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Describing the heterotopic gastric mucosa (inlet patch) located in the esophagus with cases

Olgular eşliğinde özofagusta lokalize heterotopik gastrik mukozayı (inlet patch) tanıyalım

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Abstract

Aim: The inlet patch, also called as the heterotopic gastric mucosa, is often located in proximal esophagus and is generally asymptomatic. These lesions are rarely polypoid and mostly have a patchy pattern. In the literature, there are only few cases of inlet patches that show a malignant progression following a metaplasia- dysplasia- adenocarcinoma sequence. In our study, we aimed to present the endoscopic and morphological features of our case series.

Methods: The study, which was conducted in two clinics, included the inlet patch cases diagnosed in esophagus biopsy materials between 2016 and 2019. The slides and the demographic data of the cases were re-analyzed.

Results: Among 4190 cases whose esophageal biopsies were examined, 63 inlet patches (1.5%) were diagnosed. Thirty four cases were male and 29 were female. Age range was 16-82 years. The cases were mostly located in proximal esophagus and the size of the lesions ranged between 0.2-3.5 cm. One of the four cases with polypoid appearance was microscopically diagnosed as a hyperplastic polyp. The most common gastric type epithelium was the oxyntic type. Helicobacter pylori was observed in four cases, and intestinal metaplasia and low-grade dysplasia were observed in one. No malignancy was diagnosed in our series.

Conclusion: Although benign, the inlet patch is significant due to its risk of progression to malignancy. Thus, obtaining biopsies from each lesion endoscopically considered as inlet patch is recommended. This will help determine the precise incidence of the inlet patch and more importantly, identify neoplasia earlier.

Keywords: Inlet patch, Esophagus, Polyp, Dysplasia

Öz

Amaç: Heterotopik gastrik mukoza olarak da adlandırılan inlet patch sıklıkla proksimal özofagusta lokalizedir. Genellikle asemptomatiktir. Polipoid yapıda seyrek saptanan bu lezyonlar, sıklıkla endoskopik olarak yamasal tarzda izlenir. Literatürde metaplazi-displazi-adenokarsinom sekansını takiben malign progresyon gösterebilen az sayıda inlet patch olguları yer almaktadır. Çalışmamızda inlet patch tanılı olgu serimizi endoskopik ve morfolojik özellikleriyle sunmayı amaçladık.

Yöntemler: Çalışma iki klinik üzerinden yürütüldü. Her iki klinikte 2016-2019 yılları arasında özofagusa ait biyopsi materyalleri içinde inlet patch tanısı alan olgular dahil edildi. Olgulara ait preparatlar ve demografik bilgiler tekrar gözden geçirildi.

Bulgular: Özofagus biyopsisi incelenen 4190 olgu içinde 63 olgu (%1,5) inlet patch tanısı aldı. Olguların 34'ü erkek, 29'u kadındı. Olguların yaşları 16 ile 82 arasında değişmekteydi. En sık görüldüğü yaş aralığı 30-50 yaşdı. En sık proksimal özofagusta lokalizeydi (59 olgu). Lezyonların boyutları 0,2-3,5 cm arasında değişmekteydi. Polipoid görünümdeki dört olgudan biri histopatolojik olarak hiperplastik polip tanısı aldı. En sık gözlenen gastrik tip epitel oksintik tipti (29 olgu). Helikobakter pilori dört olguda izlendi. Olgulardan birinde intestinal metaplazi ve düşük dereceli displazi saptandı. Malignite tanısı olan olgumuz yoktu.

Sonuç: Benign bir lezyon olmasına rağmen maligniteye dönüşüm riski nedeniyle inlet patch olgularının önemsenmesi gerekmektedir. Bu nedenle endoskopik incelemede inlet patch olarak saptanan her lezyondan biyopsi alınması, özellikle büyük boyut, ülser gibi farklı klinik tablo sergileyen olguların da yakın klinik takiplerinin yapılması bizlere inlet patchin gerçekte görülme sıklığının ne olduğunu ve en önemlisi gelişen neoplazilerin erken dönemde saptanmasına olanak sağlayacaktır.

