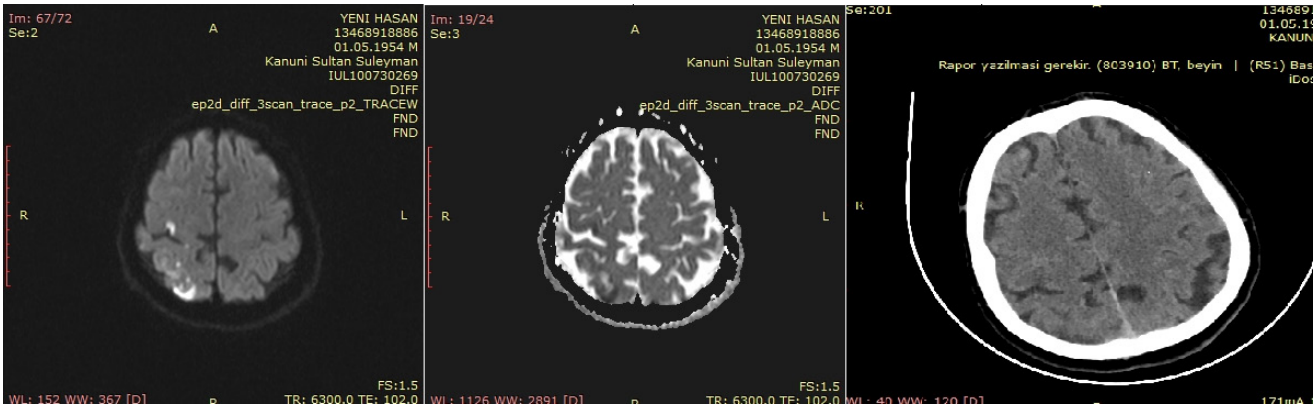
Psychological problems that can lead to loss of self-confidence, decrease in quality of life and even depression can be seen frequently in individuals with sexual dysfunction[7]. The frequency of referral to physicians with sexual disorders is low, especially due to cultural and social factors. For this reason, these herbal products, which are presented as advertising products and are easy to access, are tried to be solved in secret, and the unconscious use of these products causes serious events[8]. In this case report, we wanted to talk about the ischemic stroke patient that occurred after the herbal product used to increase sexual performance and his management in the emergency room.

Case Report

A 65-year-old male patient was admitted to the emergency department with complaints of neck pain and left arm numbness in the last 2 hours after a headache that persisted for 2 days. The patient's history was unremarkable. The patient was in good general condition, conscious and cooperatively oriented, and the blood pressure arteriole was 190/100 mmHg and other vital signs were stable. The patient's neurological examination revealed hemihypoesthesia in the left upper extremity and hypoactivity in the deep tendon reflexes. The patient was taken to the emergency department critical examination area and radiological imaging and laboratory tests were requested. In the cranial computed tomography of the patient, hypodense area in the right parietooccipital region, hyperintensity in the right parietooccipi-

Corresponding Author: Ahmet Erdur **e-mail:** ahmeterdur@yandex.com
Received: 06.04.2021 • **Accepted:** 16.12.2021
Cite this article as: Koksal A, Dikmetas C, Dogan S, Erdur A. A rare cause of acute ischemic stroke: herbal chocolate. Eurasian J Tox. 2021;3(3):46-48.

DOI: 10.51262/ejtox.910867



Picture 1: Brain Tomography and MR image of the patient

tal region in diffusion-weighted cranial magnetic resonance imaging, and hypointense appearance in the diffusion coefficient map of the same region (Picture 1).

Except for the patient's high blood sugar (287 mg/dl), no obvious pathology was found. There was no pathology in the electrocardiogram of the patient. Ischemic stroke was considered in the patient. Anticoagulant therapy, antiaggregant and antihypertensive therapy were initiated in the patient, who was consulted with neurology. It was learned that the patient, who had no problem in his history, had used a product containing cocoa butter, ginseng, cocoa powder, cinnamon, lechithin, sesame, hazelnut, and vanilla flavoring 3-5 times a day for the last 3 days when his history of stroke was deepened. It was learned that he last took it before going to bed at night. It was learned that this product used by the patient was a herbal product and was used to increase sexual performance. The patient was admitted to the neurology service for follow-up and treatment. It was learned that she was discharged after neurology follow-ups, after being advised to come to the polyclinic controls.

Discussion

Sexual dysfunctions are very common in society. One in three men experiences sexual dysfunction at least in their life. However, treatment is less under the control of a physician. Among the sexual dysfunctions, sexual anorexia, erectile dysfunction are the most common and the third most common sexual dysfunction[9].

Premature ejaculation is a common disorder at a rate of 20-30%[10]. Psychological and medical therapy should be combined in treatment. The medical treatment uses topical creams, selective serotonin reuptake inhibitors (SSRI), phosphodiesterase 5 (PDE-5) and tramadol[10,11]. Due to cultural and social factors, solutions for treatment are sought without consulting a physician. For this reason, products claimed to be harmless herbal products are preferred in easy-to-reach internet, television and similar media.

The drugs used in medical treatment are approved for use in the market after passing many tests. Side effects and possible drug interactions of herbal products are not routinely carried out. In our country, licensing and various regulations are carried out by the ministry of health and the ministry of agriculture and food in herbal products. Nevertheless, it is known that after licensing, some manufacturers can apply methods in which various chemical substances are added to increase production efficiency. The active substance sildenafil was detected in the product used by our patient, and this substance was included in the banned products list in 2019[12].

Cerebrovascular diseases (CVD), defined as stroke, are among the leading diseases that cause serious mortality and morbidity. Ischemic strokes constitute 80-85% of SVH[10]. When etiological risk factors are examined, unchangeable (age, gender, race, genetic) and changeable risk factors (hypertension, diabetes mellitus, heart diseases, atrial fibrillation, hyperlipidemia, etc.) can be detected. Except that our patient is 65 years old and male, any cardiac, metabolic, genetic, etc. There was no risk factor.

Although there are many risk factors in the etiology of ischemic stroke, these common causes may not be common in some patients. In such cases, it should be questioned whether there is any medicine or a herbal product used by the patients. As in our patient, herbal products can be used, especially with unknown and prohibited substances. With the use of these products, our patients can apply to hospitals with neurological problems as in the example.

As a result, we can say that questioning herbal products that can be used unconsciously for various purposes in patients with acute neurological complaints, apart from major risk factors, is of great importance in terms of rapid diagnosis and treatment of patients.

