

Title page

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Title: Esophageal inlet patch: Endoscopic prevalence in full sedated patients and Clinical significance.

Running title: Prevalence and Symptoms in İnlet patch

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ABSTRACT

AIM: To determine the frequency, demographic and clinical features of the heterotopic gastric mucosa (inlet patch).

MATERIALS AND METHODS: This retrospective study involves 244 patients who applied to the gastroenterology outpatient clinic with different symptoms between September 2016 and December 2019, and who were diagnosed with inlet patch in elective esophagogastroduodenoscopy. All endoscopic procedures were performed by the same clinical endoscopist. All medical records of patients including demographic and clinical features and endoscopy findings were reviewed.

RESULTS: Considering 2823 patients who underwent elective esophagogastroduodenoscopy in the same study period, inlet patch was detected in 224 (8.6%). 56.6% of the patients diagnosed with inlet patch were male and there was no statistical difference between the two genders. The mean age of the patients was 37.73 ± 13.01 years. 83.6% of the patients had only one lesion, and 58.2% had a lesion larger than 1 cm, with the largest one being 4.5 cm. Size of the smallest lesion was 0.3 cm. All of the lesions were in the proximal esophagus. 54 patients (22.1%) had at least one supraesophageal or upper esophageal symptom. The most common symptom was globus sensation (64.8%). Patients with large lesions were more likely to experience symptoms (28.2% vs. 13.7%, $p=0.008$).

CONCLUSION: Careful examination of the proximal esophagus may increase the chance of detecting inlet patch and may explain persistent symptoms in patients without a specific cause. Further understanding of the clinical significance of the disease may also prevent unnecessary diagnostic interventions.

Keywords: Inlet patch, Endoscopy, Prevalence, Globus sensation.

What's already known about this topic?

Inlet patch is a disease whose clinical importance is not fully understood, can become chronic, cause symptoms such as throat discomfort, globus sensation and difficulty swallowing, and causes many unnecessary examinations.

What does this article add?

Inlet patch is an important cause of globus sensation and the frequency of diagnosis is increased in sedated patients and this may help to prevent many unnecessary examinations in such patients.

Review criteria: how did you gather, select and analyze the information you considered in your review?

Patient information was collected retrospectively and analyzed with SPSS 21.0

Message for the clinic: what is the 'take-home' message for the clinician?

With the diagnosis of inlet patch, the etiology of symptoms such as sore throat, globus sensation and dysphagia, which have become uncomfortable and chronic in some patients, can be detected and this may help to prevent many examinations in such patients.

INTRODUCTION

Heterotopic gastric mucosa (HGM), which is also called inlet patch (IP) is characterized by congenital existence of salmon-color gastric columnar epithelial islands in the cervical esophagus. These patch-shaped islets, observed just below the upper esophageal sphincter, vary in diameter from a few millimeters to 4.5-5 cm [1-3]. An inlet patch may be slightly convex, flat, or concave, and these ectopic mucous islands, separated from normal mucous by sharp borders, can be seen as a single piece or multiple pieces. The reported incidence of endoscopically diagnosed inlet patch varies from 1% to 13.8% [4-6]. Wide variation in this incidence may be related to the anatomical localization of inlet patches and insufficient examination of the proximal esophagus by endoscopists. The increasing awareness of endoscopists about the presence of HGM and identification of its association with some symptoms increased the rate of endoscopic diagnosis of this lesion [7]. This lesion, the clinical significance of which is not exactly known yet, may cause sticking sensation, foreign body sensation and/or burning complaints in the proximal part of the esophagus. This study evaluates the incidence of inlet patch, and its association with age, gender and symptoms in the esophagogastroduodenoscopy (EGD) procedures performed by a single endoscopist under sedation, during which the proximal esophagus was carefully examined.

MATERIALS AND METHODS

This retrospective study involves 244 patients diagnosed with inlet patch from 2823 patients who applied to the gastroenterology outpatient clinic with different symptoms between September 2016 and December 2019, signed a written consent form, and underwent elective endoscopy. Patients whose endoscopic data were not clear were excluded from the study. Following full sedation under the supervision of an anesthesiologist after at least 8 hours of fasting, the patients underwent upper endoscopy performed by a single endoscopist. Proximal esophagus was examined in detail during all endoscopy procedures. Inlet patch was defined as patch-shaped lesions covered with salmon-red mucosa, the boundaries of which can be distinguished from the pearl gray esophageal mucosa (Figure 1). Demographic data of 244 patients diagnosed with inlet patch were recorded. The size of each inlet patch was determined by the top opening of the fully open biopsy forceps. The size, number and localization of the lesions were recorded. Inlet patch lesions were divided numerically into two groups, as single and multiple, and also into two groups in size, as smaller than 1 cm and larger than 1 cm. Then, the lesions were distributed according to age and gender. Globus sensation, hoarseness, voice thickening, sore throat, cough, dysphagia, and odynophagia were considered as supraesophageal and upper esophageal symptoms. The presence of these

symptoms and their association with the number and size of inlet patches were evaluated. This study was approved by the Clinical Research Ethics Committee at Health Sciences University Diyarbakır Gazi Yaşargil Training and Research Hospital (15.01.2021/621).

Statistical analysis: All statistical analyzes were performed by using statistical Package (SPSS) 21.0 software. For the significance of the difference between the two groups, the categorical variables were compared by using the Pearson's chi-squared test or Fisher's exact test, and continuous variables were compared by using Student's t test. Two-way values $p < 0.05$ were considered statistically significant.