Anahtar kelimeler: İnlet patch, Özofagus, Polip, Displazi

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Introduction

Heterotopic gastric mucosa can be observed anywhere in the gastrointestinal tract, as well as the gallbladder, abdomen, and liver [1,2]. The most common location in the gastrointestinal tract is the proximal esophagus, where it is called the inlet patch [3,4]. The lesions located just below the upper esophageal sphincter can be missed during endoscopic examination [5]. They are either patchy or circular, and polyps are rarely seen [3,6]. Though mostly asymptomatic, the inlet patch can also manifest clinically with spasm, web, esophagitis, ulceration, bleeding or extraesophageal fistula due to acid secretion from the gastric mucosa [7,8]. It may occasionally exhibit malignant progression following the metaplasia-dysplasia-adenocarcinoma sequence as in other parts of the gastrointestinal tract [9,10]. In our study, we aimed to present a series of our cases of inlet patch along with their clinicopathological findings.

Materials and methods

Our retrospective study was conducted in two centers, and included the cases diagnosed with inlet patch between 2016 and 2019. In addition to the demographic characteristics (age and gender), the endoscopic findings and pathological data of the cases (hematoxylin & eosin (H&E), histochemistry and immunohistochemistry results) were reviewed. The location of the lesion in the esophagus (upper, middle, and lower), number (single or multiple), size, appearance (patchy or polypoid) of the lesion, type of gastric epithelium, as well as concomitant inflammation, Helicobacter pylori (HP) positivity, intestinal metaplasia and dysplasia were noted. The gastric type of epithelium detected in the inlet patch biopsies were classified into three main groups as oxyntic, antral, and mixed type. For the detection of HP, Giemsa and Warthin–Starry as well as H&E stained slides were reviewed. Sydney Classification was performed for the gastric biopsies taken simultaneously with esophageal biopsies.

This study was approved by University of Health Sciences, Okmeydani Education and Research Hospital Ethic Committee, by the number 1054 on 19.11.2019.

Statistical analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. While evaluating the study data, Pearson Chi-Square test, Fisher Freeman Halton test and Fisher's Exact test were used to compare the descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) as well as the qualitative data. $P<0.05$ was considered significant.

Results

During the study, among 4190 esophageal biopsies, 63 (1.5%) were diagnosed with inlet patch, 34 (53.9%) of which were males. The ages of the patients ranged between 16 and 82 years, with mean of 42.83 (13.44) years. In the study, which also included the pediatric age group, the inlet patch was most common between 30-50 years of age (30-40 years old (n=18), 40-50 years old (n=16)). Of the lesions detected endoscopically, 59 (93.6%) were located in the proximal esophagus, three (4.7%) in the middle esophagus and one (1.5%) in the distal esophagus. The sizes of the lesions ranged between 0.2-3.5 cm. While 42 cases (66.7%) were 0.5 cm or less, 17 cases (27%) had a size of 1 cm or more. In 54 (85.7%) of the cases, there was a single focus, while 9 (14.3%) had multiple foci. In 7 of the cases with more than one focus, the size was 0.5 cm or below. In 59 cases (93.6%), the lesions were patchy, while in four, a polypoid structure was observed. The size of one of these cases was 1 cm (Figure 1).

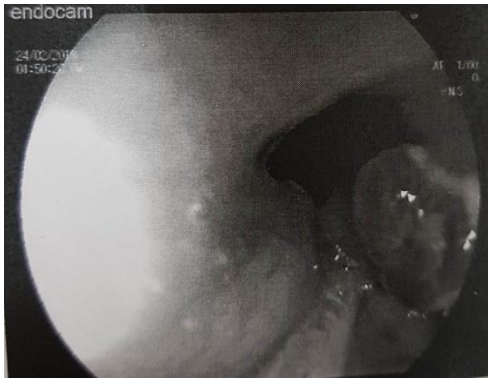

Figure 1: Endoscopic view of esophageal polyp which is located at tenth cm of esophagus

Histopathologically, oxyntic type of epithelium was observed in 29 cases (46.1%), the antral type, in 24 cases (38.1%) and the mixed type, in 10 cases (15.8%). Chronic inflammation was found in 32 cases (50.8%), while in 22 cases (34.9%) active inflammation was also present. Nine patients (14.3%) had no signs of inflammation. HP was detected in four cases (6.3%). While one of these cases had chronic inflammation, three had signs of chronic active inflammation. Histopathological examination of one of the lesions with a polypoid appearance was reported as a hyperplastic polyp (Figure 2). Other lesions had mucosal edema leading to polypoid appearance. Intestinal metaplasia and low-grade dysplasia were detected in one of the cases (Figure 3, 4) which was a single, 0.5 cm lesion found in an 82-year-old patient. This case is still under follow up.