References

1. Ernst E,Pitler MH.Risks associated with herbal medicinal products. Wien Med Wochenschr 2002;152:183-189.

2. Gianni LM, Dreitlein WB. Some popular OTC herbals can interact with anticoagulant therapy. US Pharmacist 1998;23:80-86
3. Bush TM, Rayburn KS, HollowaySW,et al. Adverse interactions between herbal and dietary substances and prescription medications: aclinicalsurvey. Altem Ther Health Med2007 ;13:30-35.
4. İncesu C .Cinsel işlev ler ve cinsel işlev bozuklukları . Klinik Psikiyatri Dergisi 2004; 7(Ek3): 3-13.
5. Mert DG, Özen NE. Genel psikiatri polikliniğine başvuran kadın hastalarda cinsel işlev bozukluğu ve ilişkili sosyokültürel parametrelerin değerlendirilmesi. Klinik Psikiyatri Derg 2011;14.85-93.
6. Hariri AG,Karadağ F, Gurol DT, Aksoy UM, Texcan AE. Sexual problems in a sample of Turkish psychiatric population.Compr Psychiatry 2009;50:353-360.
7. Kennedy SH, Rizvi S (2009). Sexual dysfunction, depression, and the impackt of anti depressants. J Clin Psychopharmarcol, 29:157-164.
8. Uzun MB, Aykaç G, Özçelikay G, Bitkisel ürünlerin yanlış kullanımı ve zararları. Lokman Hekim Journal, 2014;4(3):1-5.
9. İncesu C. Cinsel işlev ve cinsel işlev bozuklukları. Klinik Psikiyatri Derg 2004;7:3-13.
10. Hatzimouratidis K, Amar E, Eardley I, et al. Guidelines on male sexual dysfunction: erectile dysfunction and prematüre ejaculation. Eur Urol 2010;57:804-814.
11. Waldinger MD, Zwinderman AH, Schweitzer DH, Olivier B. Relevance of methodologicaldesingfort he interpretation of efficacy of drugtreatment of prematüre ejaculation : a systematic review and meta –analysis . Int J ImpotRes 2004;16:369-381.
12. Tarım Orman Bakanlığı Gıda ve Kontrol Genel Müdürlüğü internet sitesi taklit,tağşiş ,ilaç etken maddesi ilavesi duyuruları 12.10.2019 duyurusu, Erişim: https://www.tarimorman.gov.tr/GKGM/Duyuru/411/kamuoyuna duyurulur bağlantsı son erişim :15.10.2019
13. Weinberger J. Stroke. 2, Pennsylvania ;Handbooks in HealthCare Co.,2002.

Case Report

Eurasian Journal of Toxicology

Steven Johnson Syndrome Due to Allopurinol Use

Evrim Kar[1], Abdullah Algın[1], Hatice Şeyma Akça[1], Serdar Özdemir[1], Serkan Emre Eroğlu[1]

[1]Department of Emergency Medicine, Health Sciences University, Ümraniye Education and Research Hospital, Istanbul, Turkey.

Abstract

Steven Johnson syndrome is a severe cutaneous adverse reaction that develops especially against drugs and has an increasing incidence. The mortality rate in the elderly population is quite high compared to other age groups. Rapid diagnosis, early recognition, and discontinuation of the responsible drug reduce the mortality rate in patients admitted to the emergency department. The most important step in treatment is supportive treatment.

We present a 70-year-old woman with a history of hypertension, coronary artery disease, known renal failure, and adrenal insufficiency. Steven Johnson syndrome developed. We emphasized that the use of allopurinol due to known renal failure and hyperuricemia increased the mortality rate by causing acute kidney damage, and after its rapid diagnosis and treatment, it positively affected mortality. The patient was admitted to the internal medicine service with a pre-diagnosis of Steven Johnson syndrome in the emergency department and was discharged with recommendations after 26 days of hospitalization.

Because of the rapid spread and rapid deterioration of the general condition in severe cutaneous reactions such as Steven Johnson, mortality is important to make a rapid diagnosis, to determine the etiology, and to start treatment early.

Keywords: steven johnson syndrome, allopurinol, drug adverse effect.

Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are diseases mentioned together in the literature and are severe cutaneous adverse reactions characterized by extensive separation of the epidermis and mucous membrane erosions[1]. The most basic feature that distinguishes SJS from TEN is that it goes with less than 10% body surface area involvement, with an annual incidence of 1.5-1.8 / 1.000.000[2]; It is considered a small form of toxic epidermal necrolysis with an average mortality rate of 1-5%[3]. At least 50% of the cases occur due to drugs[1]. Various antiepileptic drugs, sulfonamide antibiotics, allopurinol, antiretroviral drugs and oxicam analgesics have been identified as triggers of SJS[4].

The clinic begins with fever, sore throat, runny nose, and myalgia. Subsequently, painful rash lesions that spread rapidly occur. The prognosis depends on the degree of skin peeling and the development of secondary bacterial infections. In uncomplicated cases, lesions heal within 1-2 weeks without any sequelae[3]. The first- and third-day measurements named "scorten", which consists of age, malignancy, blood urea nitrogen, glucose, pulse, serum bicarbonate level, and body level, developed by Bastuji-Garin et al. used as[5,6] Identifying the causative drug and discontinuing it early is very important for the survival of patients with SJS[7]. This situation shows the importance of rapid clinical diagnosis in patients admitted to the emergency department.

In this case report, it is aimed to present a patient with SJScaused by allopurinol and discuss it in the light of current literature.

Case Report

A 74-year-old female patient was admitted to the emergency department with the complaint of diffuse maculopapular erythematous, itchy rashes that started from the trunk, back and progressed to the palmar faces of the hands and feet, and swallowing difficulties, keeping less than 10% of the total body surface area. It was learned that the patient, who did not have a history of allergy, used allopurinol, which was initiated 14 days ago due to hyperuricemia, amlodipine 10 mg for hypertension, atorvastatin 40 mg for coronary artery disease and hyperlipidemia, and warfarin 5 mg due to a history of arrhythmia. On physical examination, his general condition was moderate, and his GlasgowComa Scale was 14. In vital parameter analysis; blood pressure: 100/50 mmHg, SaO_2: 97%, heart rate: 95 /minute, fever: 37.8^{0}C. In the tachypneic patient, bilateral respiratory sounds were

Corresponding Author: Evrim Kar **e-mail:** evrmkar@gmail.com

Received: 04.05.2021 • **Accepted:** 28.12.2021

Cite this article as: Kar E, Algin A, Akca HS, Ozdemir S, Eroglu SE. Steven johnson syndrome due to allopurinol use. Eurasian J Tox. 2021;3(3):49-51.

