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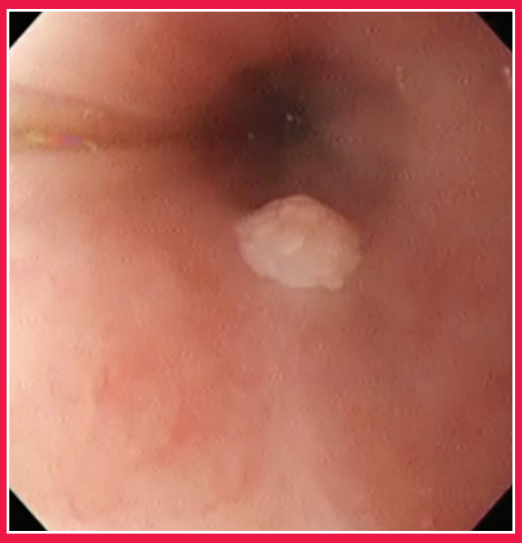
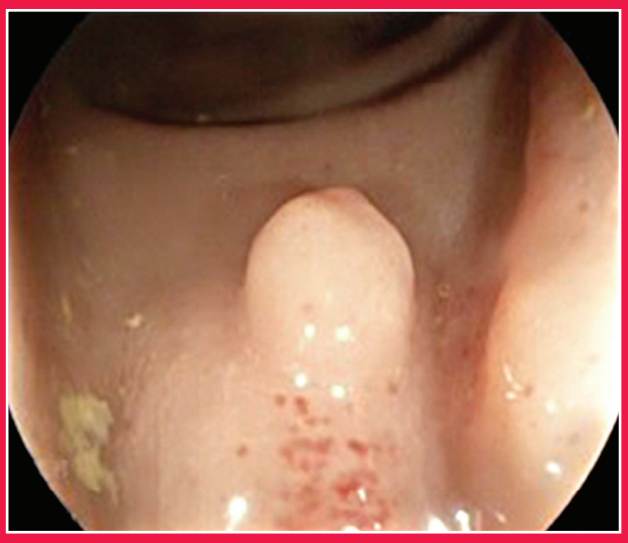


Endoscopic view of squamous papilloma in the distal esophagus of the patient.



İnverte rektal divertikülün 9-10 mm çapında rektal polip olarak görünümü. Polipoid görünüm.

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Nisan 2023; Cilt: 22 Sayı: 1
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Özgün Araştırmalar/Original Articles

Olgu Sunumları/Case Reports

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ORIGINAL ARTICLE

Endoscopic ultrasound-guided fine needle aspiration for benign liver diseases: Single-center experience

Benign karaciğer hastalıklarında endoskopik ultrason eşliğinde ince iğne aspirasyonu: Tek merkez deneyimi

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Departments of [1]Gastroenterology and [2]Internal Medicine, Düzce University School of Medicine, Düzce, Turkey

Background and Aims: To report the efficacy and safety results of our initial experience with the endoscopic ultrasound-guided liver biopsy. **Materials and Method:** Retrospective analysis of a prospectively maintained database in a tertiary care referral center. Consecutive patients who had endoscopic ultrasound-guided liver biopsy for benign parenchymal diseases, using a 19 gauge fine needle with single-pass, three actuations and wet suction technique between June 2022 and December 2022 were included. Patient demographics, procedure-related parameters and the quality of specimens were investigated. **Results:** The technical success was 100%. Of the 16 patients, four had a second procedure due to inadequate sampling. The median total sample length, the median number of pieces and the median length of the longest piece in fragmented samples, and the median number of complete portal tracts were 11 mm (range, 0.2-2.5), 9.6 (range 0-20), 0.2 mm (range 0.2-1.5) and 3.5 (range 0-19) respectively. None of the patients had any adverse events following the procedure. **Conclusion:** Endoscopic ultrasound-guided liver biopsy may be an alternative to other liver biopsy procedures but further studies are needed to determine the ideal needle type and technique.

Key words: Endoscopic ultrasonography, fine needle aspiration biopsy, liver diseases

Giriş ve Amaç: Endoskopik ultrason kılavuzluğunda karaciğer biyopsisi ile ilgili ilk deneyimimizin etkinlik ve güvenlik sonuçlarını bildirmek. **Gereç ve Yöntem:** Üçüncü basamak merkezimizde, ileriye dönük olarak tutulan bir veri tabanının geriye dönük analizi yapıldı. Haziran 2022 ile Aralık 2022 tarihleri arasında, benign parankimal hastalıklar nedeniyle, tek geçişli, üç hamleli ve ıslak aspirasyon tekniği ve 19 gauge ince iğne kullanılarak endoskopik ultrason kılavuzluğunda karaciğer biyopsisi uygulanan ardışık hastalar çalışmaya dahil edildi. Hastaların demografik bilgileri, işlem ile ilgili parametreler ve örneklerin kalitesi değerlendirildi. **Bulgular:** Teknik başarı %100 idi. Toplam 16 hastadan dördüne yetersiz örnekleme nedeniyle ikinci kez işlem uygulandı. Medyan toplam numune uzunluğu, medyan parça sayısı ve parçalanmış numunelerdeki en uzun parçanın medyan uzunluğu ve tam portal yolların medyan sayısı sırayla 11 mm (aralık, 0.2-2.5), 9.6 (aralık, 0-20), 0.2 mm (aralık 0.2-1.5) ve 3.5 (aralık 0-19) olarak bulundu. İşlem sonrası hiçbir hastada yan etki görülmedi. **Sonuç:** Endoskopik ultrason kılavuzluğunda karaciğer biyopsisi, diğer karaciğer biyopsi prosedürlerine bir alternatif olabilir, ancak ideal iğne tipini ve tekniğini belirlemek için daha fazla çalışmaya ihtiyaç vardır.

Anahtar kelimeler: Endoskopik ultrasonografi, ince iğne aspirasyon biyopsisi, karaciğer hastalıkları

INTRODUCTION

Despite the increasing knowledge about hepatic parenchymal diseases and the routine use of non-invasive markers, liver biopsy (LB) is still the gold-standard diagnostic tool in some patients. Historically liver tissue sampling was performed by either percutaneous (PLB) or transjugular (TJLB) routes. The sampling success of these methods has been demonstrated by numerous studies in the literature, but they have some significant risks. PLB can cause adverse events such as bleeding, pneumothorax, infection, bile leakage, and most commonly pain. Even death may ocur (1). Pain is less of an issue in TJLB but it can cause adverse events such as bleeding, hematoma, arrhythmias, and vascular

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damage and the sample quality can be somewhat lower compared to PLB (2,3).

Recently, endoscopic ultrasound (EUS)-guided liver biopsy (EUS-LB) has emerged as an intriguing alternative to these methods because it has advantages such as preventing injury to surrounding organs by providing real-time high-resolution images, increasing needle passage safety thanks to its Doppler feature, increasing patient comfort by applying anesthesia and shortening recovery time (4). There are many studies in the literature using techniques such as aspiration, slow-pull, dry or wet suction, and needles of different sizes such as 19 gauge, 22 gauge, and 25 gauge or types such as aspiration needles (FNA) or biopsy needles (FNB) to obtain the best possible core samples (5). Although the superiority of these techniques is still controversial, they are still obtaining better specimens than PLB and TJLB (6).

We herein report our initial experience of EUS-LB in a cohort of 15 patients, the sampling quality, and the safety of the procedure.

MATERIALS and METHOD

We performed a retrospective analysis of our prospectively maintained database. Consecutive patients who underwent EUS-LB procedures at our tertiary care referral center between June 2022 and December 2022 were included. Demographic information of the patients, procedure parameters, and tissue examination results were recorded. This study was performed per the principles of the Declaration of Helsinki, and the study protocol was approved by the local ethics committee (Date: 21.12.2022, number: 2022/220).

Patient Selection

Patients aged between 18 to 65 years old were included after obtaining written informed consent. The exclusion criteria were patients who underwent EUS-LB for targeted mass lesions, patients who had malignancy, patients that had decompensated cirrhosis, coagulopathy (platelets < 50.000 µ/mL and INR > 1.5), use of anticoagulant agents, patients who had altered anatomy and pregnancy.

Endoscopy Procedure

All procedures were performed under endoscopist-directed anesthesia, using a combination of midazolam, propofol, and ketamine with monitored anesthesia care. Patients were placed in a semi-prone position. Jaw-thrust maneuver and oxygen at a rate of 3 L/min were administered routinely.

All procedures were performed by the same endoscopist, who performed > 500 diagnostic and interventional EUS procedures annually. A standard linear echoendoscope (EG34-J10U, Pentax Medical, Hoya Corp, Japan) was used. The patients were followed up until the Modified Aldrete Score > 9 after the procedure, and then they were discharged (7).

EUS-LB Technique

All biopsies were performed with a standard 19 gauge FNA needle (Acquire, Boston Scientific, Marlborough, USA). Biopsy needles were used without stylets and primed with diluted heparin (1:1 ratio) to obtain samples by wet-suction technique to prevent clot formation. All the biopsies were performed from the left lobe of the liver as one pass and three actuations only, using 20 cc suction.

https://drive.google.com/file/d/1DMcRlsS62xsl98KqNOsXHhyH_4U_wp6m/view

Sample Preparation and Examination

The specimens were transferred to cassettes and flushed with saline to remove residual clots and then placed into formic acid. After obtaining tissue blocks, a pathologist examined the specimens

and determined the number of complete portal tracts, total sample length, number of pieces, and the length of the longest piece if the sample is fragmented.

Study Outcomes

Designed as a feasibility and safety study, the primary outcome of the study was technical success, and the quality of the samples was defined as total sample length > 15 mm and the number of complete portal tracts > 6. The secondary outcome was the rate of adverse events.

Statistical Analysis

SPSS for Windows version 22.0 (IBM, Armonk, NY, USA) was used for statistical analysis. Descriptive data were expressed as means ± standard deviation, medians (min – max), and numbers with frequencies, as appropriate. Only descriptive analysis was performed due to the small sample size and the study design.

RESULTS

Between June 2022 and December 2022, a total of 16 EUS-LB procedures were performed on 15 patients of which seven were female. The mean age was 56.8 ± 7.3 years and the mean body-mass index was 29.9 ± 3.4 kg/m^2. The most common indication for EUS-LB procedure was chronic hepatitis-B infection because our national health care policy mandates the assessment of liver parenchyma for therapy considerations. The technical success was 100%. Of the 16 procedures, four had a second procedure due to inadequate sampling. The median total sample length, the median number of pieces and the median length of the longest piece in fragmented samples, and the median number of complete portal tracts were 11 mm (range, 0.2 - 2.5), 9.6 (range 0 - 20), 0.2 mm (range 0.2 - 1.5) and 3.5 (range 0 - 19) respectively (Figure 1). None of the patients had any adverse events following the procedure and were discharged after a mean time of 82 ± 16 minutes (Table 1).

DISCUSSION

In this study, we reported our initial experience with EUS-LB, its diagnostic efficacy, and safety for benign parenchymal liver diseases in a tertiary care referral center.

Diagnostic percutaneous liver biopsy is a 100-year-old procedure, but despite improved technology and patient care, its technical aspects and adverse

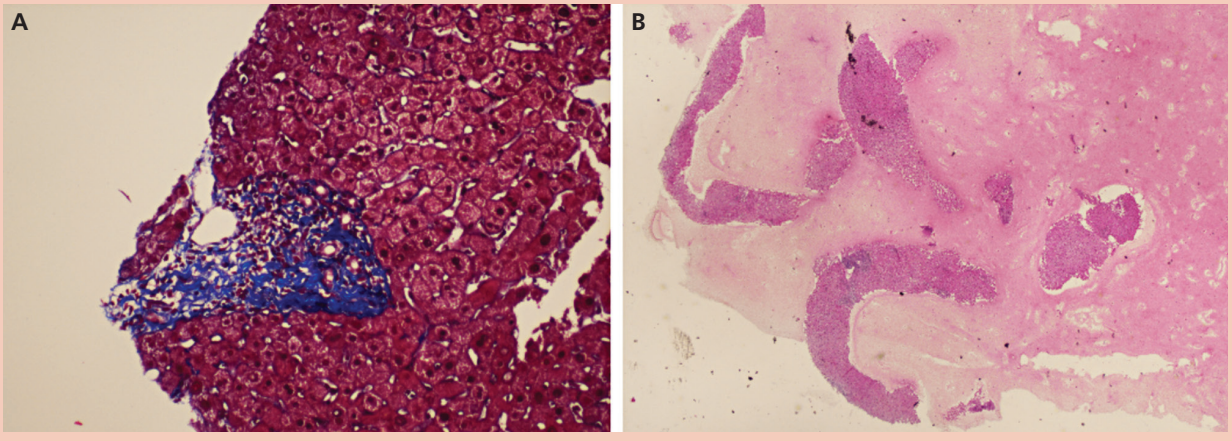

Figure 1. Biopsy specimens. **A.** Complete portal triads. **B.** Length of specimens.

Table 1 Patient characteristics, procedure related parameters and quality of specimens

Age (years, mean ± SD)	56.8 ± 7.3
Sex (n, M/F)	8/7
BMI (mean, kg/m^2)	29.9 ± 3.4
Indication (n, %)	CHB (14,93%) Unexplained transaminitis (1,7%)
Procedure time (min, mean ± SD)	6.3 ± 1.2
Quality of specimens	
Total sample length (mm), median (min - max)	11 (0.2 - 2.5)
Number of pieces (n), median (min-max)	9.6 (0 - 20)
Longest piece in fragmented samples (mm), median (min-max)	0.2 mm (0.2 - 1.5)
Complete portal tracts, median (min-max)	3.5 (0 - 19)
Time to discharge (min, mean ± SD)	82 ± 16

SD: Standard deviation; M: Male; F: Female; BMI: Body mass index; CHB: Chronic hepatitis B.

events have not changed significantly through this time (8). However, since its inception in 2007, different techniques and accessories have been produced to improve the EUS-LB procedure (9). These developments ignited a quest to find the ideal technique and the type of needle because the data in the literature is conflicting. Previous studies are highly heterogenous considering the number of passes, actuations, and the type of aspiration but the latest data support the single-pass, three actuations, wet suction technique (10). In our study, we also adopted this technique. The samples are obtained from the left lobe of the liver by single pass, three actuations, and wet suction technique. The type of needle also is up for debate. In the study by Mohan et al. (11) 19 G FNA needles had better outcomes compared to other needle types. But other studies found that FNB needles perform better compared to FNA needles (12,13). The rate of adverse events does not vary with technique, but rates are higher when FNB needles are used (14). Considering this data about safety, we used FNA needles. Indeed, we did not encounter any adverse events compared to the cumulative adverse event rate of 9.7%, irrespective of needle type and technique (13).

In our study, we found the median total sample length, the median number of pieces, and the median length of the longest piece in fragmented samples, and the median number of complete portal tracts was 11 mm (range, 0.2 - 2.5), 9.6 (range 0 - 20), 0.2 (range 0.2 - 1.5) and 3.5 (range 0 - 19) respectively. Our findings showed that, in 16 procedures, 12 of the samples did not meet the primary outcome criteria but of those 12, eight could get a diagnosis. These findings are also inferior compared to the literature. In the first study to perform EUS-LB with a 19 G FNA needle, the median number of complete portal tracts was nine and the median total sample length was 36.9 mm (15). Other studies which used 19 G FNA needles have also reported higher numbers of complete portal tracts and total sample lengths, up to 14 and 38 mm, respectively (4,6). It should be noted that in these studies, at least two passes and even three passes were performed but in our study, we only performed single-pass. The lower number of passes can explain these results because as the number of passes increases, the total sample length and the number of complete portal tracts also increase (10). We hypothesize that the increased number of frag-

mented samples can be explained by the indication of EUS-LB as in our cohort, all but one biopsy was performed in patients with chronic hepatitis-B infection. In these patients, the increased fibrosis can cause sample fragmentation (16).

This study has some limitations. First of all, this is a single-center, observational study without randomization and a control group. Another limitation is the low number of patients. Finally, the technique that we used may cause the lower rates of sample adequacy as these results may not be extrapolated to all clinical settings.

As a conclusion, our study showed that EUS-LB using 19 G FNA needles can be safe but comparing to the other techniques and needle types, the sample adequacy may be insufficient. Additional studies with a larger cohort using different techniques and needle types should be performed.

Ethics Committee Approval: *The study protocol was approved by Düzce University Clinical Researches Ethics Committee (Date: 21.12.2022, number: 2022/220).*

Informed Consent: *All patients signed the written informed consent*

Conflict of Interest Statement: *None*

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REFERENCES

1. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD; American Association for the Study of Liver Diseases. Liver biopsy. Hepatology 2009;49:1017-44.
2. Kalambokis G, Manousou P, Vibhakorn S, et al. Transjugular liver biopsy–indications, adequacy, quality of specimens, and complications–a systematic review. J Hepatol 2007;47:284-94.
3. Meng HC, Lin HC, Huang CC, et al. Transjugular liver biopsy: comparison with percutaneous liver biopsy. J Gastroenterol Hepatol 1994;9:457-61.
4. Diehl DL, Johal AS, Khara HS, et al. Endoscopic ultrasound-guided liver biopsy: a multicenter experience. Endosc Int Open 2015;3:E210-5.
5. Rangwani S, Ardeshna DR, Mumtaz K, et al. Update on endoscopic ultrasound-guided liver biopsy. World J Gastroenterol 2022;28:3586-94.
6. Pineda JJ, Diehl DL, Miao CL, et al. EUS-guided liver biopsy provides diagnostic samples comparable with those via the percutaneous or transjugular route. Gastrointest Endosc 2016;83:360-5.
7. Aldrete JA. The post-anesthesia recovery score revisited. J Clin Anesth 1995;7:89-91.
8. Bravo AA, Sheth SG, Chopra S. Liver biopsy. N Engl J Med 2001;344:495-500.
9. Mathew A. EUS-guided routine liver biopsy in selected patients. Am J Gastroenterol 2007;102:2354-5.
10. Ching-Companioni RA, Johal AS, Confer BD, et al. Single-pass 1-needle actuation versus single-pass 3-needle actuation technique for EUS-guided liver biopsy sampling: a randomized prospective trial (with video). Gastrointest Endosc 2021;94:551-8.
11. Mohan BP, Shakhatreh M, Garg R, Ponnada S, Adler DG. Efficacy and safety of EUS-guided liver biopsy: a systematic review and meta-analysis. Gastrointest Endosc 2019;89:238-46.
12. Ching-Companioni RA, Diehl DL, Johal AS, Confer BD, Khara HS. 19 G aspiration needle versus 19 G core biopsy needle for endoscopic ultrasound-guided liver biopsy: a prospective randomized trial. Endoscopy 2019;51:1059-65.
13. Baran B, Kale S, Patil P, et al. Endoscopic ultrasound-guided parenchymal liver biopsy: a systematic review and meta-analysis. Surg Endosc 2021;35:5546-57.
14. Zeng K, Jiang Z, Yang J, Chen K, Lu Q. Role of endoscopic ultrasound-guided liver biopsy: a meta-analysis. Scand J Gastroenterol 2022;57:545-57.
15. Stavropoulos SN, Im GY, Jlayer Z, et al. High yield of same-session EUS-guided liver biopsy by 19-gauge FNA needle in patients undergoing EUS to exclude biliary obstruction. Gastrointest Endosc 2012;75:310-8.
16. Malik AH, Kumar KS, Malet PF, et al. Correlation of percutaneous liver biopsy fragmentation with the degree of fibrosis. Aliment Pharmacol Ther 20041;19:545-9.

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ORIGINAL ARTICLE

Helicobacter pylori colonization density may have an important role in the development of celiac disease

Helicobacter pylori kolonizasyon yoğunluğu çölyak hastalığının gelişmesinde önemli rol oynayabilir

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Background and Aims: The aim of this study was to investigate the relationship between celiac disease and *Helicobacter pylori* infection and to compare the severity of celiac disease and *Helicobacter pylori* infection in adults according to the modified Marsh score. **Materials and Methods:** This study included 148 patients with celiac disease and 240 control patients without celiac disease who underwent endoscopy for various reasons in a tertiary hospital. Age, gender, endoscopy indications, descriptive characteristics, complaints, serological, endoscopic and histopathological findings of the patients were recorded and analyzed. **Results:** *Helicobacter pylori* colonization in the celiac disease patients was 43.9% and in control group was 57.5% (p = 0.009). *Helicobacter pylori* positivity rate was significantly lower in Marsh 2, 3A, 3B, 3C groups (p = 0.04). Pearson correlation analysis revealed a significant but weak negative relationship between the severity of *Helicobacter pylori* and celiac disease (r = -.109, p = 0.031). When Marsh score was increasing, *Helicobacter pylori* grade decreased. **Conclusion:** The current study indicated that the incidence of *Helicobacter pylori* infection was lower in adults with celiac disease compared to control patients, and *Helicobacter pylori* colonization density was associated with milder duodenal lesions in celiac patients. *Helicobacter pylori* colonization may have a protective role in the development of celiac disease.