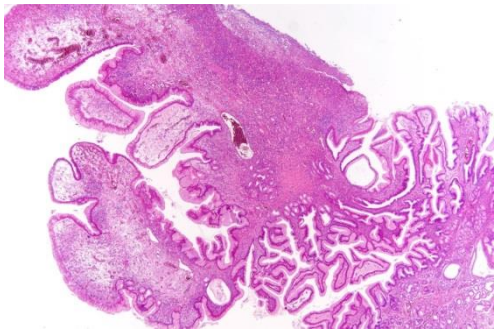

Figure 2: Hyperplastic polyp (H&E x20)

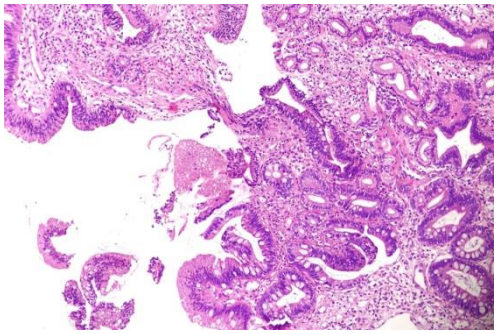

Figure 3: Intestinal metaplasia and low grade dysplasia in inlet patch focus (H&E x200)

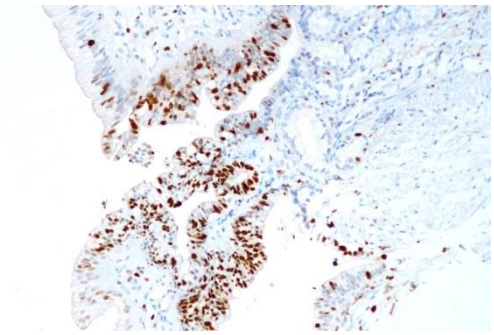

Figure 4: Dysplastic epithelium with Ki-67 proliferative activity (x200)

Chronic inflammation was found in 25 cases (39.6%), chronic active inflammation was detected in 24 cases (38.1%), intestinal metaplasia was found in 7 cases (11.1%), HP was found in 29 cases (46.1%) and 1 case (1.5%) had low grade dysplasia in gastric mucosa. HP was observed in the inlet patch foci as well as the stomach in four patients. With respect to gender, the age distribution of the cases, lesion sizes, gastric epithelium types, inlet patch gastric HP and inflammation were not significantly different (P=0.100, P=0.340, P=0.261, P=0.613, P=0.346).

No statistically significant relationship was found between the presence of HP, gastric epithelial types of the inlet patch foci and the size of lesions (P=0.463, P=0.062). Among cases where HP was and was not observed in the inlet patch foci, there was no significant difference regarding findings of chronic inflammation, chronic active inflammation, intestinal metaplasia, and dysplasia in stomach (P=0.239).

Demographic features and endoscopic findings are presented in Table 1 and histopathological findings, in Table 2.

Table 1: Demographic and endoscopic characteristics of the patients

	n (%)
Age (years)	42.83 (13.44) (min 16- max 82)
Gender	
Female	29 (46.1%)
Male	34 (53.9%)
Location	
Proximal esophagus	59 (93.6%)
Middle esophagus	3 (4.7%)
Lower esophagus	1 (1.5%)
Size	
≥5 mm	42 (66.7%)
6-9 mm	4 (6.3%)
≤10 mm	17 (27%)
Number of foci	
Single	54 (85.7%)
Multiple	9 (14.3%)
Appearance	
Patchy	59 (93.6%)
Polypoid	4 (6.3%)

Table 2: Histopathological findings in heterotopic gastric mucosa and accompanying gastric mucosa

Findings	n (%)
Cell type (heterotopic gastric mucosa)	
Oxyntic	29 (46.1%)
Antral	24 (38.1%)
Mixed	10 (15.8%)
Histopathological findings (heterotopic gastric mucosa)	
Chronic inflammation	32 (50.7%)
Chronic active inflammation	22 (34.9%)
Helicobacter pylori	4 (6.3%)
Intestinal metaplasia	1 (1.5%)
Dysplasia	1 (1.5%)
Histopathological findings (accompanying gastric mucosa)	
Chronic inflammation	25 (39.6%)
Chronic active inflammation	24 (38.1%)
Helicobacter pylori	29 (46.1%)
Intestinal metaplasia	7 (11.1%)
Dysplasia	1 (1.5%)