DOI: 10.51262/ejtox.932679

Table 1. Initial Laboratory Findings of Patient

Albumin: 23 g/dL	Lipase: 42 U/L
Leukocyte: 3.59 u/L	Amylase: 88 U/L
Neutrophil: 2.15 U/L	Gamma glutamyl transferase: 203 U/L
Eosinophil: 0 U/L	Sodium: 132 mEq/L
Hemoglobin: 10.5 g/dL	Potassium: 4.3 mEq/L
Hematocrit: 31.2%	Chlorine: 114 mEq/L
Platelet: 116 U/L	Calcium: 6.7 mg/dL
Creatinine: 1.89 mg/dL	Corrected Calcium: 8
Blood urea nitrogen: 143 mg/dL	C-Reactive Protein: 3.9 mg/dL
Uric acid: 10.5 mg/dL	pH: 7.27
INR: 1.32	pCO_2: 29.8 mmHg
Prothrombin time: 17.4 seconds	HCO_3: 13.5 mmol/L
Lactate dehydrogenase: 462 U/L,	Lactate: 1.9 mmol/L
Alanine transaminase: 38 U/L	Base minus: -11.9 mmol/L
Aspartate transaminase: 52 U/L	

decreased, and basal rales were present. There was minimal tenderness in the abdomen. There were dry oropharynx, hemorrhagic ulcerated crusts on the oral mucosa and widespread erythematous squamous rashes on the body. The Nikolsky sign was positive.

There was no abnormality other than atrial fibrillation on electrocardiography. Initial laboratory findings are shown in table 1.

Patient was hospitalized with diagnosis of SJS secondary to allopurinol.In medical treatment allopurinol was stopped, fluid replacement planned, and broad-spectrum antibiotics as ciprofloxacin 400 mg twice a dayfor 5 days and deltacortril5 mg once a day for 5 days was started. During follow-up, growth of methicillin-resistant Staphylococcus aureus in blood culture and growth of Pseudomonas and Enterobacter in urine culture were observed. Daptomycin 1 x 10 mg/kg/day and teicoplanin 400 mg twice a dayas loading dose and 400 mg once a day as maintenance dose were started orally. The patient's initial SCORTEN scale value was 3, and the probable mortality rate was 35.3. Although no examination regarding the histopathology results of the skin biopsy for the definitive diagnosis of the disease was obtained, the clinical diagnosis was a priority disease and the patient received a response to the treatment, even the SCORTEN scale value was 2on the 3rd day and the possible mortality rate decreased to 12.1. The patient was discharged on the 26th day without any complication.

Discussion

SJS is a rare severe epidermolysis adverse cutaneous reaction associated with drug use[7]. Its frequency is higher in women than men, and it occurs at all ages, but its frequency increases with age[8]. In our study, we aimed to present a case in which squamous erythematous rashes on the skin of an elderly female patient, thought to be secondary to drug reaction, regressed with allopurinol discontinuation.

Allopurinol is used to reduce serum uric acid levels in patients with gout and hyperuricemia[9]. Although the clinical process is usually within 1-3 weeks after drug intake, the disease usually occurs within the first 2 months[10]. In our case, there was a clinical course with painful lesions with rash after fever and myalgia, which occurred after the use of allopurinol 14 days ago. In a retrospective cohort study by Kim et al. in which 65,625 patients using allopurinol, 45 of whom were hospitalized for severe, cutaneous adverse reactions, using the drug data analysis system, the risk of developing SJS in allopurinol users was 10 times higher than in those who did not use allopurinol. found that[11]. Frey et al. found that the risk of SJS increased in allopurinol users in a case-control study created by matching SJS patients with and without allopurinol in a 1: 4 manner, which was previously validated by SJS[12].

Although adverse reactions seen with allopurinol are rare, the mortality rate of SJS cases caused by allopurinol

is 25%.[13] Various scoring systems are used to predict mortality in patients diagnosed with SJS. SCORTEN, ALDEN, ICNARC, APACHE are some of the scales used in predicting mortality. In a study by Lerch et al. Dated 2018, they concluded that the "SCORTEN" mortality severity scale in SJS is superior to other scoring systems such as ALDEN, APACHE II and ICNARC[6] In our patient, the SCORTEN scale was used to predict mortality, and the initial mortality While the rate was 35.3%, the 3-day mortality rate was 12.1%.

Sepsis and multiple organ failure are the most important causes of death[14]. The aim of treatment is to prevent the development of these complications. The most important step is early diagnosis and discontinuation of suspected drug or drugs. Providing fluid and electrolyte balance and nutritional support, protection from infection, respiratory support, adjustment of external temperature, pain and anxiety management, skin and wound care are the other steps of treatment[15]. Our patient was discharged after 26 days with drug discontinuation and fluid, antibiotics, and supportive therapy.

As a result; although we do not deal with the diseases with skin reaction in the emergency service as seriously as the care of other patients with hemodynamic instability, we think that this case report will create an important awareness in the literature on behalf of the emergency department management perspective in order to recognize patients with such drug reactions and with high mortality.