Key words: Celiac disease, endoscopic findings, *Helicobacter pylori*, Marsh score

Giriş ve Amaç: Bu çalışmanın amacı çölyak hastalığı ile *Helicobacter pylori* enfeksiyonu arasındaki ilişkiyi araştırmak ve modifiye Marsh skoruna göre erişkinlerde çölyak hastalığı ile *Helicobacter pylori* enfeksiyonunun şiddetini karşılaştırmaktır. **Gereç ve Yöntem:** Bu çalışmaya 3. basamak bir hastanede tanı alan 148 çölyak hastası ve çeşitli nedenlerle endoskopi yapılan 240 kontrol hastası dahil edildi. Hastaların yaş, cinsiyet, endoskopi endikasyonları, tanımlayıcı özellikleri, şikayetleri, serolojik, endoskopik ve histopatolojik bulguları kaydedildi ve analiz edildi. **Bulgular:** Çölyak hastalarında *Helicobacter pylori* kolonizasyonu %43.9, kontrol grubunda %57.5 idi (p = 0.009). *Helicobacter pylori* pozitiflik oranı Marsh 2, 3A, 3B, 3C gruplarında anlamlı olarak daha düşüktü (p = 0.04). Pearson korelasyon analizi, *Helicobacter pylori*'nin şiddeti ile çölyak hastalığı arasında zayıf ancak anlamlı negatif bir ilişki ortaya koydu (r = -.109, p = 0.031). Marsh skoru arttıkça *Helicobacter pylori* derecesi düştü. **Sonuç:** Mevcut çalışma, çölyak hastalığı olan erişkinlerde kontrol hastalarına göre *Helicobacter pylori* enfeksiyonu insidansının daha düşük olduğunu ve *Helicobacter pylori* kolonizasyon yoğunluğunun çölyak hastalarında daha hafif duodenal lezyonlarla ilişkili olduğunu göstermiştir. *Helicobacter pylori* kolonizasyonu, çölyak hastalığının gelişiminde koruyucu bir role sahip olabilir.

Anahtar kelimeler: Çölyak hastalığı, endoskopik bulgular, *Helicobacter pylori*, Marsh skoru

INTRODUCTION

Celiac disease (CD) is a chronic inflammatory disease that involves the proximal small intestine, triggered by exposure to gluten in genetically predisposed individuals, accompanied by autoimmune reactions mediated by T cells (1). The prevalence of CD has been reported to be approximately 1% in the USA and European countries, and it has been stated that there has been an increase in the risk of CD in the last 50 years (2,3).

While some of the environmental factors are blamed as risk factors for the development of CD; a number of environmental factors have been asso-

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ciated with a reduced incidence of CD in a limited number of studies. One of these environmental factors was *Helicobacter pylori (H. pylori)* infection (4). However, conflicting results have been reported in the literature regarding *H. pylori* for the risk of CD (5-7). On the other hand, several recent studies reported that *H. pylori* infection is not only associated with pathologies of gastroduodenal discomfort; but also plays an important role in some non-gastric diseases (8,9).

The aim of this study was to investigate the relationship between CD and *H. pylori* infection and to compare the severity of CD and *H. pylori* infection in adults according to the modified Marsh score.

MATERIALS and METHODS

Study Population and Design

This study included 148 patients over the age of 18 who underwent endoscopy with a preliminary diagnosis of CD and 240 control patients without CD who underwent endoscopy for various reasons between 1th February 2018 and 1th Fabruary 2022 in a tertiary hospital. The local ethics committee approved the study (the protocol number that was attributed by the ethics committee Prof. Dr. Ilhan Varank Sancaktepe Hospital, Health Science University of was: 00163385893/50, and the date of approval by the ethics committee was 12 April 2022), which was carried out following the Declaration of Helsinki, 1964, and later revisions.

Celiac antibody [tissue transglutaminase immunoglobulin A (Ig A) antibody] positivity was confirmed in all patients. At the diagnosis, Ig A deficiency was ruled out. Age, gender, endoscopy indications and descriptive characteristics of the patients were recorded. Clinical complaints, serological findings, endoscopic findings and pathology reports of the cases were reviewed retrospectively. Patients known to have received eradication therapy for *H. pylori* and patients with insufficient biopsy sampling were excluded from the study. In the study, antrum and corpus biopsy preparations of the patients were stained with hematoxylin eosin and modified Giemsa dyes and examined under light microscopy. Preparations were evaluated for *H. pylori* as none (-), low (+), moderate (++), and high (+++) according to bacterial density by Sydney classification.

Modified Marsh classification (Marsh-Oberhuber) was used for the diagnosis of celiac disease. The patients were classified as Marsh 1, Marsh 2, Marsh 3A, Marsh 3B, Marsh 3C. All cases were evaluated and reported by two experienced pathologists.

Statistical Analysis

Statistical analysis was performed using SPSS software (Statistical Package for the Social Sciences, version 22.0, SPSS Inc., Chicago, USA). Continuous data were defined as mean ± standard deviation, while categorical data were defined as percentages. The median value was used for the variables that did not show normal distribution. Fisher's exact test for categorical variables and Student's t test for numerical variables were used to evaluate statistical differences between patients in the celiac patient and control groups. In statistical analysis, correlations were evaluated with Pearson's correlation coefficient. $P < 0.05$ was considered statistically significant.

RESULTS

There were 148 patients in the celiac group and 240 patients in the control group. 72.3% (n = 107) of the patients were women in the celiac group; and 64.2% (n = 154) control group. Mean age of celiac group was 33 ± 9.5 years and control group was 34 ± 8.1 years (Table 1). In the CD group, the youngest patient was 18 years old and the oldest patient was 62 years old. There was no statistically significant difference between the two groups in terms of mean age ($p = 0.251$). Chronic diarrhea (43.9%) in the CD

group and dyspeptic complaints (61.3%) in the control group were the most common indications for endoscopy. Antral gastritis, pangastritis, peptic ulcer and mass was found to be significantly lower in the celiac group than in the control group in terms of endoscopic findings (p = 0.014) (Table 2).

H. pylori colonization in the celiac group was 43.9% and 57.5% in the control group (p = 0.009) (Table 3). When Marsh 2, 3A, 3B, 3C groups were evaluated in celiac patients, the *H. pylori* positivity rate was significantly lower in each group than the control patients (p = 0.04) (Table 4). Pearson correlation analysis revealed a significant but weak negative relationship between the severity of *H. pylori* and CD (r = -.109, p = 0.031). In celiac patients, when celiac Marsh score was increasing, *H. pylori* grade was decreased.

Table 1 Comparison of demographic data, admission complaints and laboratory results between groups.

		Celiac Disease			Control Group			
		N	%	Mean	N	%	Mean	p
Sex	Male	41	27.7%		86	35.8%		0.098
	Female	107	72.3%		154	64.2%		
Age		148		33 (±9)	240		34 (±8)	0.251
Symptoms	Diarrhea	65	43.9%		14	5.8%		**< 0.001**
	Weight loss or inability to gain	4	2.7%		17	7.1%		
	Dyspepsia or GERD	46	31.1%		147	61.3%		
	Stomach ache	2	1.4%		18	7.5%		
	Abdominal distention, indigestion	5	3.4%		23	9.6%		
	Anemia, low ferritin or vitamin deficiency	19	12.8%		21	8.8%		
	Antibody positivity	7	4.7%		0	0.0%		
Hemoglobin (gr/dL)				11.1 (± 2)			13 (± 2)	**< 0.001**
Ferritin (ng/mL)				13 (7*)			41 (26*)	**< 0.001**

* Median was used instead of standard deviation for independent data showing nonparametric distribution. Pearson chi-square test was used to compare categorical variables, and independent Student's T test was used to compare parametric variables. P < 0.05 was considered statistically significant.
GERD: Gastroesophageal reflux disease.

Table 2 Comparison of endoscopic diagnoses between groups.

	Celiac Disease		Control Group		
	N	%	N	%	p
Normal	30	20.3%	1	0.4%	**0.014***
Antral gastritis	35	23.6%	66	27.5%	
Pangastritis	39	26.4%	86	35.8%	
Bulbus ulcer	11	7.4%	27	11.3%	
Gastric ulcer	0	0.0%	2	0.8%	
Hiatal hernia, LES failure	16	10.8%	29	12.1%	
Esophagitis	17	11.5%	25	10.4%	
Mass lesion	0	0.0%	4	1.7%	

*p <0.05 was considered statistically significant. LES: Lower esophageal sphincter.

Table 3 Presence and degree of *H. pylori* between groups.

		Celiac Disease		Control Group		
		N	%	N	%	p
H. pylori presence	*H. pylori* (-)	83	56.1%	102	42.5%	**0.009***
	H. pylori (+)	65	43.9%	138	57.5%	
H. pylori grade	*H. pylori* (-)	83	56.1%	102	42.5%	**0.017***
	H. pylori (+)	36	24.3%	61	25.4%	
	H. pylori (++)	17	11.5%	55	22.9%	
	H. pylori (+++)	12	8.1%	22	9.2%	

*p <0.05 was considered statistically significant.

Table 4 The relationship between CD Modified Marsh score and *H. pylori*.

Celiac Score (Modified Marsh Score)	Presence of *H. pylori*				
	H. pylori (+)		*H. pylori* (-)		
	N	%	N	%	p
Normal duodenal biopsy	128	63.1%	96	51.9%	**0.04***
Intraepithelial lymphocyte (> 40/100 enterocytes)	11	5.4%	5	2.7%	
Crypt hyperplasia (Marsh 2)	15	7.4%	20	10.8%	
Mild villus atrophy (Marsh 3A)	38	18.7%	45	24.3%	
Middle villus atrophy (Marsh 3B)	8	3.9%	15	8.1%	
Total villus atrophy (Marsh 3C)	3	1.5%	4	2.2%	

*p <0.05 was considered statistically significant

DISCUSSION

This study revealed a negative significant relationship between CD and *H. pylori* infection. In addition, duodenal damage was less common in celiac patients in the presence of *H. pylori* infection. When the *H. pylori* density increased, duodenal damage (according to the modified Marsh classification) had decreased. This inverse relationship between CD and *H. pylori* supported the idea that *H. pylori* infection may have a protective effect in terms of CD (4).

There are prevalence studies in the literature in which the diagnoses of *H. pylori* infection were made serologically (6,10,11). In the studies of Crabtree et al. in the adult CD group and Luzza et al. in the pediatric CD group, the prevalence of *H. pylori* was not different from the control group (10,11). Konturek et al. reported an increased *H. pylori* seroprevalence among patients with the diagnosis of CD, suggesting a potential possible relationship between *H. pylori* virulence and CD (6). In addition, Jozefczuk et al. reported that the incidence of *H. pylori* in the pediatric patient group diagnosed by urea breath test was similar to the control group (12). The fact that histopathology was not used in the diagnosis of *H. pylori* in these studies can be considered a handicap, because the gold standard for the diagnosis of *H. pylori* is histopathological evaluation (13). Later on, studies on histopathological diagnosis increased in the literature. Rostami-Nejad et al. compared dyspep-

tic and celiac patients in two similar studies conducted consecutively (14,15). In their first study in 2009, they included serology and histology and in the second study in 2011, they conducted the study based on histology. In both studies, the prevalence of *H. pylori* was not statistically different between the two groups.

On the other hand, there are studies suggesting that *H. pylori* infection may be protective against celiac disease. Ciacci et al. evaluated the prevalence of *H. pylori* in the adult CD group and found the incidence of *H. pylori* to be significantly lower in the CD group (5). Lebwohl et al. reported the incidence of *H. pylori* in the CD group significantly lower for all age groups (4). They also evaluated the effect of *H. pylori* infection on duodenal damage in the same study. The prevalence of *H. pylori* was 4.2% in the Marsh 3A group, and 4.5% in the Marsh 3B/3C group (4). In Villanacci et al's study of 80 *H. pylori* -infected celiac patients, milder duodenal damage was observed (16). In another study with adult patients, the percentages of *H. pylori* in Marsh grade 1/2 and grade 3 lesions were 50% and 33%, respectively. This finding supported that the rate of *H. pylori* infection was higher in lower grade CD patients (17). This result brought up the possibility that the presence of *H. pylori* infection may alleviate the duodenal damage in the CD group. However, that was not confirmed by the multicenter study of Bayrak et al. They found *H. pylori* infection to be significantly lower in CD patients, yet the presence of *H. pylori* was not associated with duodenal damage (18). A meta-analysis consisted of 25 studies (12 with adult patients, 13 with pediatric patients) suggested that *H. pylori* infection might be a protective factor in celiac disease, since the prevalence of *H. pylori* infection was found to be lower in celiac patients than in the control group (19).

Studies investigating the relationship between *H. pylori* and dudeonal damage have been based on the Marsh classification. Comparisons were made by recategorizing the Marsh classification. In studies comparing the Marsh 1/2 and Marsh 3 groups, statistically insignificant differences were found between the two groups (7,16,18,20). There are also studies in which Marsh 3 is categorized within itself. Although there was a difference between the two groups comparing Marsh 3A/B and C, this difference was still not statistically significant (18,21-23). Yue et al. reported in their meta-analysis that the presence of *H. pylori* infection did not affect the celiac classification in these studies (19). In the current study, the prevalence of *H. pylori* infection was lower in the celiac disese group, and in this respect, it was compatible with Yue et al's meta-analysis (19). However, the most important difference of our study was that *H. pylori* infection affected the modified Marsh classification in CD patients. In our study, we performed separate analyzes for Marsh 2, 3A, 3B and 3C without categorizing and combining the Marsh classification, and evaluated the *H. pylori* rates. Correlation analysis had been used to reveal the possible relationship between the presence of infection and the degree of duodonal damage in the CD group. According to the modified Marsh score, we found a lower *H. pylori* positivity rate in 2, 3A, 3B and 3C. In the subsequent correlation analysis, there was a significant weak-negative relationship between *H. pylori* density and CD severity. In other words, we noticed that duodenal damage (according to the modified Marsh score) had decreased as the *H. pylori* density increased in CD patients. As Amlashi et al. mentioned in their meta-analysis, which is consistent with our study, this negative relationship may mean a protective role of *H. pylori* in celiac patients (24).

There are some opinions on this subject in the literature. It has been reported that chronic *H. pylori* infection may alter the T-cell response and this may result in a decrease in the incidence of CD.

This condition was stated by Lebwohl et al. as the 'hygiene hypothesis' (4). On the other hand, *H. pylori* -induced regulatory T cells in the gastric mucosa can affect the cellular response to gluten in the intestinal wall, and that *H. pylori* can modulate and reduce gastroduodenal permeability (25). In addition, Caminero et al. proposed that *H. pylori* could alter the immunogenicity of ingested gluten through modification of gastric pH or cross-talk between them (26). Although all these claims are unclear for now; it makes sense that the incidence of CD would be lower in patients with *H. pylori* infection, and duodenal damage may be less common in patients infected with *H. pylori*.

One of the limitations of our study was that socioeconomic factors such as ethnicity, household size, low family income, and inadequate living conditions were not taken into account in our study. Despite our limitations, one of the strengths of our study was that the relationship between duodenal damage and the presence of *H. pylori* was evaluated by correlation analysis. In addition, the diagnosis of *H. pylori* infection was made histologically, and patients who had taken antibiotics in the last 1 month before the procedure were excluded from the study. Another strength of our study was the use of clinical, serological, endoscopic and histopathological parameters in the diagnosis of CD.

In conclusion the current study indicated that the incidence of *H. pylori* infection was lower in adults with CD compared to control patients, and *H. pylori* colonization was associated with milder duodenal lesions in CD patients. This may suggest that *H. pylori* colonization has a protective role in the development of CD. However, since some conditions such as the socioeconomic status of the patients were not evaluated in the study, the interpretation of the results should be done carefully. Systematic, large-scale, cohort studies are required to clarify the causal relationship between *H. pylori* infection and celiac disease.

Ethics: *This study was approved by Prof. Dr.Ilhan Varank Sancaktepe Hospital, Health Science University, Ethics Committee on April 12, 2022, with the number 00163385893/50.*

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REFERENCES

1. Lebwohl B, Sanders DS, Green PHR. Coeliac disease. Lancet 2018;391:70-81.
2. Rubio-Tapia A, Ludvigsson JF, Brantner TL, et al. The prevalence of celiac disease in the United States. Am J Gastroenterol 2012;107:1538-44.
3. Mustalahti K, Catassi C, Reunanen A, et al. Coeliac EU Cluster, project epidemiology. The prevalence of celiac disease in Europe: results of a centralized, international mass screening project. Ann Med 2010;42:587-95.
4. Lebwohl B, Blaser MJ, Ludvigsson JF, et al. Decreased risk of celiac disease in patients with *Helicobacter pylori* colonization. Am J Epidemiol 2013;178:1721-30.
5. Ciacci C, Squillante A, Rendina D, et al. *Helicobacter pylori* infection and peptic disease in coeliac disease. Eur J Gastroenterol Hepatol 2000;12:1283-7.
6. Konturek PC, Karczewska E, Dieterich W, Hahn EG, Schuppan D. Increased prevalence of *Helicobacter pylori* infection in patients with celiac disease. Am J Gastroenterol 2000;95:3682-3.
7. Aydogdu S, Cakir M, Yuksekkaya HA, et al. *Helicobacter pylori* infection in children with celiac disease. Scand J Gastroenterol 2008;43:1088-93.
8. Liu R, Liu Q, He Y, et al. Association between *Helicobacter pylori* infection and nonalcoholic fatty liver: A meta-analysis. Medicine (Baltimore) 2019;98:e17781.
9. Wang L, Chen J, Jiang W, et al. The relationship between *Helicobacter pylori* infection of the gallbladder and chronic cholecystitis and cholelithiasis: A systematic review and meta-analysis. Can J Gastroenterol Hepatol 2021;2021:8886085.

10. Crabtree JE, O'Mahony S, Wyatt JI, et al. *Helicobacter pylori* serology in patients with coeliac disease and dermatitis herpetiformis. J Clin Pathol 1992;45:597-600.
11. Luzza F, Mancuso M, Imeneo M, et al. *Helicobacter pylori* infection in children with celiac disease: prevalence and clinicopathologic features. J Pediatr Gastroenterol Nutr 1999;28:143-6.
12. Jozefczuk J, Bancerz B, Walkowiak M, et al. Prevalence of *Helicobacter pylori* infection in pediatric celiac disease. Eur Rev Med Pharmacol Sci 2015;19:2031-5.
13. Souissi S, Makni C, Belhadj Ammar L, Bousnina O, Kallel L. Correlation between the intensity of *Helicobacter pylori* colonization and severity of gastritis: Results of a prospective study. Helicobacter 2022;27:e12910.
14. Rostami-Nejad M, Villanacci V, Mashayakhi R, et al. Celiac disease and Hp infection association in Iran. Rev Esp Enferm Dig 2009;101:850-4.
15. Rostami Nejad M, Rostami K, Yamaoka Y, et al. Clinical and histological presentation of *Helicobacter pylori* and gluten related gastroenteropathy. Arch Iran Med 2011;14:115-8.
16. Villanacci V, Bassotti G, Liserre B, et al. *Helicobacter pylori* infection in patients with celiac disease. Am J Gastroenterol 2006;101:1880-5.
17. Simondi D, Ribaldone DG, Bonagura GA, et al. *Helicobacter pylori* in celiac disease and in duodenal intraepithelial lymphocytosis: Active protagonist or innocent bystander? Clin Res Hepatol Gastroenterol 2015;39:740-5.
18. Bayrak NA, Tutar E, Volkan B, et al. *Helicobacter pylori* infection in children with celiac disease: Multi-center, cross-sectional study. Helicobacter 2020;25:e12691.
19. Yue M, Chen Q, Zhou X, et al. Is *Helicobacter pylori* Infection Associated with Celiac Disease? A Meta-analysis. Turk J Gastroenterol 2022;33:205-12.
20. Maxim R, Pleşa A, Stanciu C, et al. *Helicobacter pylori* prevalence and risk factors among children with celiac disease. Turk J Gastroenterol 2019;30:284-9.
21. Narang M, Puri AS, Sachdeva S, et al. Celiac disease and *Helicobacter pylori* infection in children: Is there any Association? J Gastroenterol Hepatol 2017;32:1178-82.
22. Agin M, Batun I, Ozdemir S, Doran F, Tumgor G. Prevalence of *Helicobacter pylori* in Turkish children with celiac disease and its effect on clinical, histopathological, and laboratory parameters. Arch Med Sci 2019;15:1475-81.
23. Lasa J, Zubiaurre I, Dima G, Peralta D, Soifer L. *Helicobacter pylori* prevalence in patients with celiac disease: results from a cross-sectional study. Arq Gastroenterol 2015;52:139-42.
24. Amlashi FI, Norouzi Z, Sohrabi A, et al. A systematic review and meta-analysis for association of *Helicobacter pylori* colonization and celiac disease. PLoS One 2021;16:e0241156.
25. Lionetti E, Catassi C. New clues in celiac disease epidemiology, pathogenesis, clinical manifestations, and treatment. Int Rev Immunol 2011;30:219-31.
26. Caminero A, Galipeau HJ, McCarville JL, et al. Duodenal bacteria from patients with celiac disease and healthy subjects distinctly affect gluten breakdown and immunogenicity. Gastroenterology 2016;151:670-83.