Discussion

Pathogenesis of the inlet patch is still not fully understood [8]. The most accepted hypothesis is that it is a congenital anomaly which results from the incomplete transformation of columnar epithelium into the squamous epithelium during embryonic development. Inlet patch is generally asymptomatic and detected incidentally during endoscopic examination [8]. Since most of the studies are retrospective, there is no exact data on its frequency. Rates ranging from 0.1% to 18% are reported in the literature [7,8,11]. The rate increases even more in autopsies [7]. It is often difficult to notice due to the contraction of the upper esophageal sphincter, and the attention of the endoscopist also affects its detection [3,5]. In our study, patients diagnosed with inlet patch were incidentally detected during endoscopic examination. Our study was retrospective, and the inlet patch rate was compatible with the literature.

Inlet patch can be detected at any age including the pediatric group. While the incidence in the pediatric group is between 0.1-6%, this rate varies between 0.1-18% in adults [8,11,12]. Our study included a wide age range, and one patient was in the pediatric group [1,8]. In studies, the incidence of males is slightly higher than that of females and our study was compatible with the literature in this regard. Inlet patch foci have a velvety, dark pink appearance endoscopically, and are usually found as single or multiple patchy foci [7,13,14]. In our study, while a single focus was observed in endoscopic examination in most of the cases, there were nine cases with two or more foci and our rates were similar to those reported in the literature.

Polyp development is rare in inlet patch cases [8,14]. The number of hyperplastic polyps diagnosed in cervical esophagus is very low in the literature [6,15]. In our study, we present a case located in the esophagus and diagnosed as a hyperplastic polyp (1 cm). The most common mucosa detected in the inlet patch foci is the oxyntic mucosa, which is followed by the antral type [13,14,16]. In our study, in accordance with the literature, the oxyntic type mucosa was seen more frequently.

Microscopic examination may be accompanied by mononuclear inflammatory cells (plasma cells and lymphocytes), polymorphonuclear leucocytes and HP in these foci at varying rates [8,14,17]. Studies report that 0-86% of cases with gastric HP may also have HP in the inlet patch foci [13,16]. Oral route and gastroesophageal reflux is reported among the causes of colonization of HP in the inlet patch foci [18]. In our study, HP was observed in the inlet patch foci in four cases.

Histopathologically, intestinal metaplasia may accompany the inlet patch, but dysplasia and adenocarcinoma are extremely rare [7,9,10,19]. According to some authors, lack of histopathological correlation of each inlet patch case is the reason for the low rate of neoplasia [3]. In our study, only one of our patients had a low-grade dysplasia, which was accompanied by intestinal metaplasia. We did not have a case diagnosed as adenocarcinoma. The inlet patch cases, generally known as benign lesions, remain stable during their follow up [14]. Since most of them are asymptomatic, there is no accepted standard treatment. Thus, some authors find endoscopic follow up sufficient for asymptomatic cases without taking a biopsy [16]. However, because of the possibility of neoplastic development,

some authors also recommend taking a biopsy to determine the presence or absence of preneoplastic or neoplastic lesions from endoscopically detected lesions [3,16]. Proton pump inhibitors can provide dramatic improvement for symptomatic patients [20]. In cases diagnosed with dysplasia and neoplasia, argon plasma coagulation, endoscopic mucosal resection, endoscopic submucosal dissection, and radiofrequency ablation can be performed [8].

Limitations

Our study has a few limitations. First, this study was planned retrospectively. Second, the number of cases was few, and one case was diagnosed with preneoplasia, which was excluded.

Conclusions

The incidence of our inlet patch cases was consistent with the literature in terms of the presence of the gastric type epithelium, HP, intestinal metaplasia, and dysplasia. Our case diagnosed with a hyperplastic polyp is of particular importance for the literature. Since the inlet patch, which is a benign lesion, has the potential to transform into malignancy, we need to obtain more information about these lesions and their significance. Therefore, taking biopsies from each lesion suspected of being an inlet patch in endoscopic examination, and performing a close clinical follow up, especially in patients with different clinical features such as large size and ulcers, will allow us to identify the precise frequency of the inlet patch and most importantly, detect early neoplasms. In our daily routine, we think that our study will increase awareness especially for endoscopists and pathologists and may be a guide for further studies that will be conducted among larger patient groups.

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