References

1. Roujeau JC, Stern RS. Severe Adverse Cutaneous Reactions to Drugs. N Engl J Med. 1994;331(19):1272–85.
2. Paulmann M, Mockenhaupt M. Schwere arzneimittelinduzierte Hautreaktionen: Klinik, Diagnostik, Ätiologie und Therapie. JDDG - J Ger Soc Dermatology. 2015;13(7):625–43.
3. Schneider JA, Cohen PR. Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: A Concise Review with a Comprehensive Summary of Therapeutic Interventions Emphasizing Supportive Measures. Adv Ther. 2017;34(6):1235–44.
4. Mockenhaupt M, Viboud C, Dunant A, Naldi L, Halevy S, Bavinck JNB, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis: Assessment of medication risks with emphasis on recently marketed drugs. The EuroSCAR-study. J Invest Dermatol. 2008;128(1):35–44.
5. Bastuji-Garin S, Fouchard N, Bertocchi M, Roujeau JC, Revuz J, Wolkenstein P. Scorten: A severity-of-illness score for toxic epidermal necrolysis. J Invest Dermatol. 2000;115(2):149–53.
6. Lerch M, Mainetti C, Terziroli Beretta-Piccoli B, Harr T. Current Perspectives on Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. Clin Rev Allergy Immunol. 2018;54(1):147–76.
7. Harr T, French LE. Stevens-Johnson syndrome and toxic epider- mal necrolysis. Chem Immunol Allergy. 2012 Jan;97:149–66.
8. Roujeau JC , Guillaume JC, Fabre JP, Penso D ,Fléchet ML, Girre JP.Toxic epidermal necrolysis (Lyell syndrome). Incidence and drug etiology in France, 1981-1985. Arch Dermatol 1990;126:37-42.
9. Ramasamy SN, Korb-Wells CS, Kannangara DR, Smith M,WangN,Roberts D et al. (2103) Allopurinol hypersensitivity: a systematic review of all published cases, 1950–2012. Drug Saf36, 953–80
10. Mockenhaupt M. Severe drug-induced skin reactions: clinical pattern, diagnostics and therapy. J Dtsch Dermatol Ges. 2009;7:142-60.
11. Kim SC, Newcomb C, Margolis D,RoyJ,Hennessy S. Severe cutaneous reactions requiring hospitalization in allopurinol initiators: a population-based cohort study. Arthritis Care Res. 2013;65(4):578–584.)
12. Frey N, Bodmer M, Bircher A, Jick SS, Meier CR, Spoendlin J. Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis in Association with Commonly Prescribed Drugs in Outpatient Care Other than Anti-Epileptic Drugs and Antibiotics: A Population-Based Case–Control Study. Drug Saf [Internet]. 2019;42(1):55–66. Available from: https://doi.org/10.1007/s40264-018-0711-x
13. Saito Y, Stamp LK, Caudle KE, Hershfield MS, McdonaghEM,Callaghan JT. (2016) Clinical Pharmacogenetics Implementation Consortium (CPIC) guide- lines for human leukocyte antigen B (HLA-B) genotype and allopurinol dosing: 2015 update. Clin Pharmacol Ther 99, 36–7.
14. Ghislain PD , Roujeau JC: Treatment of severe drug reactions: Stevens-Johnson syndrome, toxic epidermal necrolysis and hyper- sensitivity syndrome. Dermatol Online J 2002;8:5.)
15. Chave TA, Mortimer NJ, Sladden MJ, Hall AP, Hutchinson PE: Toxic epidermal necrolysis: current evidence, practical management and future directions. Br J Dermatol 2005;153:241-53.

Case Report
Eurasian Journal of Toxicology

Tianeptin (İlaç Kötüye) Kullanımına Bağlı Toksik Lökoensefalopati: Olgu Sunumu

İlknur Güçlü Altun[1], Harika Köşlük Gürler[2], Banu Özen Barut[1]

[1]Kartal Dr. Lütfi Kırdar Şehir Hastanesi, Nöroloji Kliniği. İstanbul, Türkiye.
[2]Kartal Dr. Lütfi Kırdar Şehir Hastanesi, Anesteziyoloji ve Reanimasyon Kliniği, İstanbul, Türkiye.

Abstract

Beyin manyetik rezonans görüntüleme (MRG) ile beyaz cevherin detaylı görüntülenmesi sonucu lökotoksik sendromlar ayrıntılı tanımlanabilmiştir. Toksik lökoensefalopati (TL), lökotoksik ajanlara bağlı serebral beyaz cevher bozukluğudur ve klinik spektrumu oldukça geniştir. Birçok ajanın bu tabloya neden olabileceği bildirilmiştir. Literatürde de benzer örneği olan tianeptin kullanımı sonucu oluşan genç yaşta toksik lökoensefalopati tablosu sunulmuştur.

Anahtar sözcükler: Lökoensefalopati, tianeptin, toksik

Giriş

Toksik lökoensefalopati (TL), lökotoksik ajanlara maruz kalmanın neden olduğu serebral beyaz cevher bozukluğudur. Beyin manyetik rezonans görüntüleme (MRG) öncesinde beyinde toksik bozukluklar nöropatolojik olarak tanımlanırdı. MRG ile beyaz cevherin detaylı görüntülenmesi bir dizi lökotoksik sendromu ortaya çıkardı. TL hafif, geçici bilişsel işlev bozukluğundan konfüzyon, koma ve ölüme kadar giden geniş klinik çeşitliliği içerir ve maruziyet meydana geldikten çok sonra ortaya çıkabilir[1].

Akut toksik lökoensefalopati (ATL), tedaviden sonra veya hastalık seyrinin erken döneminde toksinin kesilmesinin ardından düzelebilen potansiyel olarak geri dönüşümlü bir durumdur; MRG'de, ATL değişken olarak FLAIR / T2WI üzerinde anormal sinyale sahiptir, ancak anormallikler tipik olarak normal görünen beyaz maddeye (NAWM) göre DWI'de hiperintensite ve eşlik eden ADC haritalarında hipointensite olarak görülebilir. ATL tipik olarak periventriküler beyaz cevherden subkortikal beyaz cevhere uzanan yolları yaygın olarak simetrik bir dağılımda etkiler. Vakaların az bir kısmında, atipik tutulum alanları bazal gangliyonlar, talamus, beyin sapı, kapsula interna ve serebellumu içerir[2].

ATL'nin kesin patofizyolojik mekanizması bilinmemekle birlikte, ön histolojik kanıtlar, çeşitli endotel hasarlarının daha sonra ve genellikle intramiyelinik ödemle sonuçlandığını göstermektedir[3,4]. Yetişkinlerde ATL'nin en yaygın nedenleri arasında kemoterapötik ajanlar, immünosupresan tedavi, yasa dışı ilaç kullanımı ve özellikle opioid aşırı kullanımından kaynaklanan aşırı ilaç kullanımı yer alır. Benzodiazepin ve bazı antidepresanların aşırı ve kötüye kullanımının toksik lökoensefalopatiye neden olduğu literatürde bildirilmiştir. Burada genç yaşta tianeptin kötüye kullanımı ile ilişkili ATL olduğu düşünülen bir olgu paylaşılmıştır.

Olgu Sunumu

23 yaşında kadın hasta 2020 Haziran'ında bilinç kaybı nedeniyle acil servise getirildi. Hastanın yakınlarından; odasından çıkmaması ve sürekli uyuması üzerine yanına gidildiğinde ağzından köpük geldiği, morardığı ve uyandırılamadığı öğrenildi. Hastanın tıbbi geçmişinde intihar öyküsünün olduğu, düzensiz bir şekilde ne kadar süre ve ne kadar dozda olduğu tam öğrenilemeyen pregabalin, mirtazapine ve tianeptin kullanımının olduğu öğrenildi. Alkol ya da madde kullanımı bildirilmedi.

Acile başvurduğunda hastanın bilinci kapalı, solunumu zayıf ve oksijen saturasyonu düşük olduğundan entübe edilerek yoğun bakım ünitesine yatırıldı. Hastanın pupilleri izokorik, bilateral ışık refleksi ve okulosefalik refleksi alınıyordu. Ağrılı uyarana yanıt ve patolojik refleksi yoktu.