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ÖZGÜN ARAŞTIRMA

HbsAg seviyesinin HBV DNA ve karaciğer fibrozisi ile ilişkisi

The relationship of HbsAg level with HBV DNA and liver fibrosis

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Giriş ve Amaç: Kovalent olarak kapalı dairesel DNA düzeyinin kronik hepatit B hastalarında hastalığın aktivitesini öngörmede klinik önemi bulunmaktadır. Kovalent olarak kapalı dairesel DNA düzeyinin dolaylı bir göstergesi olan hepatit B yüzey antijeni düzeyi, kronik hepatit B hastalarının yönetiminde hepatit B virüs-DNA düzeyi ile birlikte önemli rol alabilir. Çalışmamızda, hepatit B nedeni ile karaciğer biyopsisi yapılan hastaların fibrozis skorları, hepatit B virüs-DNA ve hepatit B yüzey antijeni seviyelerinin hepatit B zarf antijeni durumu dikkate alınarak kıyaslanması amaçlandı. **Gereç ve Yöntem:** 2017-2020 yılları arasında kronik hepatit B nedeni ile karaciğer biyopsisi yapılan hastaların biyopsi sonuçları, retrospektif kesitsel olarak değerlendirildi. Biyopsi sonucunda fibrozis değerleri hepatit B zarf antijeni durumu göz önüne alınarak değerlendirildi. **Bulgular:** Çalışma grubunu 71 (%55.4) erkek, 57 (%44.5) kadın toplam 128 hasta oluşturdu. Ortalama yaş erkeklerde 41.58 ± 14.27, kadınlarda 43.63 ± 12.13 idi (p: 0.38). Hepatit B zarf antijeni pozitif hastalarda hepatit B yüzey antijeninin hepatit B virüs-DNA (p: < 0.01, r: 0.46), nekroinflamatuvar aktivite (p: 0.03, r: -0.38) ve fibrozis (p: < 0.01, r: -0.73) ile korele olduğu görüldü. Hepatit B zarf antijeni negatif hastalarda hepatit B yüzey antijen seviyesi fibrozis ile ilişkili olarak saptanmadı. Ancak ileri fibrozisi olan hastalarda hafif fibrozisi olanlara göre hepatit B virüs-DNA anlamlı olarak yüksek (p: < 0.01) beraberinde hepatit B yüzey antijeni seviyeleri ise anlamlı olarak daha düşük saptandı (p: < 0.01). **Sonuç:** Hepatit B yüzey antijeni seviyeleri hepatit B zarf antijeni pozitif hastalarda fibrozisi ön görmede faydalı olmakla birlikte hepatit B yüzey antijeni negatif hastalarda fibrozisi öngörmede başarısı hepatit B zarf antijeni pozitif hastalar kadar iyi saptanmamıştır.

Anahtar kelimeler: Hepatit B, fibrozis, HbsAg seviyesi

Background and Aims: The level of covalently closed circular DNA has clinical significance in predicting the activity of the disease in patients with chronic hepatitis B. Hepatitis B surface antigen level, which is an indirect indicator of covalently closed circular DNA level, may play an important role together with hepatitis B virus-DNA level in the management of chronic hepatitis B patients. In this study, it was aimed to compare the fibrosis scores, hepatitis B virus-DNA and hepatitis B surface antigen titers of the patients who underwent liver biopsy due to hepatitis B, taking into account the hepatitis B e-antigen status. **Materials and Method:** Biopsy results of patients who underwent liver biopsy for chronic hepatitis B between 2017-2020 were evaluated retrospectively, cross-sectionally. Fibrosis values in biopsy results were evaluated considering Hepatitis B e-antigen status. **Results:** The study group consisted of 128 patients, 71 (55.4%) male and 57 (44.5%) female. The mean age was 41.58 ± 14.27 in men and 43.63 ± 12.13 in women (p: 0.38). In hepatitis B e-antigen positive patients, hepatitis B surface antigen was found to be correlated with hepatitis B virus-DNA (p: < 0.01, r: 0.46), necroinflammatory activity (p: 0.03, r: -0.38) and fibrosis (p: < 0.01, r: -0.73). In hepatitis B e-antigen negative patients, hepatitis B surface antigen was not found to be associated with fibrosis. However, patients with advanced fibrosis had significantly higher hepatitis B virus-DNA (p: < 0.01) and hepatitis B surface antigen titers were significantly lower (p: < 0.01) compared to patients with mild fibrosis. **Conclusion:** Although hepatitis B surface antigen titers are useful in predicting fibrosis in hepatitis B e-antigen positive patients, its success in predicting fibrosis in hepatitis B surface antigen negative patients was not as good as in hepatitis B e-antigen positive patients.

Key words: Hepatitis B, fibrosis, HbsAg

GİRİŞ

Kronik hepatit B dünya genelinde 257 milyon insanı kronik olarak enfekte eden, siroz veya hepatosellüler kanser (HSK) gibi komplikasyonlar nedeni ile yılda 887 bin kişinin öldüğü önemli bir sağlık problemidir (1). Kronik hepatit B enfeksiyonu değişik fazlar içerir. Bu fazların ayrımı hepatit B virüs (HBV) DNA, hepatit B zarf antijeni (HbeAg) ve onun antikoru (anti-Hbe), hepatit B yüzey antijeni

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(HbsAg) ve onun antikor (anti-Hbs) düzeyine göre belirlenir (2). İmmün tolerans fazında HBV DNA değerleri yüksek, karaciğer transaminazları ve karaciğer histolojisi normal sınırlarda ve HbeAg pozitif saptanır. Zaman içinde toleransın kaybolması ile HBV DNA değerlerinde, transaminazlarda dalgalanmalar ve karaciğer histolojisinde bozulmalar meydana gelmeye başlamaktadır.

HbsAg transkripsiyonel olarak aktif kovalent olarak kapalı dairesel DNA (cccDNA) moleküllerinin translasyonu veya genoma entegre viral sekansların translasyonu yolunu içeren çeşitli yollarla üretilmektedir (3). Daha önceleri sadece tanı amaçlı kullanılan HbsAg; son yıllarda hastalık aktivitesini öngörme, antiviral tedavinin monitörizasyonu ve tedaviye yanıtı gösterme amacıyla da kullanılmaya başlanmıştır (4). Ayrıca yüksek HbsAg değerleri hastalığın komplikasyonları açısından da risk doğurmaktadır. REVEAL çalışmasında (5) başlangıç serum HbsAg seviyeleri, hastalık progresyonu ile anlamlı şekilde ilişkili saptanmıştır (HbsAg < 100, 100 - 999 ve ≥ 1.000 IU/ ml değerler için sırası ile siroz için %4.8, %8.8 ve %16.2; HSK için %1.4, %4.5 ve %9.2).

Kronik Hepatit B seyrinde, HbsAg seviyesi ile HBV DNA ve karaciğer fibrozisi arasındaki ilişkiye yönelik çeşitli çalışmalar yapılmış ve çelişkili sonuçlar elde edilmiştir (6-12). Biz bu çalışmada Hepatit B nedeniyle karaciğer biyopsisi yapılan hastalarda HbsAg seviyesinin; HbeAg durumu, HBV DNA düzeyi ve fibrozis derecesi ile ilişkisini incelemeyi amaçladık.

GEREÇ ve YÖNTEM

Hasta Seçimi

Ocak 2017-2020 tarihleri arasında kronik hepatit B nedeni ile karaciğer biyopsisi yapılan hastalar değerlendirildi. Çalışmamız retrospektif kesitsel özellikte bir çalışma olup, Erzurum Bölge Eğitim ve Araştırma Hastanesi yerel etik kurul onayı (06.04.2020 tarih ve 2020/07-79 karar no) alındıktan sonra başlatıldı. Kronik hepatit B nedeni ile biyopsi yapılan hastalar çalışmaya dahil edildi. Biyopsi sonucu yetersiz saptanan, alkolik hepatit, otoimmün hepatit veya HSK hikayesi olan hastalar ve başlangıçta antiviral kullanan hastalar çalışma dışı bırakıldı.

Karaciğer Biyopsi İşlemi ve Laboratuvar Tetkikleri

Karaciğer biyopsisi, 12 saatlik açlık sonrası ultrason eşliğinde 18 G iğne ile yapıldı. %10'luk formaldehit solüsyonunda fikse edildikten sonra patolog tarafından değerlendirildi. Değerlendirme Ishak skorlaması üzerinden yapıldı (13). Nekroinflamatuvar aktivite (HAİ) 18, fibrozis 6 puan üzerinden değerlendirildi. Fibrozis skorları yok/hafif (0 - 1), orta (2 - 3) ve ağır (4 - 6) arasında gruplandırıldı.

Bütün kan tetkikleri 12 saatlik açlık sonrası ve karaciğer biyopsisi uygulanmadan önceki 3 günlük süre içerisinde yapıldı. Aspartat aminotransferaz (AST), alanin aminotransferaz (ALT), gama glutamil transferaz (GGT), alkalen fosfataz (ALP) içeren biyokimyasal testler architect c16000 (Abbott) cihaz ile çalışıldı. HbsAg, HbeAg architect i2000SR (Abbott Laboratories, Chicago, IL, ABD) marka cihaz ile çalışıldı. Yardımcı reaktifler kullanılarak mikropartikül enzim immünolojik testi ile kantitatif (quantitative) ölçüldü. HbsAg'nin saptama aralığı 0.05 ile 1000 IU/ml'dir. HbsAg üst saptama sınırını aşarsa dilüsyonlu olarak yeniden çalışıldı. HBV DNA Qiagen rotor-gene Q marka cihaz ile real time PCR tekniği ile çalışıldı.

İstatiksel Analiz

İstatistiksel değerlendirmeler için SPSS versiyon 17.0 (SPSS Inc, Chicago, IL, USA) kullanıldı. Normal dağılım gösteren sayısal değişkenler ortalama ± SD olarak, normal dağılım göstermeyenler ise ortalama (minimum - maksimum) olarak gösterildi. Kategorik değişkenler sayı ve yüzde olarak

gösterildi. Normal dağılım göstermeyen sayısal değişkenlerin gruplar arası karşılaştırmasında Mann-Whitney U ve Kruskall-Wallis H testleri kullanıldı. Kategorik değişkenler $\chi 2$ ve Fisher's exact test ile karşılaştırıldı. Karaciğer fibrozisi ve nekroinflamasyon ile HbsAg, HBV DNA (log10) ve diğer karaciğer fonksiyon testleri arasındaki ilişki için Pearson ve Spearman korelasyon analizi kullanıldı. Gruplar arasındaki fibrozis skorlarının HbsAg ve HBV DNA (log10) arasındaki ilişki ANOVA testi ile değerlendirildi.

BULGULAR

Çalışmaya 71 erkek, 57 kadın toplam 128 hasta dahil edildi. Ortalama yaş kadınlarda 43.63 ± 12.13, erkeklerde 41.58 ± 14.27 yıl idi (p: 0.38). Ortalama HbsAg seviyesi 3878.67 ± 133.16 IU/ml, HBV DNA (log10) seviyesi ise 5.46 ± 0.15 IU/ml olarak hesaplandı. Hastaların 98 (%69.5) tanesi HbeAg negatif, kalan 30 (%21.3) tanesi HbeAg pozitif saptandı. HbeAg pozitif hasta grubu istatistiksel olarak anlamlı ölçüde daha genç olup, AST, ALT, GGT, ALP, HbsAg ve HBV DNA (log10) HbeAg pozitif grupta anlamlı olarak daha yüksek idi. Karaciğer biyopsi incelemelerinde nekroinflamatuvar aktivite ve fibrozis açısından gruplar arasında anlamlı bir fark izlenmedi (Tablo 1).

HbsAg ve HBV DNA (log10) değerleri ile karaciğer fibrozisi arasında anlamlı bir ilişki saptanmadı [HbsAg ve HBV-DNA (log10) için p değerleri sırası ile 0.42 ve 0.61]. Nekroinflamatuvar aktivite ile HBV DNA (log10) arasında hafif düzeyde anlam-

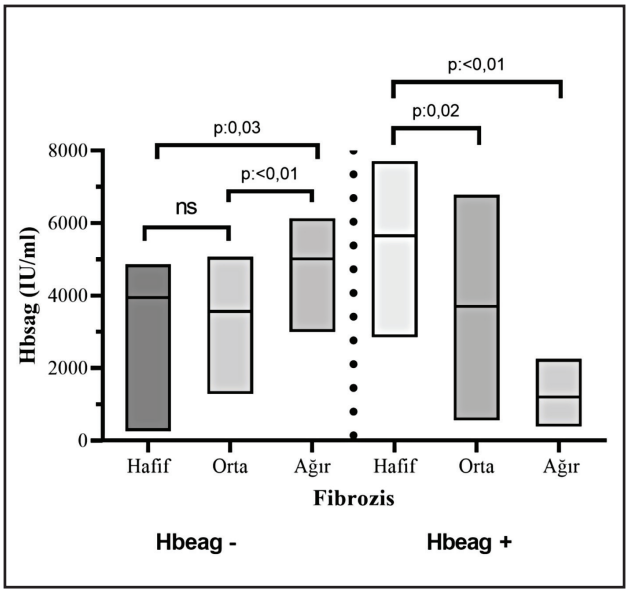
Tablo 1 Hastaların laboratuvar ve karaciğer biyopsi sonuçları

	HbeAg Pozitif n: 30	HbeAg Negatif n: 98	P Değeri
Cinsiyet (erkek) n (%)	17 (%13.3)	54 (%42.2)	0.52
Yaş (mean ± SD)	33.9 ± 11.14	45.12 ± 12.9	< 0.001**
AST mg/dl (mean ± SD)	47.40 ± 22.96	32.75 ± 20.73	0.01**
ALT mg/dl (mean ± SD)	71.13 ± 39.70	42.24 ± 36.72	< 0.001**
GGT mg/dl (mean ± SD)	34.50 ± 19.16	26.17 ± 16.77	0.02**
ALP mg/dl (mean ± SD)	85.63 ± 20.85	75 ± 26.22	0.04**
Karaciğer histolojisi			
Nekroinflamasyon*	6.53±1.73	5.97 ± 1.93	0.07
Minimal (0 - 4) n (%)	3 (%2.5)	17 (%13.9)	0.21
Hafif (5 - 8) n (%)	24 (%19.7)	64 (%52.5)	0.19
Orta (9 - 12) n (%)	3 (%2.5)	10 (%8.2)	0.53
Şiddetli (13 - 18) n(%)	0	1 (%0.8)	0.75
Fibrozis*	2.26 ± 1.11	2.64 ± 1.35	0.62
Yok/hafif (0 - 1) n (%)	8 (%6.7)	20 (%16.7)	0.61
Orta (2 - 3) n (%)	17 (%14.2)	49 (%40.8)	0.83
Şiddetli (4) n (%)	4 (%3.3)	13 (%10.8)	0.88
Siroz (5 - 6) n (%)	1 (%0.8)	8 (%6.7)	0.31
HBV DNA (log 10) IU/ml ± SD	7.35 ± 1.71	4.92 ± 1.22	< 0.001**
HbsAg IU/ml ± SD	3901.4 ± 1254.2	3804.2 ± 2161.1	< 0.001**

AST: Aspartat aminotransferaz; ALT: Alanin aminotransferaz; GGT: Gama glutamil transferaz; ALP: Alkalen fosfataz; * sınıflamada Ishak skorlama kullanılmıştır
** P < 0.05 istatiksel analiz için anlamlı kabul edilmiştir.

lı bir ilişki mevcut idi (r: 0.22, p: 0.01). HbsAg ile nekroinflamatuvar aktivite arasında anlamlı bir ilişki saptanmadı (Tablo 2).

HbeAg pozitif grupta HbsAg seviyesi ile HBV DNA (log10) arasında pozitif korelasyon mevcut iken; nekroinflamatuvar aktivite ve fibrozis ile negatif korelasyon izlendi. HbeAg negatif hastalarda HbsAg seviyesi ile karaciğer histolojisi ve HBV DNA (log10) arasında anlamlı korelasyon izlenmedi (Tablo 3). Fibrozis skorları ile HbsAg seviyeleri açısından yapılan değerlendirmede ise HbeAg negatif gruptaki ileri fibrozisli hastalarda hafif ve orta fibrozise göre HbsAg seviyeleri anlamlı olarak yüksek saptanırken (p: <0.01); HbeAg pozitif olan grupta ise fibrozis derecesi ilerledikçe HbsAg seviyelerinin anlamlı olarak azaldığı gözlemlendi (Şekil 1).



Şekil 1 Gruplara göre HbsAg titresi ve fibrozis arasındaki ilişki.

Tablo 2 Hastaların karaciğer histolojisi ile HbsAg ve HBV DNA ile arasındaki ilişkileri

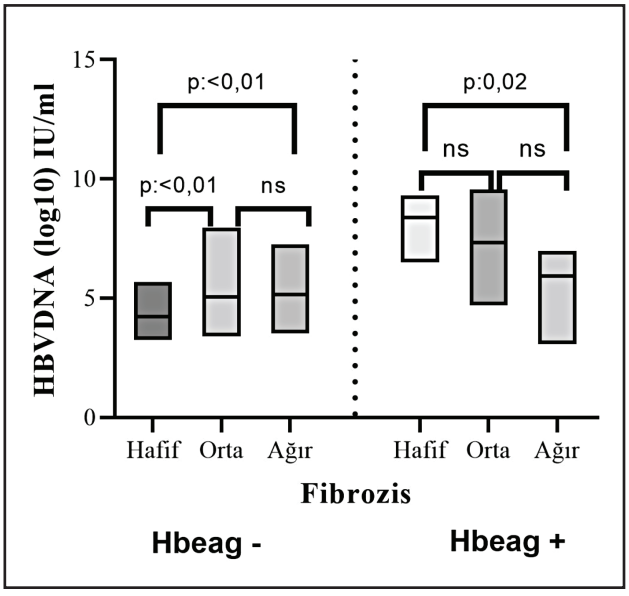
	Nekroinflamatuvar Aktivite		Fibrozis	
	r	p	r	p
HbsAg	0.13	0.14	0.07	0.42
HBV DNA (log10)	0.22	0.01*	0.04	0.61

Tablo 3 Grupların karaciğer histolojisi ile HbsAg, HBV-DNA ve karaciğer enzim değerleri arasındaki ilişkileri

	Nekroinflamatuvar Aktivite		Fibrozis		HbsAg Seviyesi	
HbeAg Negatif Grup	r	p	r	p	r	p
AST	0. 41	< 0.01*	0.20	< 0.04*	0.09	0.34
ALT	0.39	< 0.01*	0.13	0.20	0.13	0.20
GGT	0.22	0.02*	0.10	0.30	0.01	0.90
ALP	0.13	0.20	0.07	0.48	0.2	0.05
HBV DNA (log10)	0.27	< 0.01*	0.19	0.05	0.04	0.64
HbsAg Seviyesi	0.08	0.42	0.22	0.06		
HbeAg Pozitif Grup						
AST	0.45	0.01*	0.48	< 0.01*	-0.05	0.77
ALT	0.47	0.01*	0.45	0.01*	-0.12	0.50
GGT	0.28	0.03*	0.07	0.68	0.14	0.94
ALP	-0.32	0.08	0.27	0.13	0.09	0.63
HBV DNA (log10)	-0.30	0.10	0.14	0.35	0.46	< 0.01*
HbsAg Seviyesi	-0.38	0.03*	-0.73	< 0.01*		

AST: Aspartat aminotransferaz; ALT: Alanin aminotransferaz; GGT: Gama glutamil transferaz; ALP: Alkalen fosfataz, HBV DNA: Hepatit B virüs DNA; HbsAg: Hepatit B yüzey antijeni.

Fibrozis skorları ile HBV DNA (log10) düzeyleri açısından yapılan değerlendirmede ise, HbeAg negatif gruptaki hafif fibrozisi olan hastalarda orta ve ağır fibrozisi olanlara göre anlamlı olarak HBV DNA (log10) düzeyleri daha düşük saptanmış olup, HbeAg pozitif grupta ise hafif fibrozisi olan hastalarda HBV DNA (log10) düzeyleri ise anlamlı olarak yüksek izlendi (Şekil 2).



Şekil 2 Gruplara göre HBV DNA ve fibrozis arasındaki ilişki.

TARTIŞMA

Çalışmamızda HbsAg seviyesinin, HbeAg pozitif hastalarda HBV DNA (log10) ile pozitif; nekroinflamatuvar aktivite ve fibrozis ile negatif korele seyrettiği görüldü. HbeAg negatif hastalarda ise, HbsAg seviyesi ile karaciğer fibrozisi ve HBV DNA düzeylerinde anlamlı birliktelik izlenmedi.

HbsAg seviyesi HbeAg'nin pozitif saptandığı immüntolerans fazında, HBV DNA ile birlikte yüksek seyretmektedir (8,9). Karaciğer histolojisinde normal veya minimal değişikliklerin izlendiği bu dönemin sonunda daha düşük HbsAg titreleri ve dalgalı HBV DNA düzeyleri ile karakterize immünklirens faz gelmektedir. Bu dönemle ilişkili en dikkat çekici çalışmalardan biri 2010 yılında Chan ve ark. tarafından yapmış, HbsAg düzeyi düşüşünün HbeAg serokonversiyonu ile ilişkili olduğu ve HbsAg düzeyinin >1 log IU/ml düşmesinin immüntoleran dönemdeki hastalarda immün kontrol için bir belirteç olabileceği önerilmiştir (14). Peignoux ve ark. da 406 hastayı kapsayan çalışmalarında, çalışmamıza benzer şekilde HbeAg pozitif hastalarda düşük HbsAg düzeylerinin fibrozisin şiddeti ile ilişkisini vurgulamışlardır (p: < 0.01 r: 0.43) (15). Tüm HBV genotiplerini içeren bir Fransız çalışmasında ise, HbsAg seviyesi F0 - F1'de F2 - F4 hastalarından önemli ölçüde daha yüksek saptanmış (4.63 ± 0.58'e karşı 3.84 ± 1.01 log10 IU/ml, p: < 0.001) ve orta-şiddetli fibrozis ayrımı için HbsAg eşik düzeyini 3.85 (log10) IU/ml olarak önermişlerdir (16). HbeAg pozitif hastalarda giderek artan şiddetli karaciğer fibrozunun neden daha düşük serum HbsAg ve HBV DNA seviyeleri ile ilişkili olduğunun mekanik açıklaması belirsizdir. Hastalık artışı sırasında giderek daha güçlü bir hümoral bağışıklık tepkisi, HbsAg'nin salgıdan ziyade hücreler içinde tutulmasına veya konağın viral replikasyonu destekleme yeteneğinin azalmasına bağlı olabileceği speküle edilebilir (15). Bu grup hastalarda HbsAg ile HbeAg seviyesi veya spontan HbeAg serokonversiyonu arasında bir ilişki çalışmamız da dahil çoğu çalışmada saptanmamıştır (14,17). Ancak yapılan çalışmalarda, HbeAg serokonversiyonundan sonraki 1 yıl içerisinde HbsAg < 1.000 IU/ml düşen hastalarda, 6 yıl içerisinde HbsAg klirensinin yüksek olduğu belirtilmektedir (18,19).

HbeAg negatif hastalarda ise HbsAg düzeyi fibrosizden ziyade HBV DNA düzeyi ile birlikte inaktif taşıyıcı ile kronik HbeAg negatif hepatit B ayrımında oldukça faydalı gibi gözükmektedir (17,20). HbsAg (< 1.000 IU/mL) ve HBV DNA'nın (≤ 2.000 IU/mL) olduğu durumlarda inaktif taşıyıcının tanımlanmasında tanısal doğruluk %94.3 ve pozitif prediktif değer (PPV) %87.9 olarak saptanmıştır

(21). REVEAL çalışmasında ise aynı eşik değerleri kullanıldığında genotip B ve C ile enfekte taşıyıcılarda tanısal doğruluk %78 ve PPV %83'dür (22). Çalışmamızda fibrozis skorları ile HbsAg seviyeleri arasında anlamlı korelasyon izlenmedi. Ancak ileri fibrozisli hastalarda HbsAg değerlerinin HBV DNA ile birlikte ileri fibrozis olmayanlara göre anlamlı yüksek olduğu görüldü. Bu yönde HbeAg negatif kronik hepatit B hastalarında Yunanistan'dan yapılmış bir çalışmada HBV DNA düzeylerine göre hastalar 3 gruba bölünmüş, HBV DNA değeri yüksek (> 20 000IU/ml) olan grupta HbsAg, ALT ve fibrozis değerlerinin daha yüksek olduğu bildirilmiştir (23). Çalışmamıza benzer ALT ile HbsAg değerleri arasında ilişki saptanmayan bir diğer çalışma Jaroszewicz ve ark. tarafından yapılmıştır (17). İlginç olarak takiplerinde HbeAg negatif hastalarda düşük replikatif fazda iken hepatit alevlenme görülenlerde HbsAg titresinin 3 kat daha yüksek olduğunu saptamışlardır.

Çalışmamızın retrospektif doğasının yanı sıra bir diğer kısıtlaması HBV DNA düzeyinin 2000 IU/ml altında olan hastaların sayıca az olmasıdır. Her ne kadar HbsAg titresi ile fibrozisin değerlendirilmesi öncelikli amacımız olsa da bu durumda az sayıdaki düşük viremi olan hastalarda fibrozisin değerlendirmesi yanıltıcı olabilmektedir.

Sonuç olarak, dinamik bir süreç olan HBV enfeksiyonunda özellikle HbeAg pozitif hastalarda HbsAg düzey ölçümü, hastalarda tedavi planlanması amacıyla önemli yeri olan fibrozis derecesinin tayininde anlamlı sonuçlar verebilir. Bu konu ile ilgili daha değerli bilgilerin edinebilmesi amacıyla daha geniş çapta çalışmalara ihtiyaç vardır.

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KAYNAKLAR

1. Zampino R, Boemio A, Sagnelli C, et al. Hepatitis B virus burden in developing countries. World J Gastroenterol 2015;21:11941-53.
2. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol 2017;67:370-98.
3. Seeger C, Mason WS. Hepatitis B virus biology. Microbiol Mol Biol Rev 2000;64:51-68.
4. Liaw YF. Clinical utility of hepatitis B surface antigen quantitation in patients with chronic hepatitis B: A review. Hepatology 2011;54:E1-9.
5. Cornberg M, Wong VWS, Locarnini S, et al. The role of quantitative hepatitis B surface antigen revisited. J Hepatol 2017;66:398-411.
6. Liu SQ, Zhu XJ, Sun XH, Li M, Gao YQ. [Characteristic of liver pathology in HBeAg-positive and HBeAg-negative chronic hepatitis B patients with mildly elevated ALT]. Zhonghua Gan Zang Bing Za Zhi 2012;20:348-52.
7. Zeng DW, Liu YR, Dong J, et al. Serum HBsAg and HBeAg levels are associated with liver pathological stages in the immune clearance phase of hepatitis B virus chronic infection. Mol Med Rep 2015;11:3465-72.
8. Nguyen T, Thompson AJV, Bowden S, et al. Hepatitis B surface antigen levels during the natural history of chronic hepatitis B: A perspective on Asia. J Hepatol 2010;52:508-13.
9. Zeng LY, Lian JS, Chen JY, et al. Hepatitis B surface antigen levels during natural history of chronic hepatitis B: A Chinese perspective study. World J Gastroenterol 2014;20:9178-84.
10. Viganò M, Lampertico P. Clinical implications of HBsAg quantification in patients with chronic hepatitis B. Saudi J Gastroenterol 2012;18:81-6.
11. Li J, Sun X, Fang J, et al. Analysis of intrahepatic total HBV DNA, cccDNA and serum HBsAg level in Chronic Hepatitis B patients with undetectable serum HBV DNA during oral antiviral therapy. Clin Res Hepatol Gastroenterol 2017;41:635-43.
12. Wiegand J, Wedemeyer H, Finger A, et al. A decline in hepatitis B virus surface antigen (HBsAg) predicts clearance, but does not correlate with quantitative HBeAg or HBV DNA levels. Antivir Ther 2008;13:547-54.

13. Ishak K, Baptista A, Bianchi L, et al. Histological grading and staging of chronic hepatitis. J Hepatol 1995;22:696-9.

14. Chan HL, Wong VW, Wong GL, et al. A longitudinal study on the natural history of serum hepatitis B surface antigen changes in chronic hepatitis B. Hepatology 2010;52:1232-41.

15. Martinot-Peignoux M, Carvalho-Filho R, Lapalus M, et al. Hepatitis B surface antigen serum level is associated with fibrosis severity in treatment-naïve, e antigen-positive patients. J Hepatol 2013;58:1089-95.

16. Marcellin P, Martinot-Peignoux M, Asselah T, et al. Serum levels of hepatitis B surface antigen predict severity of fibrosis in patients with E antigen-positive chronic hepatitis B. Clin Gastroenterol Hepatol 2015;13:1532-9.e1.

17. Jaroszewicz J, Serrano BC, Wursthorn K, et al. Hepatitis B surface antigen (HBsAg) levels in the natural history of hepatitis B virus (HBV)-infection: a European perspective. J Hepatol 2010;52:514-22.

18. Tseng T, Liu C, Su T, et al. Serum hepatitis B surface antigen levels predict surface antigen loss in hepatitis B e antigen seroconverters. Gastroenterology 2011;141:517-25.

19. Fung J, Wong DKH, Seto WK, et al. Hepatitis B surface antigen seroclearance: Relationship to hepatitis B e-antigen seroclearance and hepatitis B e-antigen-negative hepatitis. Am J Gastroenterol 2014;109:1764-70.

20. Yakut M, Bektas M, Seven G, et al. Characterization of the inactive HBsAg carrier state with 3 year follow-up. J Hepatol 2011;54(Suppl 1):S159.

21. Brunetto MR, Oliveri F, Colombatto P, et al. Hepatitis B surface antigen serum levels help to distinguish active from inactive hepatitis B virus genotype D carriers. Gastroenterology 2010;139:483-90.

22. Liu J, Yang H, Lee M, et al. Serum levels of hepatitis B surface antigen and DNA can predict inactive carriers with low risk of disease progression. Hepatology 2016;64:381-9.

23. Papatheodoridis GV, Manesis EK, Manolakopoulos S, et al. Is there a meaningful serum hepatitis B virus DNA cutoff level for therapeutic decisions in hepatitis B e antigen-negative chronic hepatitis B virus infection? Hepatology 2008;48:1451-9.

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ORIGINAL RESEARCH

Endoscopic findings are not different in patients with upper gastrointestinal bleeding with COVID-19

COVID-19'lu üst gastrointestinal sistem kanamalı hastalarda endoskopik bulgular farklı değildir

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Background and Aims: Coronavirus disease-2019 is an emerging disease of global public health concern. We aimed to evaluate the demographic data, clinical properties, risk factors and endoscopy findings of coronavirus disease-2019 patients with upper gastrointestinal system bleeding. **Materials and Method:** Patients who underwent endoscopy for upper gastrointestinal bleeding between July 2, 2020 and January 29, 2021 and were diagnosed with severe acute respiratory syndrome coronavirus-2 confirmed by polymerase chain reaction were included in the study. In this retrospective study patients with gastrointestinal bleeding were compared as 1:2 case-control. Coronavirus disease-2019 patients who underwent endoscopy for upper gastrointestinal bleeding and the control group were compared retrospectively in terms of demographic data, comorbid diseases, bleeding symptom, drugs administered, laboratory parameters, time between bleeding symptom and endoscopy, endoscopy findings, gastrointestinal bleeding treatment, and mortality rates. **Results:** Forty Covid-19 patients (23 males, mean age ± SD, 65.92 ± 12.97) and 80 non-Covid-19 control patients (43 males, mean age ± SD, 66.17 ± 15.61) who underwent endoscopy for upper gastrointestinal bleeding were compared. The most common bleeding symptom was melena in both groups (50% vs 60%). Hospitalization in intensive care unit (47.5% vs 20%, P = 0.004) and need for mechanic ventilation (22.5% vs 5%, p = 0.006), use of corticosteroids were more common in coronavirus disease-2019 group (30% vs. 2.5%, p = 0.000). The need for erythrocyt replacement were not different between the groups [median (min - max) 1.5 (0 - 13) vs 0.5 (0 - 22), p = 0.397]. Use of low molecular weight heparin was statistically more common in coronavirus disease-2019 group (32.5% vs 5%, p=0.00). Time elapsed until the performance of endoscopy in terms of hours was significantly longer in coronavirus disease-2019 group (62.97 ± 84.59 vs. 21.85 ± 33.91, p = 0.006). The most common endoscopic finding was gastroduodenal ulcer in both groups. No significant differences were seen in terms of rebleeeding rates. Mortality rate was statistically higher in coronavirus disease-2019 group (37.5% vs 8.8%, p = 0.000). **Conclusions:** Until more precise guidelines for the management of gastrointestinal bleeding in COVID-19 patients are developed, a case-by-case decision should be made on whether to perform endoscopy and the timing of the procedure, after multidisciplinary assessments are made in terms of patient status, response to medical therapy, treatment resources, and assessment of risks.

Key words: Covid-19, gastrointestinal bleeding, anticogulant

Giriş ve Amaç: Kovid-19 hastalığı, küresel halk sağlığı endişesi yaratan yeni ortaya çıkan bir hastalıktır. Üst gastrointestinal sistem kanaması olan Kovid-19 hastalarının demografik verilerini, klinik özelliklerini, risk faktörlerini ve endoskopi bulgularını değerlendirmeyi amaçladık. **Gereç ve Yöntem:** 2 Temmuz 2020 - 29 Ocak 2021 tarihleri arasında üst gastrointestinal sistem kanaması nedeniyle endoskopi yapılan ve polimerize zincir reaksiyon ile doğrulanmış ağır akut solunum sendrom-koronavirüs-2 tanısı konan hastalar çalışmaya alındı. Gastrointestinal sistem kanaması olan Kovid-19'lu hastalar retrospektif olarak karşılaştırıldı. Üst gastrointestinal sistem kanaması nedeniyle endoskopi yapılan Kovid-19 hastaları ile kontrol grubu retrospektif olarak demografik veriler, komorbid hastalıklar, kanama semptomu, uygulanan ilaçlar, laboratuvar parametreleri, kanama semptomu ile endoskopi arasındaki süre, endoskopi bulguları, gastrointestinal kanama tedavisi ve ölüm oranları açısından karşılaştırıldı. **Bulgular:** Üst gastrointestinal sistem kanaması nedeniyle endoskopisi yapılan 40 Kovid-19 hastası (23 erkek, ortalama yaş ± SD, 65.92 ± 12.97) ve 80 Kovid-19 hastalığı olmayan kontrol (43 erkek, ortalama yaş ± SD, 66.17 ± 15.61) hastası karşılaştırıldı. Her iki grupta da en sık görülen kanama semptomu melena idi (%50'ye karşı %60). Yoğun bakım ünitesinde yatış (%47.5'e karşı %20, p = 0.004) ve mekanik ventilasyon ihtiyacı (%22.5'e karşı %5, p = 0.006), kortikosteroid kullanımı (%30'a karşı %2.5, p = 0.000) Kovid-19 hastalığı grubunda daha yaygındı. Eritrosit replasmanı ihtiyacı gruplar arasında farklı değildi [medyan (min - maks) 1.5 (0-13) vs 0.5 (0-22), p = 0.397]. Düşük moleküler ağırlıklı heparin kullanımı Kovid-19 hastalığı grubunda istatistiksel olarak daha yaygındı (%32.5'e karşı %5, p = 0.00). Endoskopi performansına kadar geçen süre, saat olarak Kovid-19 hastalık grubunda anlamlı olarak daha uzundu (62.97 ± 84.59 vs. 21.85 ± 33.91, p = 0.006). Her iki grupta da en sık görülen endoskopik bulgu gastroduodenal ülserdi. Tekrar kanama oranları açısından anlamlı bir fark görülmedi. Ölüm oranı Kovid-19 hastalığı grubunda istatistiksel olarak daha yüksekti (%37.5'e karşı %8.8, p = 0.000). **Sonuç:** Kovid-19 hastalarında gastrointestinal sistem kanamalarının yönetimine ilişkin daha kesin kılavuzlar geliştirilinceye kadar, hastanın durumu, medikal tedaviye yanıt, tedavi kaynakları ve risklerin değerlendirilmesi açısından multidisipliner değerlendirmeler yapıldıktan sonra, endoskopi yapılıp yapılmayacağına ve işlemin zamanlamasına vaka bazında karar verilmelidir.

Anahtar kelimeler: Kovid-19, gastrointestinal kanama, antikogülan

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INTRODUCTION

Coronavirus disease 2019 (Covid-19), an infectious disease caused by coronavirus 2 (SARS-CoV-2) is characterized by severe acute respiratory failure (1). The typical presentation of coronavirus disease is pulmonary infiltrations associated with fever, cough, and dyspnea (2). Even though the involvement of the respiratory system is the most common manifestation, gastrointestinal tract can be affected as well. Gastrointestinal tract symptoms include nausea, vomiting, diarrhea, abdominal pain, and gastrointestinal bleeding (3). Some observational studies suggest that the risk of gastrointestinal (GI) bleeding may be increased in patients with Covid-19 (4-6). The first-line treatment of acute gastrointestinal bleeding is an endoscopic approach after appropriate resuscitation. Endoscopic guidelines mostly recommend endoscopy procedures should be performed within the first 24 hours in acute upper GI bleeding (7). But endoscopic procedures carry a high risk for health care workers due to aerosol production (8). Due to the risk of transmission, there seems to be a trend towards the conservative treatment of Covid-19 positive patients with GI bleeding consisting of pharmacotherapy, transfusion, and close hemodynamic monitoring (6,9,10). As a result, gastrointestinal pathologies have not been clarified yet in Covid-19 positive patients with GI bleeding. We aimed to present demographic, clinical data, risk factors, and endoscopy findings in patients with Covid-19 positive GI bleeding who underwent endoscopy in a tertiary center retrospectively.

MATERIALS and METHODS

In this single tertiary care center (Ankara City Hospital, Turkey), retrospective study patients with GI bleeding were compared as 1:2 case-control. The Covid-19 group was defined as upper GI bleeding Covid-19 patients confirmed with polymerase chain reaction (PCR) positivity and the control group was defined as upper GI bleeding patients who were confirmed not to have Covid-19 using laboratory, clinical, and imaging data. Endoscopy was performed on all patients in both groups. Patients in the endoscopy database from July 6, 2020, when the first Covid-19 positive case was received, to January 29, 2021, who underwent endoscopy for upper gastrointestinal bleeding were included in the study. Endoscopy patients with upper GI bleeding were selected from this endoscopy database. Patient files were searched and demographic data, data about comorbid diseases, GI bleeding symptom, medications used especially antiplatelet and anticoagulant drugs, laboratory parameters, the time period between the bleeding symptom and endoscopy procedure, endoscopic findings, treatments for GI bleeding (medical, endoscopic, radiologic, surgery) were extracted from electronic medical records. The endpoint of the study was the discharge or exit of the patients. Over acute upper GI bleeding was accepted as symptoms such as hematemesis, melena, hematochezia, blood in a nasogastric tube, blood coming from ostomy site, syncope, or drop of hemoglobin more than 2 units. Covid-19 positivity was defined as Covid-19 PCR positivity in nasopharyngeal swabs. The control group was selected from upper GI bleeding patients to whom endoscopy was performed and with no previous history of Covid-19 disease and with no fever, cough, and respiratory difficulty at the time of endoscopy. Patients in the control group were Covid-19 PCR negative, an antibody against Covid-19 was negative (Immunoglobulin G + Immunoglobulin M), and they did not have any Covid-19 findings radiologically Covid-19 PCR negativity was accepted only if the test was performed within the 24 hours before endoscopy. Patients younger than 18 years of age, with suboptimal endoscopy reports and pregnant patients were excluded.