Hastanın ciddi aspirasyon pnömonisi saptandı ve yoğun bakımda entübe olarak takip edildi. Biyokimyasal parametrelerinde Glukoz:203mg/dl üre:23 mg/dl kreatinin:0.23 mg/dl AST:83 U/L ALT:74 U/L Na:144 mmol/L K: 3.7 mmol/L Ca:7.7 mg/dl vardı, kan tablosunda lökosit ve CRP yüksekliği hakimdi. Hastada toksikoloji çalışması yapılamadı. Beyin görüntülemesinde kranial BT 'sinde yay-

Corresponding Author: İlknur Güçlü Altun **e-mail:** ilknurguclu@yahoo.com
Received: 06.08.2021 • **Accepted:** 09.11.2021
Cite this article as: Altun IG, Gurler HK, Barut BO. Tianeptin (ilaç kötüye) kullanimina bağli toksik lökoensefalopati: olgu sunumu. Eurasian J Tox. 2021;3(3):52-55.

gın ödem gözlendi. Yatak başı EEG'sinde jeneralize 2-3 hz delta frekansında yavaş dalga aktivitesi izlendi, zemin aktivitesi izlenmedi. (Figür 1) Hastanın genel durumu nedeniyle MRG yapılamadığından düzenli EEG takipleriyle kontrolü yapıldı. Daha sonra hastanın kliniğinde gözlerinin sağa deviye olduğu sol kolunda klonik atımların eşlik ettiği fokal başlangıçlı bilateral tonik-klonik nöbetlerin eşlik etmesi üzerine levetirasetam yükleme ve idame tedavisi başlandı. Hastanın EEG 'leri non konvulzif status epileptikus kriterlerini tam olarak karşılamamakla birlikte nöbetlerinin sık tekrarlaması üzerine status dozunda sedasyon yapıldı ve kontrol EEG'sinde zemin aktivitesinin düzeldiği görüldü. (Figür 3) Hastanın taşikardi ve ajitasyonu nedeniyle tedavisine klonazepam eklendi. Genel durumunda biraz düzelme saptanan ve uyanıklığı sağlanan hastanın çekilen beyin MRG sonucu toksik lökoensefalopatinin karakteristik beyaz cevher hasarını gösterdi. (Figür 2) Yaklaşık 3 aylık yoğun bakım takibinin sonunda hastanın nörolojik muayenesinde uyanık, sözel iletişime girdiği, tetraparezik, derin tendon reflekslerinin canlı olduğu tespit edildi. Trakeostomi ile takip edilen hastanın halen fizik tedavi ve rehabilitasyon süreci devam etmektedir.

Tartışma

Radyolojik olarak kraniyal MRG ile toksik lökoensefalopati tanısı alan bu olguda hastanın kullandığı ilaçlardan yola çıkarak bu kliniğe en olası neden olabilecek ajanın tianeptin olduğu düşünülmüştür[5].

Tianeptin, serotonin alımını artıran, dopamin sinyalini artıran, glutamat sinyalini modüle eden ve mu (μ) ve delta$^{\delta}$ opioid reseptörlerini uyaran atipik bir trisiklik antidepresandır[6,7,8].

Tianeptin anksiyolitik ve öforik etkileri nedeniyle de kullanılabilmektedir[9]. Tianeptin bağımlılığı ve anksiyete, terleme, miyalji, titreme ve depresyondan oluşan bir yoksunluk sendromu tanımlanmıştır.Tianeptin aşırı doz ölümleri, 4.000 ila 18.000 ng / mL arasında değişen serum konsantrasyonları ile ilişkilidir[10].

Literatürde benzer bir vakanın tianeptin düzeyinin aşırı yüksek saptandığı ve hastanın kabulünden 19 gün sonra öldüğü bildirilmiştir[11]. Bu olguda olduğu gibi bilinç kaybı tablosu ile başvurmuştur ve kranial görüntülemede supratentoryal simetrik beyaz madde tutulumu izlenmiştir. Her iki olgunun klinik ve kranial görüntüleme bulguları benzerdir, literatürdeki olgudan farklı olarak bu olguda toksikolojik çalışma yapılamamıştır ve hastanın prognozu daha iyi seyretmiştir.

Bu olguda tianeptinin uzun süre, yüksek doz kullanımına; pregabalin ve mirtazapinin eklenmesiyle bilinç kaybı gelişen ve epileptik nöbetler ile seyreden klinik tabloya dikkat çekilmiştir. Bu vakada toksikoloji paneli çalışılamadığından nedensellik tam olarak ortaya konamasa da , olgunun literaturdeki vaka ile benzerliği tianeptine bağlı toksik lökoensefalopati tanısını desteklemektedir. Hastanın GABA üzerinden etki eden pregabalin ve SSRI olan mirtazapin kullanımının toksik etkiyi pekiştirmiş olabileceği düşünülmüştür.

Toksik lökoensefalopati hipoksiye bağlı lökoensefalopati ile karışabilse de nörogörüntüleme bulguları ile ayırt edilebilir. Geri döndürülebilir bileşenlerden bağımsız olarak difüzyon üzerindeki anormalliklerin dağılımını FLAIR üzerindeki dağılımla karşılaştırarak hipoksik iskemik ensefalapati (HIE) ve toksik lökoensefalopatinin ayırt edilebileceği gösterilmiştir. Ayrıca FLAIR üzerindeki kortikal hiperintensiteler HIE'yi akut toksik lökoensefalopatinin sadece periventriküler beyaz cevher bulgularından ayırır.