Endoscopic classification of upper GI bleeding was defined according to international guidelines

(11,12). Endoscopic treatments were recorded. Radiologic and surgical treatments were recorded in patients with endoscopic treatment failure. General mortality rates were recorded.

Ethics

This study was conducted with the permission of the Ministry of Health of Turkish Government. Ethics board permission was granted from Ankara Yıldırım Beyazıt University Faculty of Medicine with the reference number 26379996150/40. The data entry was made without using any identity information (i.e., name) thereby patient anonymity was assured.

Statistics

In this retrospective study, discrete variables such as the need for ventilation and the rate of intensive care unit admission were presented in terms of absolute values and percentages. Continuous variables, such as ferritin, hemoglobin, hematocrit levels were expressed and summarized based on mean, standart deviation (SD), median and interquartile range values. Frequencies were expressed per hundred (%) separately for Covid-19 and non-Covid-19 patients with 95% confidence interval (CI). For the comparison of Covid-19 and non-Covid-19 patients (i.e., control group), the $\chi 2$ test and cross-tab analysis were utilized to analyze the frequency differences in discrete variables. In particular, frequencies for the use of low molecular weight heparin and mortalities (i.e., mortality rates) were compared using Chi-square tests and cross-tabs analysis. On the other hand, Student t test were conducted to compare Covid-19 patients with non-Covid-19 patients in terms of hemoglobin levels, Hematocrit levels, lymphocyte count, platelet count, international normalised ratio (INR), blood urea nitrogen (BUN), creatinine, blood cell count, ferritin levels. In all comparisons, statistical significance was accepted if the p-value was < 0.05. All analyses were conducted with the SPSS (v.24) statistical software package (IBM Corp., Armonk, NY). After the analyses were conducted, post-hoc analysis of "observed power" was made by using the obtained sample and effect size. For the comparisons of ferritin levels and white blood cell counts, the power of the analysis was found to be more than 0.80 threshold level. For instance, using an alpha level of .05, an effect size of .76, and sample sizes of 40 and 59 for Covid-19 and non-Covid -19 patient groups respectively, we found the post hoc statistical power to be .98 using G*power analysis.

RESULTS

Fourty Covid-19 positive patients with upper GI bleeding in whom endoscopy was performed and 80 non- Covid-19 controls with upper GI bleeding and endoscopy performed during the same period were selected for this retrospective study. Basic demographic data of both groups are presented in Table 1.

The most common bleeding symptom was melena in both groups. According to Chi-Square Analysis, the rate of intensive care unit admission and the need for mechanical ventilation were found to be more prevalent in Covid-19 group. Besides, the use of corticosteroids was more frequently observed in the Covid-19 group compared to non-Covid-19 patients. The use of low molecular weight heparin (LMWH) was statistically more common in the Covid-19 group (32.5% vs 5%, $p = 0.00$). Remarkably, there were no significant differences in terms of packed red blood cell replacement between the groups [median (min-max) 1.5 (0-13) for Covid-19 group vs 0.5 (0-22), $p = 0.397$ for non-Covid-19 group]. Besides packed red blood cell replacements, statistically significant differences were not obtained between two groups for minimum or maximum hemoglobin levels, hematocrit levels, lymphocyte count, platelet count, INR, BUN, creatinine.

Table 1 Demographic and clinical data of with Covid-19 GI bleeding patients and non-Covid-19 GI bleeding patients.

	Group 1 (n = 40)	Group 2 (n = 80)	p value
Gender (Female/Male)	17/23	37/43	0.697
Age (years)	65.92 ± 12.97	66.17 ± 15.61	0.931
Comorbidity, n (%)	33 (82.5)	67 (83.8)	1
Hypertension	50 (50)	38 (47.5)	0.049
Diabetes	19 (47.5)	26 (32.5)	0.162
Coronary arter disease	6 (15)	21 (26.3)	0.246
Cancer	7 (17.5)	10 (12.5)	0.644
Cirrhosis	2 (5)	7 (8.8)	0.370
Chronic renal failure	6 (15)	7 (8.9)	0.237
Neurological disease	5 (12.5)	17 (21.3)	0.359
COPD	5 (12.5)	2 (2.5)	**0.04**
Congestive heart failure	2 (5)	0 (0)	0.109
Other	1 (2.5)	11 (13.8)	**0.045**
History of peptic ulcer, n (%)	5 (12.5)	6 (7.5)	0.282
Use of corticosteroids, n (%)	12 (30)	2 (2.5)	**0.000**
Bleeding symptom, n (%)			
Melena	20 (50)	48 (60)	0.471
Hematemesis	10 (25)	25 (31.25)	0.619
Hematochesia	4 (10)	3 (3.75)	0.167
Drop of hemoglobin	2 (5)	0 (0)	0.109
Blood in NG tube	3 (7.5)	1 (1.25)	0.107
Blood in ostomy	1 (2.5)	1 (1.25)	0.557
Syncope	0 (0)	2 (2.5)	0.443
Hospitalization in intensive care unit, n (%)	19 (47.5)	16 (20)	**0.004**
Oxygen treatment, n (%)			
Room air	20 (50)	69 (87.3)	**0.000**
Low flow	6 (15)	5 (6.3)	**0.111**
High flow	5 (12.5)	2 (2.5)	**0.040**
Mechanical ventilation	9 (22.5)	4 (5)	**0.006**
ES replacement median (min - max)	1.5 (0-13)	0.5 (0-22)	0.397
Medical treatment for bleeding, %			0.354
PPI infusion	37 (92.5)	75 (93.8)	
PPI + somatostatin infusion	2 (5)	5 (6.2)	
PPI x 2	1 (2.5)	0 (0)	
Rebleeding, %	6 (15)	4 (5)	0.068
Exitus, %	15 (37.5)	6 (7.5)	**0.000**

COPD: Chronic obstructive pulmonary disease, NG: Nasogastric, ES: Erythrocyte suspension, PPI: Proton pump inhibitor.

Independent sample t-tests revealed that white blood cell count and ferritin levels were statistically higher in the Covid-19 group. Albumin levels were statistically lower in the Covid-19 group (Table 2). Time spent until endoscopy procedure (hours) (defined as the time from emergency department

Table 2 Laboratory findings of Covid-19 GI bleeding patients and non-Covid-19 GI bleeding patients

	Group 1 (n = 40)	Group 2 (n = 80)	p value
Hgb max, g/dL	11.94 ± 0.37	11.53 ± 0.25	0.358
Hgb min, g/dL	7.93 ± 0.41	7.99 ± 0.26	0.895
Htc	25.72 ± 1.36	26.19 ± 0.82	0.759
White blood cell count, 103 μL^{-1}	14628 ± 2797	8471 ± 599	**0.037**
Lymphocyte, 10^3 μL^{-1}	1255 ± 341	1686 ± 247	0.316
Platelet count, 10^3 μL^{-1}	228350 ± 26205	239116 ± 12194	0.671
INR	4.21 ± 2.89	1.52 ± 0.17	0.360
BUN, mg/dL	91.77 ± 9.46	74.58 ± 6.47	0.132
Cr, mg/dL	1.53 ± 0.21	1.24 ± 0.13	0.237
D-Dimer, ng/mL	4.28 ± 1,28	3.73 ± 0,99	0,736
Ferritin, (µg/L)	781.39 ± 180	164.26 ± 36.39	**0.002**
LDH (U/L)	339.48 ± 25.28	279.15 ± 37.96	0.189
C-reactive protein (g/L)	0.77 ± 0.12	0.45 ± 0.11	0.062
Albumin (g/L)	30.86 ± 1.19	34.91 ± 0.8	**0.006**

Hgb: Hemoglobin, Htc: Hematocrit, INR: International normalized ratio, BUN: Blood urea nitrogen, Cr: Creatinine, LDH: Lactic dehydrogenase.

admission to endoscopy in outpatients and time from the first appearance of bleeding symptoms to endoscopy in already hospitalized patients) was significantly longer in Covid-19 patients.

There were no significant differences in terms of endoscopy findings between Covid-19 and the non-Covid-19 group. The most common endoscopic finding was a gastroduodenal ulcer in both groups. Due to a low number of cases, other endoscopic findings could not be compared but 2 cases of candida esophagitis were detected in the Covid-19 group and erosive gastritis was numerically more common (17.5% vs 7.5%). There were no differences in terms of Forrest classification of gastroduodenal ulcers. Similarly, there were no differences in terms of endoscopic management between the groups (Table 3). No differences were not noted in terms of medical treatment of upper GI bleeding (p = 0.354). Two patients needed surgical treatment for GI bleeding. No surgical treatment was needed for patients in the non-Covid-19 group but 1 patient underwent embolization by interventional radiology. The rate of rebleeding did not differ between the groups. Mortality rate of Covid-19 patients were significantly higher than non-Covid-19 group (37.5% vs 7.5%, p = 0.000) (Table 1). The cause of mortality was due to GI bleeding in only 1 patient out of 15 in the Covid-19 group while in the non-Covid-19 group 4 out of 6 patients died due to upper GI bleeding.

DISCUSSION

Endoscopy guidelines recommend that, upper GI endoscopy be performed in the first 24 hours upon admission (7). This approach enables to determine to cause of bleeding, estimate the risk of rebleeding/mortality, and apply therapeutic measures if necessary. A therapeutic approach to GI bleeding has been affected during the Covid-19 pandemic. In clinical practice, this 24-hour recommendation can be ignored due to some reservations. This delay might be due to respiratory failure and difficulty of oxygenation of the patients with accompanying

Table 3 Endoscopic outcomes of Covid-19 and non-Covid-19 patients with upper GI bleeding.

	Group 1 (n = 40)	Group 2 (n = 80)	p value
Endoscopy findings			0.276
Gastric ulcer, n (%)	5 (12.5)	11 (13.75)	
Duodenal ulcer, n (%)	9 (22.5)	18 (22.5)	
Gastroduodenal ulcer, n (%)	1 (2.5)	4 (5)	
Erosive gastritis, n (%)	7 (17.5)	6 (7.5)	
Varix, n (%)	2 (5)	5 (6.25)	
Mallory Weis tear, n (%)	0 (0)	1 (1.25)	
Pangastropathy, n (%)	9 (22.5)	12 (15)	
Candida esophagitis, n (%)	2 (5)	0 (0)	
Other, n (%)	2 (5)	13 (16.25)	
AD, n (%)	1 (2.5)	2 (2.5)	
No visible source, n (%)	2 (5)	8 (10)	
Ulcer, Forrest classification, n	15	33	0.429
Forrest 1a, n (%)	0 (0)	1 (3)	
Forrest 1b, n (%)	1 (6.7)	4 (12)	
Forrest 2a, n (%)	4 (26.6)	2 (6)	
Forrest 2b, n (%)	1 (6.7)	3 (9)	
Forrest 2c, n (%)	2 (13.4)	8 (24)	
Forrest 3, n (%)	7 (46.6)	15 (46)	
Endoscopic intervention, n	40	80	0.339
None, n (%)	32 (80)	59 (73.75)	
Injection, n (%)	3 (7.5)	3 (3.75)	
Cautery, n (%)	1 (2.5)	1 (1.25)	
Hemoclip, n (%)	3 (7.5)	3 (3.75)	
Injection, cautery, n (%)	0 (0)	6 (7.5)	
Injection, hemoclip, n (%)	0 (0)	3 (3.75)	
APC, hemoclip, n (%)	0 (0)	1 (1.25)	
EBL, n (%)	1 (2.5)	2 (2.5)	

AD: Angiodysplasia, APC: Argon plasma coagulation, EBL: Endoscopic band ligation

cardiopulmonary complications or upper GI endoscopy being a highly aerosol producing procedure causing risk of transmission (13). This observation has been confirmed in our study. The time period between emergency department admission in outpatients and appearance of first bleeding symptom in hospitalized patients and endoscopy was significantly longer in the Covid-19 group. Gonzales R et al. have shown that endoscopy was performed 30% less in Covid-19 patients with upper GI bleeding (14). On the other hand daily, GI endoscopy practice has also been affected in non-Covid-19 patients in pandemic and these changes are anticipated to last in the near future. Gastroenterological procedures are decreased with the advent of the pandemic. Lantinga MA et al. have reported that gastroscopic procedures have been decreased 57% (15). This trend seems to be also affecting non-Covid-19 patients with GI bleeding. But in our study, we have shown that upper GI endoscopy was performed within 21.85 ± 33.91 hours in non-Covid-19 patients with GI bleeding.

When we evaluated the data of both Covid-19 and non-Covid-19 patients with upper GI bleeding in this single-center retrospective case-control study we saw the most common etiology was gastroduodenal ulcer. We searched the endoscopic data of 40 Covid-19 patients in this study. To our knowledge, this is one of the highest numbers of Covid-19 patients with upper GI bleeding and reports of endoscopic procedures. When we searched the current literature we could see case series or fewer patients with endoscopic procedures (6,16,17). None of these studies included a comparison with non-Covid-19 GI bleeding patients. Gonzales et al. performed endoscopy in 39 Covid-19 patients with upper GI bleeding in the emergency department before hospitalization. Peptic ulcer was the most common finding in these patients with a 46.2% rate. They compared endoscopic findings with the non-Covid-19 GI bleeding group and found no significant difference (14). We also did not find a significant difference in terms of endoscopic findings between Covid-19 and non-Covid-19 groups. Generally, the most common reason for upper GI bleeding has been reported to be peptic ulcer disease (approximately 32-36%) in the literature. The other commonly reported reasons are gastritis or gastric erosions (18-22%) and duodenitis (13%) (18). In our study, we also found similar findings in Covid-19 and non-Covid-19 groups.

Observational studies suggested the beneficial effect of anticoagulant treatment on mortality rates in patients with Covid-19 related coagulopathy or a prominent increase in serum D-dimer levels (19). As a result, most hospitals integrated anticoagulant drugs into standard medical treatment. Likewise, LMWH use was significantly higher in Covid-19 patients. Anticoagulant drugs have been considered as risk factors for GI bleeding in the non-Covid-19 population. The risk of anticoagulant treatment for GI bleeding in Covid-19 patients has not been clarified yet. Trindade et al. suggested that the anticoagulant and antiplatelet drugs do not pose an increased risk of GI bleeding in Covid-19 patients (10,17). We also found that GI bleeding-related mortality was not high in Covid-19 patients despite the common use of LMWH. Likewise, rates of rebleeding were also similar in both groups.

Proton pump inhibitor (PPI) treatment had been given to all patients with a presumed diagnosis of GI bleeding. Although time period between admission/bleeding symptom to endoscopy was significantly higher in the Covid-19 group there were no significant differences in terms of the need for transfusion, endoscopic findings, rebleeding rates between Covid-19 and non-Covid-19 groups. Similarly, Mauro et al. did not find any difference in terms of mortality and rebleeding between the groups (groups were defined as patients to whom endoscopy was done in the first 24 hours, endoscopy was done after >24 hours, and patients who did not undergo endoscopic evaluation) (17). While deciding the timing of endoscopy a gastroenterologist should also consider the severity of the systemic involvement of Covid-19 disease, the presence or absence of significant respiratory involvement of the disease. Sedation and the endoscopic procedure itself may negatively affect respiratory functions. In patients, breathing room air or low flow oxygen endoscopy can be performed in the first 24 hours as guidelines recommend. On the other hand in patients receiving high flow oxygen or noninvasive positive pressure ventilation decision to perform endoscopy should be done after consideration of GI bleeding risk scores.

In this study of patients with GI bleeding, we found that Covid-19 patients had a significantly higher in-hospital mortality rate than the non-Covid-19 group. While only 1 out of 15 deaths in the Covid-19 group was due to GI bleeding this rate was 4 out of 6 in the non-Covid-19 group. Patients with GI bleeding in the Covid-19 group were shown to bleed during Covid-19 treatment, so they died from complications related to the Covid-19 disease. Our

hospital mortality rate in Covid-19 patients with GI bleeding was higher than mortality of Covid-19 patients without GI bleeding (Ates I et al. unpublished data). This may suggest that GI bleeding in Covid-19 patients is a complication advanced disease leading to a higher mortality rate. Further studies are needed to clarify whether GI bleeding has an effect on mortality rates in Covid-19 patients.

There are some limitations of our study. First of all, this is a retrospective study. Symptom evaluation of GI bleeding might have led to interobserver variations of definitions. Patients with melena were accepted as upper GI bleeding and a small fraction of these patients might be suffering from bleeding from middle or lower GI bleeding. Time to endoscopy was significantly different between the groups and medical treatment had been initiated in the meantime. This medical treatment might have changed the endoscopic findings. Another limitation of our study was the lack of data about the previous use of non-steroid antiinflammatory drugs (NSAIDs) and PPI. NSAIDs have long been known to be important in the etiology of peptic ulcer disease and most of our GI bleeding patients had a gastroduodenal ulcer.

We found similar etiologies in GI bleeding patients with or without Covid-19 infection. Although the time period between symptom/hospital admission till endoscopy was significantly longer in Covid-19 patients there were no significant differences in terms of the need for transfusion, rebleeding rates, and GI bleeding-related mortality rates from non-Covid-19 GI bleeding patients. Until definitive guidelines are developed decisions on whether to perform endoscopy and timing of the endoscopy should be made after multidisciplinary evaluation of the patient and after careful consideration of the patient's condition, response to medical treatment, risk evaluation. Finally, the decision should be individualized for each patient.

Ethics Committee: *This study protocol was approved by Ethics Committee of Ankara Yıldırım Beyazıt University Faculty of Medicine (Date: 07.07.2021, and number 40). The study was complied with The World Medical Association Declaration of Helsinki.*

Conflict of Interest: *There is no conflict of interest with any institution or person. No financial support was received.*

REFERENCES

1. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020;395:565-74.
2. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708-20.
3. Lin L, Jiang X, Zhang Z, et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. Gut 2020;69:997-1001.
4. Cavaliere K, Levine C, Wander P, Sejpal DV, Trindade AJ. Management of upper GI bleeding in patients with COVID-19 pneumonia. Gastrointest Endosc 2020;92:454-5.
5. Gadiparthi C, Perisetti A, Sayana H, et al. Gastrointestinal bleeding in patients with severe SARS-CoV-2. Am J Gastroenterol 2020;115:1283-5.
6. Martin TA, Wan DW, Hajifathalian K, et al. Gastrointestinal bleeding in patients with Coronavirus disease 2019: A matched case-control study. Am J Gastroenterol 2020;115:1609-16.
7. Gralnek IM, Stanley AJ, Morris AJ, et al. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. Endoscopy 2021;53:300-32.
8. Soetikno R, Teoh AYB, Kaltenbach T, et al. Considerations in performing endoscopy during the COVID-19 pandemic. Gastrointest Endosc 2020;92:176-83.
9. Shalimar, Vaishnav M, Elhence A, et al. Outcome of conservative therapy in coronavirus disease-2019 patients presenting with gastrointestinal bleeding. J J Clin Exp Hepatol 2021;11:327-33.
10. Trindade AJ, Izard S, Coppa K, et al; Northwell COVID-19 Research Consortium. Gastrointestinal bleeding in hospitalized COVID-19 patients: a propensity score matched cohort study. J Intern Med 2021;289:887-94.

11. Gralnek IM, Dumonceau JM, Kuipers EJ, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2015;47:a1-46.
12. Tripathi D, Stanley AJ, Hayes PC, et al; Clinical Services and Standards Committee of the British Society of Gastroenterology. U.K. guidelines on the management of variceal haemorrhage in cirrhotic patients. Gut 2015;64:1680-704.
13. Gralnek IM, Hassan C, Beilenhoff U, et al. ESGE and ESGENA Position Statement on gastrointestinal endoscopy and the COVID-19 pandemic. Endoscopy 2020;52:483-90.
14. Gonzalez Gonzalez R, Jacob J, Miro O, et al; Spanish Investigators on Emergency Situations TeAm (SIESTA) Network. Incidence, clinical characteristics, risk factors, and outcomes of upper gastrointestinal bleeding in patients with COVID-19: Results of the UMC-19-S12. J Clin Gastroenterol 2022;56:e38-e46.
15. Lantinga MA, Theunissen F, Ter Borg PCJ, et al; Trans. IT foundation study group. Impact of the COVID-19 pandemic on gastrointestinal endoscopy in the Netherlands: analysis of a prospective endoscopy database. Endoscopy 2021;53:166-70.
16. Vanella G, Capurso G, Burti C, et al. Gastrointestinal mucosal damage in patients with COVID-19 undergoing endoscopy: an international multicentre study. BMJ Open Gastroenterol 2021;8:e000578.
17. Mauro A, De Grazia F, Lenti MV, et al. Upper gastrointestinal bleeding in COVID-19 inpatients: Incidence and management in a multicenter experience from Northern Italy. Clin Res Hepatol Gastroenterol 2021;45:101521.
18. Kuftinec G, Elmunzer BJ, Amin S; North American Alliance for the Study of Digestive Manifestations of Covid-19. The role of endoscopy and findings in COVID-19 patients, an early North American Cohort. BMC Gastroenterol 2021;21:205.
19. Nadkarni GN, Lala A, Bagiella E, et al. Anticoagulation, bleeding, mortality, and pathology in hospitalized patients with COVID-19. J Am Coll Cardiol 2020;76:1815-26.

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OLGU SUNUMU

Siyanoakrilat ilişkili pulmoner emboli; Olgu sunumu

Cyanoacrylate associated pulmonary embolism: A case report

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Sirotik hastaların %50'ye yakınında özofagus ve gastrik varisler gelişir. Varisli siroz hastalarında dekompansasyon bulgusu olarak varis kanaması görülebilmektedir. Kanamalar sıklıkla özofageal varis kaynaklı kanamalardır. Gastrik varisler daha nadir kanar; ancak daha ciddi ve mortalitesi yüksek kanamalara neden olurlar. Gastrik varisler özofagus varisleri ile karşılaştırıldığında daha geniş çapta ve submukozal alanda daha derine uzanım gösterebilirler. Bu nedenle özofagus varisleri için yapılan standart endoskopik tedaviler büyük oranda etkisizdir. Siyanoakrilat tedavisinde septik ve embolik komplikasyonlar görülebildiği bildirilmiştir. Olgumuzda akut gastrik varis kanaması ile başvuran siroz hastasında siyanoakrilat tedavisi sonrası gelişen pulmoner emboli olgusu sunulmuştur.

Anahtar kelimeler: Varis, siyanoakrilat, emboli

Up to 50% of cirrhotic patients develop esophageal and gastric varices. Varicose bleeding may develop as a sign of decompensation in patients with cirrhosis with varicose veins. Bleeding is often caused by esophageal varices. Gastric varices bleed less frequently, but they cause more serious and high-mortality bleeding. Compared to esophageal varices, gastric varices may extend more widely and deeper into the deep submucosal area. Therefore, standard endoscopic treatments for esophageal varices are largely ineffective. Septic and embolic complications have been reported from cyanoacrylate treatment. In our case, a case of pulmonary embolism that developed after cyanoacrylate treatment in a cirrhosis patient who presented with acute gastric variceal bleeding is presented.

Key words: Gastric varices, cyanoacrylate, thromboembolism

GİRİŞ

Karaciğerin kronik inflamasyona maruz kalması sonucu parankimal fibröz dokusu artarak siroza ilerleyebilmektedir. Siroz ve portal ven trombozu gibi hastalıklar nedeni ile gelişen portal hipertansiyon, hastalarda varislere neden olmaktadır. Sirotik hastaların %50'ye yakınında özofagus ve gastrik varisler gelişmektedir. Varisli siroz hastalarında dekompansasyon bulgularından biri olarak varis kanaması görülebilmektedir (1,2). Varis kanama oranları %25-40 arasında bildirilmektedir (3). Varis kanaması portal hipertansiyonun en mortal komplikasyonudur. Kanamalarda mortalite oranı %20'lere çıkabilmektedir (3-6). Endoskopik tekniklerin gelişmesine rağmen portal hipertansiyonun progresif bir şekilde artma göstermesi nedeni ile tekrarlayan kanamalarda bu oran %50'lere çıkabilmektedir. Gastrik varisler özofagus varislerine oranla daha nadir kanama eğilimindedirler. Ancak kanama durumunda daha ciddi ve mortalitesi yüksek kanamalara neden olurlar. Gastrik varisler özofagus varisleri ile karşılaştırıldığında daha geniş çapta ve submukozal alanda daha derine uzanım gösterebilirler. Bu nedenle özofagus varisleri için yapılan standart endoskopik tedaviler büyük oranda etkisizdir. Karaciğer hastalığının derecesi, varisin çapı ve üzerindeki red spotların

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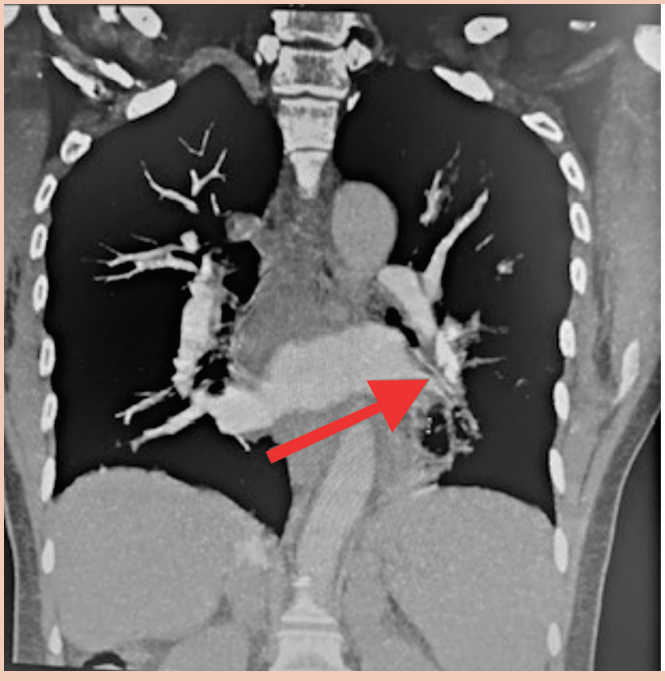
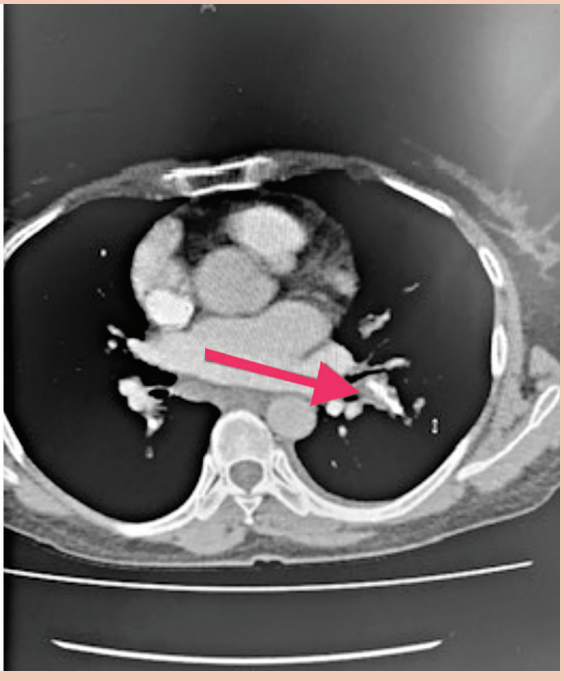
durumuna göre profilaktik tedaviler önerilmektedir. Siyanoakrilat tedavisi gastrik varislerde kanamayı %93-100 oranında kontrol altına alırken tekrar kanama oranı %10 seviyesindedir. Siyanoakrilat ile tedavi edilen gastrik varis olgularında kanama riski beta blokerler ile tedavi edilen gruba oranla daha düşüktür (7). Siyanoakrilat tedavisine bağlı septik ve embolik komplikasyonlar görülebilmektedir. Olgumuzda gastrik varis kanaması ile başvuran siroz hastasında siyanoakrilat tedavisi sonrası gelişen nontrombotik pulmoner emboli olgusu sunulmuştur.

OLGU SUNUMU

Elli dört yaşında portal ven trombozu zemininde karaciğer sirozu ile izlenen 5 yıl önce band ligasyon hikayesi olan hasta kanlı kusma hikayesi ile başvurdu. Vitalleri stabil olan hastanın laboratuvar incelemelerinde lökosit 4.7 x 10^9/L, hemoglobin (Hgb) 10.2 gr/dl (11.7 - 16), hematokrit %31, trombosit 115 x 10^9/L (150 - 400), uluslararası normalleştirilmiş oran (INR) 1.38 (0.88 – 1.17), total bilirübin 0.73 mg/dl (< 1.1), albümin 36 g/dl (35 - 52), kreatin 0.61 mg/dl tespit edildi. CHILD A (5), MELD skoru 9 olan hastaya üst gastrointestinal sistem (GİS) endoskopisi yapıldı. Özofagus distal kesimde geçirilmiş ligasyona bağlı skar izleri arasında büyük varisler izlenen hastanın fundusunda büyük boyutlu üzerinde red spotlar izlenen varisler olması nedeni ile fundal varislere yönelik siyanoakrilat tedavisi planlandı. Siyanoakrilat tedavisi sırasında komplikasyon yaşamayan hasta 24 saat sonra taburcu edildi. Taburculuktan 48 saat sonra nonspesifik solunum semptomları nedeniyle gribal semptom düşünülerek semptomatik tedavi başlandığı öğrenildi. Takiplerde şikayetlerin azalmaması üzerine kardiyopulmoner hastalıklar açısından değerlendirildi. Laboratuvar tetkiklerinde lökosit 11x10^9/L, Hgb 10 gr/dl, C reaktif protein 54 mg/L (0 - 5), troponin-T 3.13 pg/ml (3 - 14), D-dimer 540 ng/ml (0 - 243); elektrokardiyogramında sinus taşi-



Resim 1. Pulmoner arterde dens materyal.



Resim 2. Pulmoner arterde dens materyal.

kardisi saptandı. Posterior anterior akciğer grafisi normal idi. Arter kan gazında hipokarbi, hipoksisi olan hastaya pulmoner emboli ön tanısıyla pulmoner bilgisayarlı tomografi (BT) anjiografi çekiminde her iki pulmoner arterin segmental dallarında dens odaklar (Resim 1,2) izlendi. Siyanoakrilat hikayesi olan hasta ön planda siyanoakrilat embolisi olarak yorumlandı. Hastanın akut faz parametrelerinde yükseklik olması nedeni ile eş zamanlı olarak antibiyoterapi ve düşük molekül ağırlıklı heparin başlandı. Takiplerinde 1 hafta içinde şikayetleri gerileyen hasta ayaktan takip edildi. Takiplerinde ek klinik problem izlenmedi. Olgu sunumu için hastadan bilgilendirilmiş onam alındı.

TARTIŞMA

Baveno konsensusu siyanoakrilat tedavisinin gastrik varis kanamalarında kullanılmasını önermektedir (8). Siyanoakrilat tedavisi gastrik varislerin tedavisinde etkin olarak kullanılmaktadır. İşleme bağlı riskler arasında pulmoner embolizm, splenik ve portal ven trombozu, sistemik tromboembo-li, renal arter embolisi, gastrik ülser, mezenterik hematom, bakteriyel peritonitis gibi komplikasyonlar gelişebilir. Siyanoakrilat tedavisi sonrası pulmoner emboli gelişebileceği unutulmamalıdır. Parthiv Amin ve arkadaşları siyanoakrilat tedavisi sonrası gelişen nontrombotik pulmoner emboli olgusunu literatürde sunmuşlardır (9). Gastrik varislere enjekte edilen siyanoakrilat portosistemik yolla nontrombotik pulmoner emboliye neden olabilir (10). Siyanoakrilat polimerizasyonunu engellemek için yağ çözücü özelliği olan lipiodol kullanılmaktadır. Lipiodol embolisi akciğerde parankimal infiltratlar, konsolidasyon ve yüksek çözünürlüklü dens materyal olarak görülebilir (11). Siyanoakrilat tedavisi sonrası gelişen nontrombotik emboliler pıhtılaşmaya değil, pulomer arter ve dallarındaki mekanik obstrüksikogülasyona bağlı olduğundan antikoagülan tedavinin etkisi tartışılmaktadır.

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KAYNAKLAR

1. North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. A prospective multicenter study. N Engl J Med 1988;319:983-9.
2. Garcia-Tsao G, Abraldes JG, Berzigotti A, et al. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. Hepatology 2017;65:310-35.
3. Reverter E, Tandon P, Augustin S, et al. A MELD-based model to determine risk of mortality among patients with acute variceal bleeding. Gastroenterology 2014;146:412-19.
4. Tapper EB, Friderici J, Borman ZA, et al. A multicenter evaluation of adherence to 4 major elements of the Baveno Guidelines and outcomes for patients with acute variceal hemorrhage. J Clin Gastroenterol 2018;52:172-7.
5. Smith JL, Graham DY. Variceal hemorrhage: a critical evaluation of survival analysis. Gastroenterology 1982;82:968-73.
6. de Dombal FT, Clarke JR, Clamp SE, et al. Prognostic factors in upper G.I. bleeding. Endoscopy 1986;18(Suppl 2):6-10.
7. Mishra SR, Sharma BC, Kumar A, Sarin SK. Primary prophylaxis of gastric variceal bleeding comparing cyanoacrylate injection and beta-blockers: a randomized controlled trial. J Hepatol 2011;54:1161-7.
8. Ryou M, Thompson CC. Tissue adhesives: A Review, Techniques in Gastrointestinal Endoscopy 2006;8:33-7.
9. Amin P, Pannu T, Mohamed R, Watson K. Nonthrombotic pulmonary embolism secondary to cyanoacrylate embolization of gastric varices. CMAJ 2022;194:E336-7.
10. Watanabe K, Kimura K, Matsutani S, et al. Portal hemodynamics in patients with gastric varices: a study in 230 patients with esophageal and/or gastric varices using portal vein catheterization. Gastroenterology 1988;95:434-40.
11. Asah D, Raju S, Ghosh S, et al. Nonthrombotic pulmonary embolism from inorganic particulate matter and foreign bodies. Chest 2018;153:1249-65.

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CASE REPORT

Esophageal squamous cell papilloma in a child with cystic fibrosis: A rare incidental endoscopic finding

Kistik fibrozis tanılı bir çocuk hastada saptanan özofageal skuamoz hücreli papillom: Nadir ve insidental bir endoskopik bulgu

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Esophageal squamous cell papilloma is an uncommon epithelial lesion of the esophagus. Epidemiological data regarding esophageal squamous cell papilloma in children is scarce and consists of few case reports. Although the etiology of esophageal squamous cell papilloma remains unclear, chemical/mechanical irritation induced hyper-regenerative response of esophageal mucosa and human papillomavirus infection have been suggested as most probable causes. A case of a 14-year-old girl with cystic fibrosis and chronic dyspepsia had a 0.5 x 0.5 cm sessile, multilobulated, whitish and verrucous polypoid mass close to the lower esophageal sphincter removed. Histologically, a benign squamous papilloma was confirmed. Her dyspeptic symptoms suggestive for gastroesophageal reflux resolved after papilloma removal and anti-acid treatment. Esophageal squamous cell papilloma is an incidental finding at upper endoscopy. Gastroesophageal reflux disease may be responsible for distally localized papillomas. Due to its rarity in childhood, there are not any well-established management and surveillance guidelines. Esophageal squamous cell papilloma should be removed, when possible, because of the ambiguity about its malignant potential.

Key words: Squamous papilloma, esophagus, gastroesophageal reflux, cystic fibrosis, esophagogastroduodenoscopy, dyspepsia

Özofageal skuamoz hücreli papillom, özofagusun nadir görülen bir epitel lezyonudur. Çocuklarda özofageal skuamoz hücreli papillom ile ilgili epidemiyolojik veriler kısıtlıdır ve birkaç vaka raporundan oluşmaktadır. Özofageal skuamoz hücreli papillomun etiyolojisi belirsizliğini korusa da, özofagus mukozasının kimyasal/mekanik tahrişe bağlı gösterdiği hiper-rejeneratif yanıt ve human papillomavirus enfeksiyonu en olası nedenler olarak öne sürülmüştür. Kistik fibrozisli ve kronik dispepsisi olan 14 yaşında bir kız çocuğunda alt özofagus sfinkterine yakın lokalizasyonda 0.5 x 0.5 cm boyutlarında, sesil, multilobüle, beyazımsı ve verrüköz polipoid lezyon çıkarıldı. Histolojik olarak lezyonun benign skuamoz papillom olduğu gösterildi. Hastanın gastroözofageal reflü düşündüren dispeptik semptomları, lezyonun çıkarılması ve anti-asit tedavi sonrası düzeldi. Özofageal skuamoz hücreli papillom, üst endoskopide insidental olarak saptanan bir bulgudur. Distal özofageal yerleşimli papillomlardan gastroözofageal reflü hastalığı sorumlu olabilir. Çocuklukta nadir görülmesi nedeniyle, yönetimi ve takibiyle ilgili rehber önerileri yoktur. Malignite potansiyeli konusundaki belirsizlik nedeniyle mümkün olduğunda çıkarılmalıdırlar.

Anahtar kelimeler: Skuamoz papillom, özofagus, gastroözofageal reflü, kistik fibrozis, özofagogastroduodenoskopi, dispepsi

INTRODUCTION

Esophageal squamous cell papilloma (ESCP) is an uncommon epithelial lesion of the esophagus that was first described in 1959 by Adler (1). ESCPs are incidental lesions found at upper endoscopy or at autopsy and extremely rare in children. Although the etiology of ESCP is still a debate, chronic mucosal inflammation, and human papilloma virus (HPV) have been suggested to be responsible (2). Here, we report a case of a cystic fibrosis patient with chronic dyspepsia whose upper endoscopy revealed an ESCP.

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CASE REPORT

The patient was a 14-year-old girl with the diagnosis of cystic fibrosis. She was suffering from recurrent abdominal pain and had symptoms suggestive for gastroesophageal reflux. Her physical examination was normal. Routine etiologic evaluation for chronic dyspepsia including laboratory and imaging tests were inconclusive. Upper gastrointestinal system endoscopy revealed mild duodenogastric bile reflux, antral hyperemia and a 0.5 x 0.5 cm sessile, multilobulated, whitish and verrucous polypoid mass close to the lower esophageal sphincter (Figure 1). In addition to the removal of the polypoid lesion by cold forceps, routine tissue sampling from other parts of the upper gastrointestinal tract (one biopsy from each part; distal esophagus, corpus, antrum, duodenal bulb and second portion of the duodenum) was performed as suggested by current guidelines. No specific pathological finding was observed in mucosal specimens from esophagus, stomach, and duodenum. *Helicobacter pylori* was negative in gastric and duodenal specimens. Histopathological evaluation of polypectomy material was consistent with squamous papilloma (Figure 2A). Papilloma was composed of non-keratinizing squamous epithelium and no koilocytic or dysplastic change was observed. HPV infection was not detected in the papilloma. Surrounding esophageal mucosa was histologically normal with no inflammatory cell infiltration (Figure 2B). There was also no pathologic eosinophilia in the esophageal, gastric, and duodenal mucosa. Peripheral blood did not show eosinophilia at the time of procedure and the patient never had eosinophilia during her follow-up. Recommendations regarding dietary modification and body positioning were given to the patient and proton pump inhibitor therapy was started. Her symptoms were resolved on the follow up without any additional intervention. Informed consent was obtained from her parents.

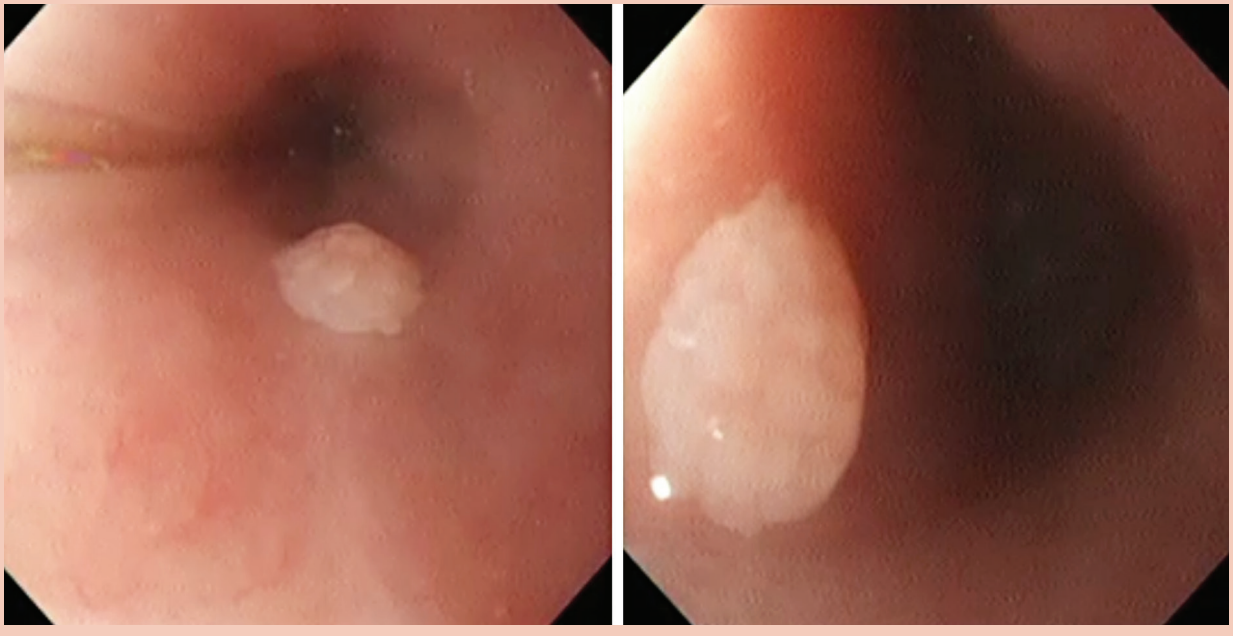

Figure 1. Endoscopic view of squamous papilloma in the distal esophagus of the patient.