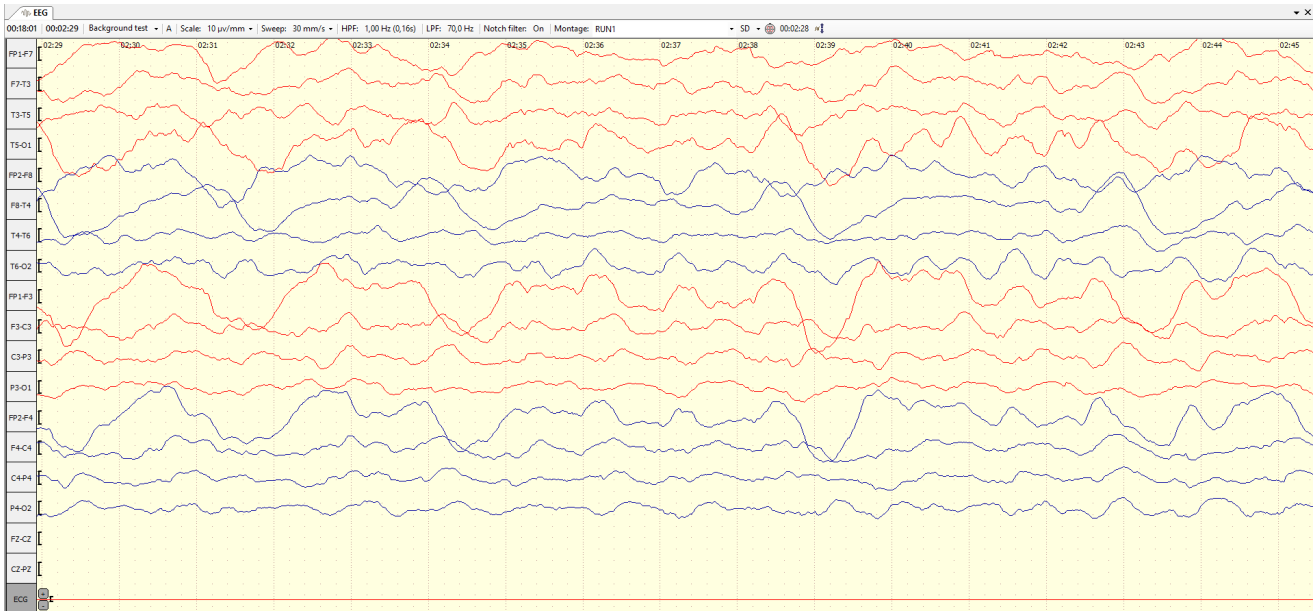
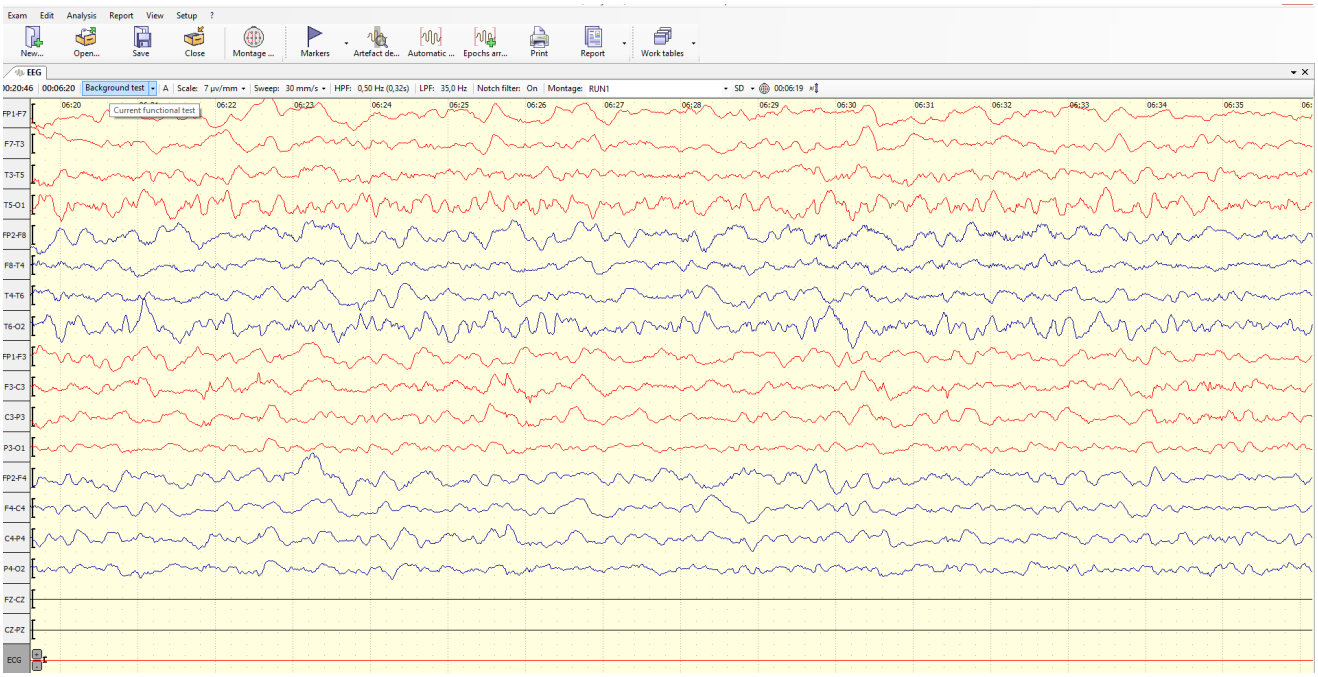
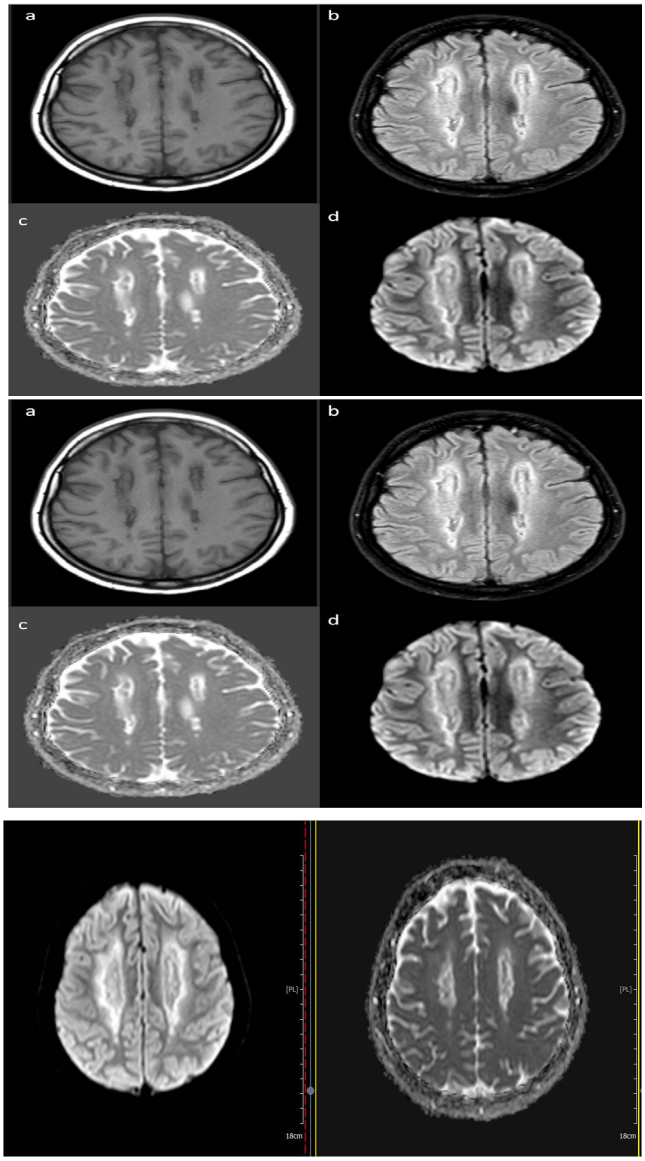


Figure 1. EEG'de jeneralize 2-3 hz delta frekansında yavaş dalga aktivitesi izlendi, zemin aktivitesi izlenmedi. (01.07.2020)



Figür 2: Kontrol EEG'de 5-6 Hz teta aktiivitesinden oluşmuş zemin aktivitesi izlendi. (12.07.2020)



Figür 3: Beyin MRG toksik lökoensefalopatinin karakteristik beyaz cevher hasarını göstermektedir.

Diğer geri döndürülebilir tablo olan posterior reversibl ensefalopati sendromunda tipik olarak FLAIR'de korteks veya subkortikal beyaz madde etkilenir ve nadiren azalmış difüzyon içerir, toksik lökoensefalopatide ise periventriküler beyaz maddenin simetrik tutulumu sözkonusudur Tianeptin, depresif sendromların tedavisi için 25 ülkede onaylanmış atipik bir antidepresandır. Toplumdaki ve yatan hasta servislerinde psikiyatri hastaları arasında Tianeptin kötüye kullanımı son yıllarda giderek artan bir şekilde rapor edilmektedir. Literatürde cinsiyet ve yaş aralığı açısından değişik bulgular bildirilmekle birlikte ölümle sonuçlanan vakalar nadir değildir. Tianeptin kötüye kullanımı ve bağımlılığı ile ilişkili en belirgin fenomen, daha fazla ilaç kötüye kullanımını sürdüren, belirgin öfori ve çekilme semptomlarıdır[7,8].

Eroin gibi yasadışı toksik maddeler, opioid gibi birçok ilaç ve kemoterapi ajanları akut toksik lökoensefalopati ile ilişkilendirilmiştir. Klinik açıdan toksik lökoensefalopatiden şüphelenildiğinde kranial görüntülemenin tanı değeri önemlidir. Tianeptin, kötüye kullanım ve bağımlılık potansiyeli olan bir ilaçtır. Önceden madde kötüye kullanımı öyküsü olan hastalara tianeptin reçetesi yazılırken dikkatli olunmalıdır ve tedavi süresince ilaç kötüye kullanımı için yakından izlenmelidir.Bu olgu tianeptin ve diğer antidepresanların kötüye kullanımına bir halk sağlığı sorunu olarak dikkat çekmek istenmiştir.

Kaynaklar

1. Filley CM, McConnell BV, Anderson CA. The Expanding Prominence of Toxic Leukoencephalopathy. J Neuropsychiatry Clin Neurosci. 2017 Fall;29(4):308-318.
2. Koksel Y, Ozutemiz C, Rykken J, Ott F, Cayci Z, Oswood M, McKinney AM. "CHOICES": An acronym to aid in delineating potential causes of non-metabolic, non-infectious acute toxic leukoencephalopathy. Eur J Radiol Open. 2019 Jun 28;6:243-257.
3. McKinney A.M. Acute toxic leukoencephalopathy: potential for reversibility clinically and on MRI with diffusion-weighted and FLAIR imaging. AJR Am. J. Roentgenol. 2009;193(1):192–206.
4. Ozutemiz C. Acute toxic leukoencephalopathy: etiologies, imaging findings, and outcomes in 101 patients. AJNR Am. J. Neuroradiol. 2019;40(2):267–275.
5. Rimkus Cde M. Toxic leukoencephalopathies, including drug, medication, environmental, and radiation-induced encephalopathic syndromes. Semin. Ultrasound CT MR. 2014;35(2):97–117.
6. McEwen BS, Chattarji S, Diamond DM, vd. Tianeptinin (Stablon) nörobiyolojik özellikleri: monoamin hipotezinden glutamaterjik modülasyona. Mol Psychiatry 2010; 15 : 237–49.
7. Springer J, Cubała WJ. Psikiyatri hastalarında Tianeptin kötüye kullanımı ve bağımlılığı: literatürdeki 18 vaka raporunun gözden geçirilmesi. J Psychoactive Drugs 2018; 1 : 1–6.
8. Lauhan R, Hsu A, Alam A, Beizai K. Tianeptine Abuse and Dependence: Case Report and Literature Review. Psychosomatics. 2018 Nov;59(6):547-553.
9. Dresse A, Rosen JM, Brems H, Masset H, Defrance R, Salvadori C. Gıdanın tianeptin ve ana metabolit kinetiği üzerindeki etkisi. J Clin Pharmacol 1988; 28 : 1115–9.
10. Baselt RC. İnsanda toksik ilaçların ve kimyasalların dağılımı. 7. baskı. Foster City, CA: Biyomedikal Yayınları; 2004.
11. Goodnough R, Li K, Fouladkou F, Lynch KL, Shah M, Smollin CG, Blanc PD. Notes from the Field: Toxic Leukoencephalopathy Associated with Tianeptine Misuse - California, 2017. MMWR Morb Mortal Wkly. Rep. 2018 Jul 13;67(27):769-770

Case Report
Eurasian Journal of Toxicology

Retained Foreign Body After Stingray Injury; A Case Report

Şeref Emre Atiş[1], Bora Çekmen[1], Öner Bozan[2]

[1] Karabuk University, Faculty of Medicine, Department of Emergency Medicine, Karabuk, Turkey
[2] Prof. Dr. Cemil Tascioglu City Hospital, Department of Emergency Medicine, Istanbul, Turkey

Abstract

Stingray is a demersal sea fish that causes widespread injury around the world. Stingray envenomation may cause local tissue injury as well as systemic effects. Although immersion of the injured area in hot water is effective in the treatment, this treatment does not provide complete relief in cases where there is a foreign body in the tissue. We presented about a case of a 22-year-old male patient with stingray tail detected in x-ray images taken after complete relief was not provided after treatment.

Keywords: stingray,injuries,foreign objects,envenomation

Introduction

Sea stingray is a deep fish species that is common in the world and has a variable number of stings on its tail and venomous glands[1]. The injury is caused by the mechanical effect of the tail, as well as the serotonin, phosphodiesterase containing poison in the gland. Serotonin content is responsible for pain in individuals, and phosphodiesterase derivatives are responsible for local tissue destruction[2]. Injury may remain local or systematic symptoms could be seen such as nausea, vomiting, diarrhea, rabdomyolysis, cardiac injury[3]. Injury is mostly related to foot or lower extremity[4]. We present a case report who was brought to our emergency department after a marine stingray injury and afterwards a retained stingray fragment was found.