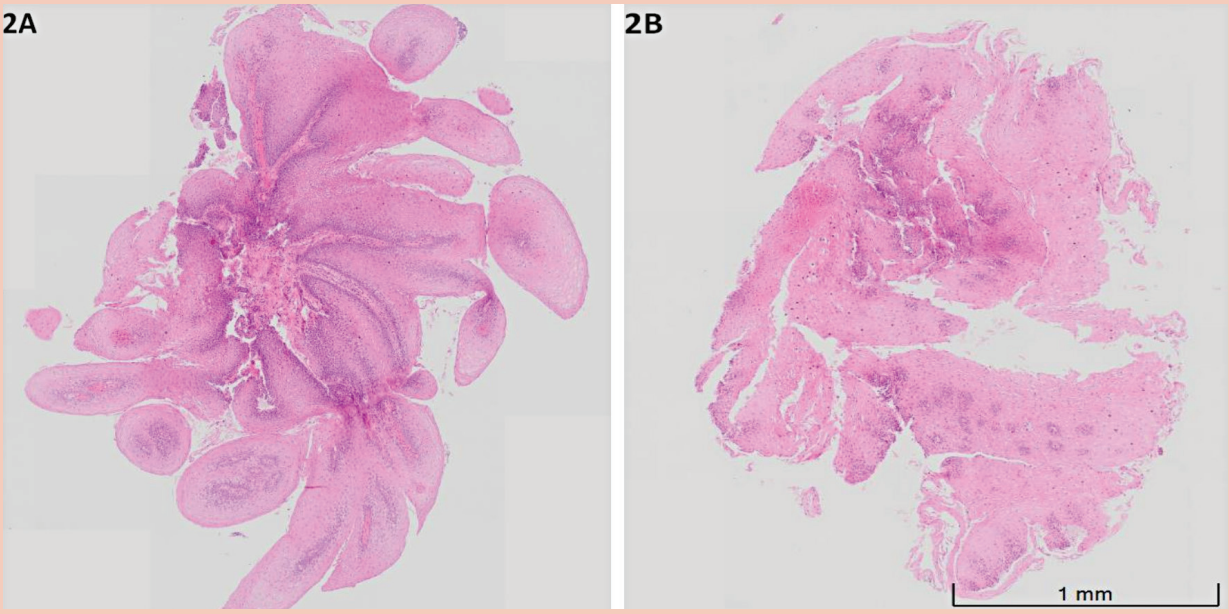

Figure 2. Histopathologic findings of esophageal biopsies. **2A.** Papillary projections lined by squamous epithelium with a fibrovascular core (hematoxylin and eosin, 4x). **2B.** Normal esophageal mucosa surrounding the papilloma (hematoxylin and eosin, 4x).

DISCUSSION

The estimated prevalence of ESCP in adult population was reported to be less than 1% in different series (3). However, epidemiological data regarding ESCP in children is scarce and mainly consists of case reports. The largest case series of ESCP in the pediatric population provided an estimated prevalence of 0.08% through a 15-year study period which approximates to 0.17% in the last 5 years of the study period indicating an increasing prevalence in time (4). The etiology of ESCP remains unclear. Chemical/mechanical irritation induced hyper-regenerative response of esophageal mucosa and HPV infection were held responsible for ESCP (5). Direct mucosal trauma (nasogastric tubes, bougienage for benign stricture, placement of a self-expanding metal stent, variceal sclerotherapy, and chronic food impaction), alcohol consumption, cigarette smoking, previous gastroesophageal surgery, hiatal hernia, and especially gastroesophageal reflux disease (GERD) have been reported to be associated with ESCP in various studies (6). The role of HPV infection in the pathogenesis of ESCP is controversial (7). HPV prevalence in esophageal papillomatous tissue was reported to be 0% - 87% in different studies (8). In the largest pediatric case series, among 12,459 children who required an upper endoscopy only 10 cases were identified with ESCP. None of the cases were tested positive for HPV and the authors concluded that reflex testing for HPV may not be beneficial nor cost effective in children (4). Among possible etiologies, GERD was the most likely cause of squamous papilloma in our patient as she had no risk factors for direct mucosal trauma, no exposure to alcohol or cigarette smoke, no history of abdominal surgery or anatomical anomaly and no histologic finding suggestive for HPV infection. She also had typical symptoms highly suggestive for GERD including heartburn and epigastric pain. In focal dermal hypoplasia, a genetic disorder known to be associated with the formati-

on of squamous papillomas, the esophageal papillomas are hypothesized to be related to the high frequency of severe gastroesophageal reflux starting in infancy (9). A potential association between esophageal papillomas and eosinophilic esophagitis has been recently reported in a pediatric case with focal dermal hypoplasia (10). The patient we present here had a single papilloma in the distal esophagus and did not have eosinophilic esophagitis and dermal hypoplasia. *H. pylori* infection was also suggested as a potential underlying etiology in one study reporting a 10-year-old child with ESCP (11). However, there has been no further evidence indicating an association between *H. pylori* gastritis and ESCP in the pediatric and adult literature. Although her symptomatology was suggestive for a possible *H. pylori* gastritis, our patient's biopsy specimens were negative for *H. pylori*.

There is no pathognomonic finding for ESCP at endoscopic evaluation. However, ESCP usually appears as a well delineated, round, sessile, verrucous-looking lesion, whitish or pinkish in color, with a soft consistency and a smooth or slightly rough surface (5). Although ESCPs are usually solitary and small (2 – 6 mm in diameter), there are reports of giant esophageal papillomas (up to 5 cm) or esophageal papillomatosis (12,13). The localization of the lesion seems to be associated with underlying etiology. While distal esophageal papillomas are likely to be associated with acid reflux, HPV is detected in a variable percentage of mid- and upper esophageal papillomas and in cases of esophageal papillomatosis (2). Lower third of the esophagus has been reported to be the main site for esophageal papilloma localization (6). However, higher prevalence in the middle esophagus was also reported from different centers in Europe and Asia (6,14,15). The results of the largest adult case series from Turkey also pointed the middle esophagus as the most frequent location of ESCPs indicating that there was no relationship between ESCP and GERD (16). However, localization of our patient's papilloma close to the lower esophageal sphincter is another factor pointing a possible role of GERD in etiology. Differential diagnosis of ESCP include glycogenic acanthosis, verrucous border of squamous cell carcinoma, verrucous carcinoma, fibrovascular polyp, inflammatory fibroid polyp, leiomyoma, granular cell tumor, squamous cell carcinoma and malignant melanoma most of which are also very rare clinical conditions in children.

ESCPs are most often asymptomatic and usually diagnosed incidentally at esophagogastroduodenoscopy performed for non-specific symptoms. However, mechanical obstruction due to giant or multiple papillomas can be seen and patients may present with dysphagia in early childhood (17). We cannot directly relate our patient's symptom resolution to ESCP removal as she also received acid suppressive treatment for GERD and duodenogastric bile reflux. Although it is widely accepted as a benign condition, there have been anecdotal reports suggesting an association between ESCP and squamous cell cancer in adults (18). More intensive evaluation of patients with large or multiple squamous papillomas has been proposed as lesions may have malignant potential (19). There has not been any report regarding malignant transformation of ESCP in the pediatric literature.

To the best of our knowledge, this is the first report in pediatric and adult literature regarding ESCP in a cystic fibrosis patient. GERD is a common manifestation in pediatric cystic fibrosis patients with a reported prevalence of 27-81% (20). The relationship between squamous cell lesions and GERD in cystic fibrosis has not been reported in children. However, higher prevalence of GERD in cystic fibrosis patients might be related with development of ESCP in this patient population. The distal localization of the lesion, the absence of other significant mechanical/chemical irritants, negative histologic findings for HPV infection, and higher

prevalence of GER in cystic fibrosis patients than normal population leave GER as the most probable cause for ESCP in our patient. Endoscopic appearance and histology of the adjacent esophageal mucosa were normal in our patient. However, neither normal macroscopic appearance nor the absence of histological abnormalities can sufficiently rule out the presence of GERD in children. It would be optimal if we could perform a pH-impedance testing to evaluate the presence and nature (acidic or alkaline) of gastroesophageal reflux in our patient however, a trial of proton pump inhibitors in the presence of typical symptoms like heartburn and epigastric pain for a definite duration (4 to 8 weeks), as we practiced in our patient, is also a suggested diagnostic test for GERD in children (21). The relief of patient's symptoms with anti-acid treatment and lifestyle modification is suggestive for GERD in our patient.

In conclusion, ESCP is an incidental finding at upper endoscopy. GERD may be responsible for distally localized papillomas. Due to its rarity in childhood, there are not any well-established management and surveillance guidelines. ESCP should be removed, when possible, because of the ambiguity about its malignant potential although no malignancies associated with ESCP was reported in children to date to the best of our knowledge. As upper endoscopy in children is a relatively invasive procedure, awareness of this lesion by the endoscopist is critical for the decision of removal at the time of endoscopy and for avoiding further unnecessary intervention.

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Informed consent: *Written informed consent was obtained from the patient's parents for publication of this case report.*

REFERENCES

1. Adler RH, Carberry DM, Ross CA. Papilloma of the esophagus: association with hiatal hernia. J Thorac Surg 1959;37:625-35.
2. Odze R, Antonioli D, Shocket D, et al. Esophageal squamous papillomas. A clinicopathologic study of 38 lesions and analysis for human papillomavirus by the polymerase chain reaction. Am J Surg Pathol 1993;17:803-12.
3. Szanto I, Szentirmay Z, Banai J, et al. [Squamous papilloma of the esophagus. Clinical and pathological observations based on 172 papillomas in 155 patients]. Orv Hetil 2005;146:547-52.
4. Tou AM, Al-Nimr AO. Esophageal squamous papilloma in children: A single-center case series. J Pediatr Gastroenterol Nutr 2021;72:690-2.
5. Mosca S, Manes G, Monaco R, et al. Squamous papilloma of the esophagus: long-term follow up. J Gastroenterol Hepatol 2001;16:857-61.
6. Takeshita K, Murata S, Mitsufuji S, et al. Clinicopathological characteristics of esophageal squamous papillomas in Japanese patients–with comparison of findings from Western countries. Acta Histochem Cytochem 2006;39:23-30.
7. Syrjanen S, Syrjanen K. HPV-associated benign squamous cell papillomas in the upper aero-digestive tract and their malignant potential. Viruses 2021;13:1624.
8. Rebeuh J, Willot S, Bouron-Dal Soglio D, et al. Esophageal squamous papilloma in children. Endoscopy 2011;43(Suppl 2)UCTN:E256.
9. Nasr Y, Salgado D, El Demellawy D, et al. Esophageal squamous cell papillomatosis arising in focal dermal hypoplasia in a 3-year-old girl. J Pediatr Gastroenterol Nutr 2018;66:e132-e134.
10. Pasman EA, Heifert TA, Nylund CM. Esophageal squamous papillomas with focal dermal hypoplasia and eosinophilic esophagitis. World J Gastroenterol 2017;23:2246-50.
11. Yang Q, Stefanovici C, Mujawar Q, et al. Esophageal squamous papilloma in a pediatric patient with Helicobacter pylori gastritis. Pediatr Dev Pathol 2018;21:105-6.
12. Inomata S, Aoyagi K, Eguchi K, Sakisaka S. Giant esophageal papilloma. Gastrointest Endosc. 2004;60:430.
13. Park SH, Bang BW, Kim HG, Shin YW, Kim L. A case of esophageal squamous papillomatosis. Korean J Intern Med. 2012;27:243.
14. Talamini G, Capelli P, Zamboni G, et al. Alcohol, smoking and papillomavirus infection as risk factors for esophageal squamous-cell papilloma and esophageal squamous-cell carcinoma in Italy. Int J Cancer 2000;86:874-8.

15. Sablich R, Benedetti G, Bignucolo S, Serraino D. Squamous cell papilloma of the esophagus. Report on 35 endoscopic cases. Endoscopy 1988;20:5-7.

16. Ekin N, Bestas R, Cetin A. Clinicopathological characteristics of patients with oesophageal squamous papilloma in Turkey and comparison with the literature data: The largest case series ever reported from Turkey. Int J Clin Pract 2021;75:e14420.

17. Singhal S, Baker RD, Khan A, et al. A rare case of esophageal papilloma due to Human papillomavirus with uncommon presentation of dysphagia in a 2-year-old child. Clin Pediatr (Phila) 2016;55:1168-70.

18. d'Huart MC, Chevaux JB, Bressenot AM, et al. Prevalence of esophageal squamous papilloma (ESP) and associated cancer in northeastern France. Endosc Int Open 2015;3:E101-6.

19. Reynoso J, Davis RE, Daniels WW, et al. Esophageal papillomatosis complicated by squamous cell carcinoma in situ. Dis Esophagus 2004;17:345-7.

20. Bongiovanni A, Manti S, Parisi GF, et al. Focus on gastroesophageal reflux disease in patients with cystic fibrosis. World J Gastroenterol 2020;26:6322-34.

21. Rosen R, Vandenplas Y, Singendonk M, et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr 2018;66:516-54.

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OLGU SUNUMU

İnverte rektal divertikül: Nadir bir kolonoskopik bulgu

Inverted rectal diverticulum: A rare colonoscopic finding

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Kolonda inverted divertikül kolonoskopide nadir görülebilen bir bulgudur. Rektumda inverted divertikül görülmesi ise çok daha nadirdir. Kolonda inverted divertiküller, kolon poliplerine benzerler. Tüm polypoid lezyonlarda dışlanmalıdırlar. Poliplerden ayırt edilmesi, polipektomi yapılması durumunda kolon perforasyonu olma riski nedeniyle çok önemlidir. İnverted rektal divertiküller kolonoskopi sırasında çok nadiren görülürler. Burada rektumda inverted divertikül saptanan nadir görülen bir vakayı sunacağız.

Anahtar kelimeler: İnverted divertikül, rektum, kolonoskopi

Inverted diverticulum in colon is very rare finding on colonoscopy. The appearance of reverse diverticulum in the rectum is much rarer. Inverted diverticulums in the colon are similar to colon polyps. They should be excluded in all polypoid lesions. Differentiation from polyps is very important because of the risk of colonic perforation in case of polypectomy. Inverted rectal diverticulums are very rarely seen during colonoscopy. Here, we will present a rare case of inverted diverticulum in the rectum.

Key words: Inverted diverticulum, rectum, colonoscopy

GİRİŞ

Kolonoskopi sırasında inverte rektal divertikül görülmesi son derece nadir bir bulgudur. Hem divertikül hem de inverte divertikül nadiren rektumda görülür. İnverte divertikül rektal polibe benzer (1). İnverte kolon divertikülünün polipten ayrımı çok önemlidir, çünkü polipektomi sırasında perforasyon gelişme riski oldukça yüksektir (2). Bu nedenle tüm kolon poliplerinin ayırıcı tanısında rektal polipler dahil inverte divertikül de mutlaka dışlanmalıdır. Burada rektal polibe benzeyen oldukça nadir görülen inverte rektal divertikül vakasını sunuyoruz.

OLGU SUNUMU

Yetmiş yaşında kadın hasta kabızlık ve şişkinlik yakınması ile kliniğimize başvurdu. Daha öncesinden bilinen hipertansiyon ve diabetes mellitus öyküsü dışında ek hastalığı yoktu. Fizik muayenede özellik yoktu. Biyokimyasal çalışmalar ve ultrasonografi normaldi. Yaşlı olması nedeniyle tarama amacı ile endoskopi ve kolonoskopi yapıldı. Endoskopide antral gastrit ve bulbit saptandı. Kolonoskopide ise dentat hattan 3-4 cm mesafede sesil rektal polip saptandı. Polip mukozası normaldi. Hava vermekle polip düzleşiyordu. Biyopsi forsepsi ile dokunulduğunda yumuşak ve içi boş

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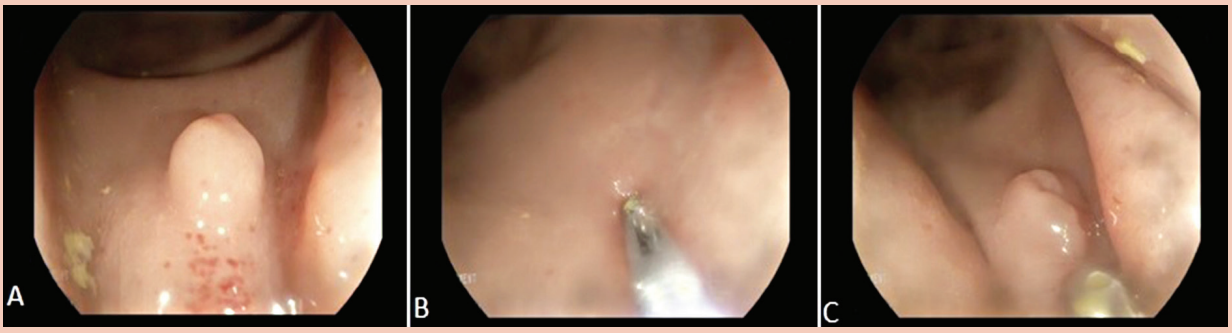

Resim 1. İnverte rektal divertikülün 9-10 mm çapında rektal polip olarak görünümü **A.** Polipoid görünüm, **B.** Biyopsi forsepsi ile dokunma ile düzleşme, **C.** Biyopsi forsepsi ile dokunma ile ortasında çöküntü oluşması.

görünümdeydi. Hava aspirasyonu sonrası polip belirgin hale geliyordu (Resim 1). Diğer kolon segmentlerinde divertiküler hastalık bulgusu yoktu. Hasta inverte rektal divertikül olarak tanı aldı. Rektal ultrasonografi yapıldı, submukozal lezyon saptanmadı. Bu yayınla ilgili olarak hastadan yazılı onam alınmıştır.

TARTIŞMA

Klinik pratikte divertiküler hastalık sıklıkla görülür. Kolon divertikülleri, kolon mukozasının ve submukozanın, kolon kas tabakasından kazanılmış herniasyonlarıdır. Kolonda divertikül formasyonunun gerçek patolojik mekanizması bilinemese de, kolon divertikülleri yaş, diyet, genetik faktörler, bozulmuş motilite, bağırsak mikrobiatası ve inflamasyonu ile ilişkilidir (3). Kolon divertiküllerinin prevalansı yaşam tarzı değişiklikleri ve yaşlanma ile artmaktadır (3,4). Kolon divertikülü olan insanların çoğu asemptomatiktir. Kolon divertikülü ilişkili semptom gelişmesi durumunda divertiküler hastalıktan söz edilir. Vakaların yaklaşık %50'si 60 yaş üzeridir (3). Kolon divertikülleri sıklıkla sigmoid kolon ve inen kolonda lokalizedir, rektal divertiküller son derece nadir olup kolon divertiküler hastalığının %1'inden azını oluşturur (5,6). Rektal divertiküllerin büyük çoğunluğu insidental olarak bulunur. Kanama, divertikülit, perforasyon, abse, fistül oluşumu, stenoz, inverte divertiküloz ve rektal prolapsus bu lezyonlara bağlı olarak gelişebilir (2,7,8-10). İnverte divertikül, divertiküllerle ilişkili nadir bir durumdur. İnverte kolon divertikülü çok nadir olup kolonoskopi sırasında yaklaşık %0.7 oranında gözlenir (11). Divertikül tepesinin lümene prolapsusu ile karakterize olup makroskobik görünüm olarak polip benzeri görünüme sebep olabilir (8,10,11).