Case Report

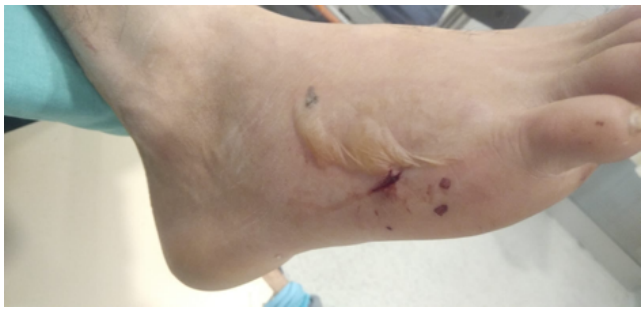
A 22-year-old male patient, who has no known disease, was admitted to the emergency room after stingray envenomation from his foot while cleaning the fishing net. He had no history of allergy and his vital signs were stable when he arrived. The patient had regional edema and an approximately 1 cm laceration in the dorsolateral region of the right foot and a bullous injury approximately 3 cm size above the laceration (Picture 1). There was no motor or sensory loss in the right foot. Initially hot water immersion treatment performed but when the pain was remaining, opioid-derived painkillers added for analgesia. He complained of severe pain again after a while during the follow-up. A radiopaque foreign body (stingray tail) was found near the 5th metacarpal bone in the x-ray radiographs of the patient (Picture 2). In laboratory creatine kinase was 377 U/L (normal range 60-300 U/L), aspartate aminotransferase was 139 U/L, alanine aminotransferase was 160 U/L (normal values 15-42, 15-50 U/L, respectively) and other values were in the normal range. The patient was consulted with Orthopedics. The foreign body in the foot was removed with local anesthesia, and the surrounding tissue was debrided. The patient was hospitalized for follow-up and antibiotic treatment, was discharged 3 days later with full recovery.

Discussion

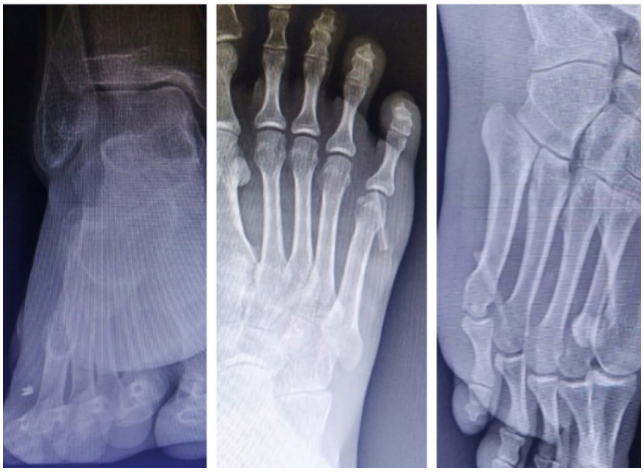
Although stingray envenomation can occur anywhere on the body depending on the area of contact, it is mostly seen in lower extremities. In a prospective study of 22 patients, the injury site was mostly determined as the plantar foot region[5], but in our case the dorsolateral area of the foot was injured. In the treatment of stingray envenomation, immersion the injured area in hot water near 30-90 minutes neutralizes the effects of the labil poison and provides relief of symptoms[2]. In addition to immersion in hot water, we added an opioid analgesic, as the patient's pain was not fully resolved. In a retrospective study of Clark et al. there was no stingray part was found in the foot on the imaging performed after injury.

Corresponding Author: Şeref Emre Atiş **e-mail:** dremreatis@gmail.com
Received: 18.10.2021 • **Accepted:** 10.12.2021
Cite this article as: Atis SE, Cekmen B, Bozan O. Retained foreign body after stingray injury; a case report. Eurasian J Tox. 2021;3(3):56-57.

DOI: 10.51262/ejtox.1011388



Picture 1. The patient had regional edema and an approximately 1 cm laceration in the dorsolateral region of the right foot and a bullous injury approximately 3 cm size above the laceration



Picture 2: A radiopaque foreign body (stingray tail) was found near the 5th metacarpal bone in the x-ray radiographs of the patient.

Suspicious imaging was provided in only one case, and no structure other than sand was detected in the wound exploration. In the same study, symptomatic reprieve was observed in all patients by immersing the affected limb in hot water and some patients with additional painkillers[3]. In another prospective study of 22 patients, no foreign body was detected after the envenomation and all patients' pain were relieved by hot water treatment or hot water plus povidin iodine application[5]. In the literature, there are only few cases which reported positive radiological imaging.[6,7]. In our case, the tail of the stingray was detected on x-ray imaging, which is rare in the literature, and this foreign body was removed and wound was debrided. Evans et al. was stated that the foreign body embedded in the wound site caused the absence of symptomatic relief and tissue necrosis[8]. In our case, pain relief was not achieved after the treatment and a tail part of the stingray was found close to the entrance with imaging techniques.

In envenomation of stingray, which is a common marine vertebrae in the coastal areas, patients who cannot be relieved by conventional treatment, retained foreign body (especially the part of the stingray tail) should be suspected and local tissue exploration with diagnostic imaging techniques are required.

References

1. Otten EJ, Blomkalns AL. Venomous animal injuries. In:Marx JA, Hockberger RS, Walls RM et al., Emergency Medicine: concept and clinical practice, 5th edition St.louis MO: Mosby; 2002:785-800.
2. Kline A. Stingray envenomation of the foot: a case report. Foot Ankle Online J 2008; 1:4.
3. Clark RF, Girard RH, Rao D, Ly BT, Davis DP. Stingray envenomation: a retrospective review of clinical presentation and treatment in 119 cases. The Journal of emergency medicine, 2007;33(1): 33-37.
4. Kamajian G, Singletary B Case Series: Stingray Envenomation. J. Urgent Care Med. 2014
5. Myatt T, Nguyen BJ, Clark RF, Coffey CH, O'Connell, CW A prospective study of stingray injury and envenomation outcomes. The Journal of emergency medicine 2018;55(2):213-217.
6. Cook MD, Matteucci MJ, Lall R, Ly BT. Stingray envenomation. Journal of Emergency Medicine 2006;30(3): 345-347.
7. Moyles BG, Wilson RC. Stingray spine foreign body in the foot. The Journal of foot surgery. 1989;28(1):30-32.
8. Evans RJ, DaviesRS. Stingray Injuries Emergency Medicine Journal 1996;13(3):224-225.