Rektal divertiküller çok nadirdir. Rektumdaki kasların intraluminal basınca direnç oluşturması, düşük intraluminal basınç ve yavaş peristaltik hareketler rektal divertikülerinin nadir olmasının nedeni olabilir (12). Rektal divertiküllerin nadir olması nedeniyle inverte rektal divertikülleri son derece nadirdir. Literatürde sadece birkaç vaka vardır (6,9).

Endoskopi sırasında inverte divertikülleri, poliplerden ayırt etmede bazı ipuçları vardır. Hava vermek veya su jeti ile müdahale inverte divertikülün eversiyonuna (düzleşmesine) neden olur. Biyopsi forsepsi ile veya başka bir endoskopik enstrümanla dokunma ile lezyon, yumuşak, çöküntülü veya düzleşmiş olarak görülür. Yüzeyindeki mukoza normal olarak izlenir. Dar band görüntülemede veya kromoendoskopi ile konsatrik halkalar şek-

linde izlenen Aurora halkaları görülür. Bazı vakalarda baryumlu kolon grafisi, bilgisayarlı tomografi veya endoskopik ultrasonografi faydalı olabilir (2,7,11-14).

İnverte rektal divertikül, polipoid bir lezyon şeklinde görülür. Biyopsi veya polipektomi perforasyon gibi ciddi komplikasyonlara yol açabilir. Tanı için bizim vakamızda olduğu gibi bazı ipuçları vardır. Endoskopik ultrasonografi veya transrektal ultrasonografinin inverte rektal divertikül tanısında önemli yöntemler olabileceğini düşünüyoruz. Bizim vakamızda; ortasında dokunmakla çöküntü olan, yüzeyinde normal mukoza olan polipoid lezyon olarak görüntüledik. Hava vermekle polip küçülüyor ve kayboluyordu. Biyopsi forsepsi ile hafifçe dokunma ile lezyon düzleşiyordu. Hava aspirasyonu ile polip boyutları artıyordu. Her ne kadar lezyon karakteristik olarak olarak inverte divertikül bulguları gösteriyorsa da endoskoik ultrasonografi ile de değerlendirdik. Endoskopik ultrasonografi bulguları da inverte rektal divertikül ile uyumluydu.

Sonuç olarak inverte rektal divertikül kolonoskopi sırasında son derece nadir görülen bir bulgudur. Bizim vakamız da göstermiştir ki, çok nadir olsa bile, polipektomi veya biyopsi ile perforasyon gibi ciddi komplikasyonlara neden olabileceğinden rektum polipoid lezyonlarının ayırıcı tanısında inverte divertikül yer almalıdır.

Çıkar Çatışması: *Tüm yazarlar, bu yayınla ilgili çıkar çatışması olmadığını beyan etmektedir.*

Tüm yazarlar yayının son versiyonunu okumuş ve onaylamıştır.

KAYNAKLAR

1. Paoluzi OA, Tosti C, Andrei F, Stroppa I, PalloneF. Look out before polypectomy in patients with diverticular disease – a case of a large, inverted diverticulum of the colon resembling a pedunculated polyp. Can J Gastroenterol 2010;24:61-3.
2. Cappell MS. The water jet deformation sign: a novel provocative colonoscopic maneuver to help diagnose an inverted colonic diverticulum. South Med J 2009;102:295-8.
3. Feuerstein JD, Falchuk KR. Diverticulosis and Diverticulitis. Mayo Clin Proc 2016;91:1094-104.
4. Tursi A, Papagrigoriadis S. Review article: the current and evolving treatment of colonic diverticular disease. Aliment Pharmacol Ther 2009;30:532-46.
5. Na SK, Jung HK, Shim KN, Jung SA, Chung SS. Iatrogenic rectal diverticulum with pelvic-floor dysfunction in patients after a procedure for a prolapsed hemorrhoid. Ann Coloproctol 2014;30:50-3.
6. Walstad PM, Sahibzada AR. Diverticula of the rectum. Am J Surg 1968;116:937-9.
7. Yusuf SI, Grant C. Inverted colonic diverticulum: a rare finding in a common condition? Gastrointest Endosc 2000;52:111-5.
8. Peixoto P, Amaro P, Sadio A, et al. A strange duodenal lesion. Rev Esp Enferm Dig 2010;102:563-5.
9. Chen CW, Jao SW, Lai HJ, Chiu YC, Kang JC. Isolated rectal diverticulum complicating with rectal prolapse and outlet obstruction: case report. World J Gastroenterol 2005;11:7697-9.
10. Ladas SD, Prigouris SP, Pantelidaki C, Raptis A. Endoscopic removal of inverted sigmoid diverticulum–is it a dangerous procedure? Endoscopy 1989;21:243-4.
11. Sáenz R, Kinney TP, Santander R, Yazigi R, Navarrete C, Gobelet J, Waye J. Divertículo colónico invertido: un hallazgo endoscópico infrecuente [Inverted colonic diverticula: an uncommon endoscopic finding]. Gastroenterol Hepatol 2008;31:285-8.
12. Fagundes RB, Motta GL, Fontana K, Fonseca CB, Binato M. Rectal diverticulum. ABCD Arq Bras Cir Dig 2011;24:339-41.
13. Merino R, Kinney T, Santander R, et al. Inverted colonic diverticulum: an infrequent and dangerous endoscopic finding [abstract]. Gastrointest Endosc 2005;61:AB257.
14. Share MD, Avila A, Dry SM, Share EJ. Aurora rings: a novel endoscopic finding to distinguish inverted colonic diverticula from colon polyps. Gastointest Endosc 2013;77:308-12.

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OLGU SUNUMU

Akut fosfat nefropatisi: İki olgu sunumu ve literatürün gözden geçirilmesi

Acute phosphate nephropathy: Report of two cases and review of the literature

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Fosfat nefropatisi; fosfat kristallerinin renal tübülleri etkilemesiyle oluşan önce akut, sonrasında kronik böbrek hasarı ile seyreden bir klinik tablodur. Kolonoskopi birçok endikasyonla sık olarak kullanılan bir yöntemdir. İşlem öncesinde hazırlık amaçlı kullanılan oral fosfat içerikli pürgatifler bu tablonun gelişimine yol açmaktadır. Nefropati gelişme riski yüksek olan gruplarda, fosfat içermeyen pürgatiflerin kullanılması önerilmektedir. Fosfat nefropatisi tedavisinde temel yaklaşım hasarın gelişimini önlemektir. Biz bu yazımızda, oral sodyum fosfat ile kolonoskopi yapılan ve işlem sonrası fosfat nefropatisi ile uyumlu akut böbrek hasarı gelişen iki vakayı sunmayı amaçladık.

Anahtar kelimeler: Fosfat nefropatisi, kolonoskopi, pürgatif

Phosphate nephropathy is a clinical picture that occurs with the effect of phosphate crystals on the renal tubules, which first progresses with acute and then chronic kidney damage. Colonoscopy is a method for direct examination of the colon performed with various indications. Oral phosphate-containing purgatives used for preparatory purposes before this procedure lead to the development of this disease. In groups with a high risk of developing nephropathy, phosphate-free purgatives are recommended during the preparation for the colonoscopy. The principal treatment for phosphate nephropathy is to prevent the development of damage. In this article, we aimed to present two cases of phosphate nephropathy who underwent colonoscopy for different indications and that oral phosphate was used during the preparation for the procedure.

Key words: Phosphate nephropathy, colonoscopy, purgative

GİRİŞ

Akut fosfat nefropatisi, fosfat kristallerinin renal tübülleri etkilemesi sonrası gelişen bir böbrek hasarı şeklidir (1). Kolonoskopi öncesi bağırsak temizliği için kullanılan oral sodyum fosfat içeren pürgatiflere bağlı gelişir (2). Hastalığın patogenezinde çeşitli hipotezler olmakla beraber, serum fosfat düzeyinde hızlı artışa eşlik eden sodyum fosfatın laksatif özelliğine bağlı volüm deplesyonu temel rol oynar. İntratübüler fosfat konsantrasyonunun artması lüminal obstrüksiyona, direkt tübüler epitel hasarına ve immün yanıtın aktivasyonuna yol açan kalsiyum fosfat tuzlarının çökmesine ve dokuda birikmesine neden olur. Kesin tanı böbrek biyopsisinde renal tübüllerde kalsinozis gözlenmesiyle konulur (3). Biz burada geri dönüşümsüz böbrek hasarına yol açabilen fakat kolaylıkla gözden kaçabilen iki fosfat nefropatisi vakasını sunuyoruz.

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OLGU SUNUMU

Olgu 1

Altmış dört yaşında kadın hastaya, üç gün önce kabızlık nedeni ile dış merkezde oral sodyum fosfatlı hazırlık sonrasında kolonoskopi yapılmıştı. İşlem öncesi kreatinin değeri normal sınırlarda (0.8 mg/dl) olan hasta, işlem sonrası 10. günde tetkik sonuçlarını göstermek üzere dahiliye polikliniğine başvurduğunda kreatinin 5.51 mg/dl saptanıp akut böbrek hasarı (ABH) ön tanısı ile nefroloji kliniğine yatırıldı. Özgeçmişinde 10 yıldır hipertansiyon öyküsü olan hasta ramipril 5 mg ve nebivolol 5 mg kullanmaktaydı. Fizik muayenesinde özellik saptanmadı. Tetkiklerinde; üre 90 mg/dl, kreatinin 5.51 mg/dl, sodyum 130 mmol/L, potasyum 4.06 mmol/L, fosfor 6.17 mg/dl, 24 saatlik idrarda 500 mg/gün protein saptandı. ELİSA negatif, otoimmün serolojik belirteçleri (anti nükleer antikor, anti-dsDNA antikoru, antinötrofilik sitoplazmik antikorları) negatifti. Üriner ultrasonografide böbrek boyutları normal olup patoloji saptanmadı. Göz dibi muayenesinde retinopati yoktu. Hastaya intravenöz hidrasyon yapıldı. Ramipril kesilerek amlodipin ve nebivolol ile tansiyon kontrolü sağlandı. Takiplerinde kreatinin değeri 2 mg/dl'ye kadar geriledi. Hastaya böbrek biyopsisi yapıldı. Biyopside tübül lümeninde kalsifikasyon, arterlerde hiperplastik değişiklikler, fokal interstisyel fibrozis, tübüler atrofi ve segmental skleroz saptandı. Hastaya etiyoloji açıklanarak öneriler ile taburcu edildi ve nefroloji poliklinik takibine alındı. Hastadan bilgilendirilmiş onam formu alınmıştır.

Olgu 2

Yetmiş sekiz yaşında erkek hastaya, tarama amaçlı kolonoskopi yapılmış ve kolonoskopi hazırlığı sırasında sodyum fosfatlı lavman kullanılmıştı. İşlem öncesinde kreatinin değeri normal aralıkta saptanan hasta işlem sonrasında 7. günde kreatinin 2 mg/dl saptanması üzerine ABH tanısı ile yatırıldı. Özgeçmişinde 20 yıldır hipertansiyon tanısı olduğu, karvedilol 12.5 mg ve perindopril 5 mg kullandığı öğrenildi. Fizik muayenesinde patoloji saptanmadı. Tetkiklerinde; üre 74 mg/dl, kreatinin 1.91 mg/dl, sodyum 137 mmol/L, potasyum 4.68 mmol/L, fosfor 7.2 mg/dl görüldü. Otoimmün serolojik belirteçleri ve ELİSA negatif saptandı, idrar tetkikinde hematüri ve proteinüri saptanmadı. Üriner ultrasonografide böbrek boyutları ve parankim kalınlığı normal saptandı. Takiplerinde renal fonksiyon testleri aynı düzeyde seyreden hastaya böbrek biyopsisi yapıldı. Biyopsi sonucunda intratübüler kalsifikasyon gözlendi. Hasta fosfat nefropatisi tanısı ile nefroloji poliklinik takibine alındı. Hastadan bilgilendirilmiş onam formu alınmıştır.

TARTIŞMA

Sunduğumuz iki hastanın da yaşları 55'in üzerinde olup, bilinen hipertansiyon tanıları ve antihipertansif ilaç kullanımları vardı. Kolonoskopi öncesinde bakılan kreatinin değerleri normaldi ve kolonoskopi hazırlıkları oral fosfatlı pürgatif ile yapılmıştı. İşlem sonrasında bakılan rutin polikliniK kontrolünde kreatinin yüksekliği saptanmış olup hastalar asemptomatikti. Yatış esnasında hastaların hidrasyon ile renal fonksiyon testlerinde tam düzelme saptanmadı ve hemodiyaliz ihtiyacı olmadı. İzlemde, ABH tablosu devam eden hastalarımıza kesin tanı amaçlı böbrek biyopsisi yapıldı. Biyopsi sonucunda fosfat nefropatisi tanısı alan hastalarımızın takipleri nefroloji polikliniğinde devam etmekte olup, kreatinin yükseklikleri sebat etmektedir.

Genellikle kolonoskopi yapılacak olan hastalara işlemden 12-24 saat önceden başlayarak iki kez 45 ml'lik oral fosfatlı lavman verilmektedir (2). Lavman sırasında intestinal emilim olmakta ve geçici hiperfosfatemi ile hipokalsemi hemen her hastada görülmektedir. Bunun yanında semptomatik hipernatremi, hiponatremi, hipokalemi, yüksek anyon açıklı metabolik asidoz ve ABH görülebilmektedir (4).

Fosfatın büyük çoğunluğu proksimal tübüllerden az miktarı distal tübüllerden emilmektedir. Günlük fosfor ihtiyacımız 1 gr/gün olmasına rağmen, kolonoskopi hazırlığı sırasında kullanılan fosfat içerikli pürgatifler bu miktarın çok üzerindedir (11.6 gr). Yüksek miktarda fosfat alımı yanında, laksatif özelliğine bağlı volüm deplesyonu fosfat nefropatisinin temelini oluşturmaktadır (5).

Fosfatlı pürgatif kullanımının yaygınlaşması sonrasında çok sayıda akut fosfat nefropatisi vakası bildirilmiştir. Colombia Üniversitesi'nde 2000-2004 yılları arasında yapılan 7349 böbrek biyopsisinin 31'inde nefrokalsinozis saptanmış olup bunların da 21'inde oral fosfat kullanımının sorumlu olduğu bildirilmiştir (6). Yayınlanan bir metaanalizde; polietilen glikol, sodyum fosfat ve sodyum bisülfat kolonoskopi hazırlığındaki etkinlikleri açısından karşılaştırılmış ve sodyum fosfat ile yapılan hazırlığın daha yeterli olduğu sonucuna varılmıştır. Sodyum fosfatın kardiyovasküler ve renal hastalığı olanlarda dikkatli kullanılması söylenmiş, fakat bu gruplarda komplikasyon riskini gösteren yeterli çalışma olmadığı belirtilmiştir (7).

2005 yılında yayınlanmış bir çalışmada oral fosfatlı lavman kullanımı sonrası ABH gelişen 21 hasta incelenmiştir. Bu hastaların %81'i kadın, %81'i beyaz ırk, %76'sında hipertansiyon olduğu görülmüştür. Hipertansiyonu olanların da %80'inin anjiotensin dönüştürücü enzim inhibitörü (ACE-İ) veya anjiotensin reseptör blokeri (ARB) kullandığı belirtilmiştir. Bu çalışmaya göre; ileri yaş, kadın cinsiyet, beyaz ırk, hipertansiyon, ilaç kullanımı gibi faktörlerin fosfat nefropatisi gelişme riskini arttırdığı öne sürülmüştür (6). 2011 yılında yayınlanan Aydınlı ve ark. tarafından yapılan çalışmada, kolonoskopi yapılan 54 hasta incelenmiş, işlem öncesi kreatinin düzeyleri normal olan hastaların %46.3'ünde oral fosfatlı kolonoskopi hazırlığı sonrası serum fosforunun yükseldiği saptanmıştır. ACE-İ veya ARB kullanmakta olan 10 hastada fosfor artışı bu ilaçları kullanmayanlara göre anlamlı yüksek saptanmıştır. Ellibeş yaş üzerindeki hastalardaki kreatinin ve kan basıncı değerlerinin diğerlerine göre de daha yüksek olduğu bildirilmiştir (8). Bizim 2 hastamız da ileri yaşta olup hipertansiyon nedeni ile ACE-İ kullanmakta idiler ve serum fosfor düzeyleri yüksekti.

Kanada'da yapılan bir çalışmada; yeterli hidrate edilmeyen, komorbiditesi ve ilaç kullanımı fazla olan hastalarda oral fosfat kullanımının daha fazla yan etki oluşturduğu, ayrıca oral fosfatın yüksek dozda kullanımının, hiperfosfatemiye bağlı gelişebilecek komplikasyon riskini arttırdığı gösterilmiştir (9). 256 hastalık bir çalışmada ise yüksek doz ile düşük doz oral fosfat güvenlik, etki ve tolerans açısından karşılaştırılmıştır. Yüksek doz fosfat kullananların kolon temizliğinin daha iyi yapıldığı fakat hasta tolerasının azaldığı ve işlem sonrası hiperfosfatemiye bağlı yan etkilere daha fazla rastlandığı gösterilmiştir (10).

Sonuç olarak, kolonoskopi farklı branş hekimlerince çeşitli endikasyonlar ile istenen yaygın bir tarama ve tanı yöntemidir. Fosfat nefropatisi geliştikten sonra spesifik bir tedavi yöntemi olmadığı için, en önemli strateji hastalığın gelişimini önlemektir. Oral sodyum fosfat kullanımının kolonoskopi hazırlığı açısından daha etkili olduğu bildirilmekle birlikte fosfatlı lavman kullanımının bazı gruplarda riskli olduğu gösterilmiştir. Kronik böbrek hastalığı, ileri yaş, kadın cinsiyet, hipertansiyon, diyabetes mellitus, konjestif kalp yetmezliği, ACE-İ/ARB kullanımı risk faktörleridir (6). Bu gruplarda, kolonoskopi hazırlığının fosfatsız lavman ile yapılması önerilmektedir. Hazırlık yapılırken de yeterli hidrasyonun sağlanması ve işlem öncesinde ACE-İ, ARB ve diüretiklerin kesilmesi, işlemden sonraki günlerde kreatinin kontrolü yapılması uygundur.

Çıkar Çatışması: *Tüm yazarlar, bu yayınla ilgili çıkar çatışması olmadığını beyan ederler.*

KAYNAKLAR

1. Balaban DH. Guidelines for the safe and effective use of sodium phosphate solution for bowel cleansing prior to colonoscopy. Gastroenterol Nurs 2008;31:327-34.
2. Gumurdulu Y, Serin E, Ozer B, Gokcel A, Boyacioglu S. Age as a predictor of hyperphosphatemia after oral phosphosoda administration for colon preparation. J Gastroenterol Hepatol 2004;19:68-72.
3. Markowitz GS, Nasr SH, Klein P, et al. Renal failure due to acute nephrocalcinosis following oral sodium phosphate bowel cleansing. Hum Pathol 2004;35:675-84.
4. Jimenez C, Gagel RF. Disorders Affecting Multipl Endocrine Systems. In: Fauci AS, Braunweld E, Kasper DL (eds.), Harrison's Principles of Internal Medicine. 17th ed. New York: McGraw-Hill Co; 2013. p.2371-2.
5. Asplin JR, Mandel NS, Coe FL. Evidence of calcium phosphate supersaturation in the loop of Henle. Am J Physiol 1996;270:F604-F13.
6. Markowitz GS, Stokes MB, Radhakrishnan J, D'Agati VD. Acute phosphate nephropathy following oral sodium phosphate bowel purgative: An underrecognized cause of chronic renal failure. J Am Soc Nephrol 2005;16:3389-96.
7. Tan JJ, Tjandra JJ. Which is the optimal bowel preparation for colonoscopy-a meta-analysis. Colorectal Dis. 2006;8:247-58.
8. Aydınlı F, Ahıshalı E, Dolapçıoğlu C, Uygur MM, Dabak R. Evaluation of the safety and afficacy of colonoscopy preparation by sodium phosphate in patients with normal creatinin values. J Kartal TR 2011;22:113-20.
9. Hookey LC, Depew WT, Vanner S. The safety profile of oral sodium phosphate for colonic cleansing before colonoscopy in adults. Gastrointest Endosc 2002;56:895-902.
10. Barclay RL. Safety, efficacy, and patient tolerance of a three-dose regimen of orally administered aqueous sodium phosphate for colonic cleansing before colonoscopy. Gastrointest Endosc 2004;60:527-33.