RESULTS

In our study, IP was endoscopically detected in 244 (8.64%) of 2843 patients who underwent EGD. The mean age of patients diagnosed with IP was 37.73 ± 13.01 . 106 (43.4%) of the patients were female and 138 (56.6%) were male. All of the IP lesions observed in the patients were located in the proximal esophagus. Single lesions were detected in 204 (83.6%) of the patients and multiple lesions in 40 (16.4%). Lesion size was less than 1 cm in 102 (41.8%) patients, and larger than 1 cm in 142 (58.2%). The smallest lesion was 0.3 cm, while the largest lesion was 4.5 cm. While no supraesophageal or upper esophageal symptom was found in 190 (77.9%) of the patients, 54 (22.1%) of the patients had at least one of the supraesophageal and upper esophageal symptoms. Globus sensation (64.8%) was the most common symptom followed by dysphagia (12.9%), and cough (11.1%). Age did not have a significant relation with the symptoms or the number and size of the lesion ($p > 0.05$). However, the patients with large lesions were more likely to experience symptoms (28.2% vs. 13.7%, $p = 0.008$). Demographic data of the patients and distribution of symptoms are given in the table 1 and table 2.

DISCUSSION

Ectopic gastric mucosa may appear anywhere along the gastrointestinal tract. When it is seen in the proximal part of the esophagus, it is called inlet patch. It was first defined by Schmidt in 1805 and it is usually located in the postcricoid area of the esophagus or just below the upper esophageal sphincter and it is considered to be a congenital anomaly. The lesion is more common when the endoscope shaft is pulled by the endoscopist very slowly from the proximal esophagus. In endoscopy, the lesions are salmon-colored and velvety, mostly round oval lesions that can be easily distinguished from the normal gray-white flat epithelium of the esophagus [8,9]. The incidence of these lesions, which are frequently ignored by endoscopists, has been reported in a wide range of 1% to 13.8%.. [3,7,8]. In this study, the incidence of inlet patch was found to be 8.64% . The mean age of the patients was

37.73 ± 13.01, and it was more common in male patients with 56.6%. The incidence rate of inlet patch in our study was higher than many reported studies. Due to the fact that all cases were performed by a single endoscopist, and the proximal esophagus was examined in detail, a higher rate was found in our study compared to many other reported studies. While inlet patch is seen at any age, it is typically seen in fifties [10]. Our study found that it is also seen at younger ages. With detailed examination of the proximal esophagus, inlet patch diagnostic efficiency can be increased. In addition, the use of NBI can increase the frequency and accuracy of diagnosis [11-13]. In our own experience, we have seen that the most important event that increases the frequency of inlet patch diagnosis is a detailed examination of the esophagus proximal.

The clinical significance of inlet patch is not known much. Inlet patch, which is mostly asymptomatic, causes supraesophageal and upper esophageal symptoms, but it is usually detected in endoscopic examinations carried out due to other gastrointestinal complaints. However, inlet patch may also appear with more serious medical problems such as pain, dysphagia, ulcer, bleeding, perforation or esophageal web[14,15]. While there are publications supporting the increase in the severity of symptoms with the size of the lesion[16,17] the relationship between acid secretion and inlet patch-related symptoms remains uncertain. Studies suggest that only a small proportion of symptomatic patients had acid secretion from inlet patch [18,19]. Patients who are symptomatic typically have laryngopharyngeal symptoms such as globus pharyngeus, sore throat, hoarseness, chronic cough, throat clearing, and dysphagia, and these symptoms are thought to occur due to irritation of the airways and vocal cords due to acid secretion [20,21]. Macha et al. [22]. showed that children with IP had a higher rate of respiratory symptoms compared to the control group. Poyrazoglu et al. [23] also reported a higher incidence of dysphagia in adults with IP. Another study shows that the frequency of upper esophageal or laryngopharyngeal symptoms did not differ between the case group and control group [24]. 54 (22.1%) of our patients with inlet patch had at least one of the supraesophageal and upper esophageal symptoms. None of our patients had severe complications. Conducted studies reported the frequency of upper esophagus and supraesophageal symptoms in inlet patch patients at rates ranging from below 20% to 70% [25]. The reason for the fact that this ratio is slightly lower in our study may be due to the fact that our study was retrospective and these symptoms were not adequately questioned. No relation was found among the frequency of symptoms, the number of lesions and the age of patients. In line with the above-mentioned publications, the

frequency of symptoms was significantly higher in patients with lesions greater than 1 cm ($p: 0.008$).

While IP is typically seen as a single lesion, it can also be seen as multiple lesions [26]. In our study, a single lesion was found in 204 (83.6%) of the IP cases, while 40 (16.4%) of the cases showed 2 or more lesions in accordance with the literature, The size of the lesions in the inlet patch can vary from a few millimeters to 4.5-5 cm [24]. In our study, while the size of lesion was less than 1 cm in 102 (41.8%) cases, it was larger than 1 cm in 142 (58.2%) patients, with the largest one being 4.5 cm.

Strictures and webs are treated with serial dilatation but should include biopsy to rule out malignancy [27] Overall, significant histological non-malignant changes or malignancies in HGM are extremely rare. Neoplastic transformations have only been reported in the adult population [28-31]. Since the first case reported by Carrie et al [32] in 1950 there have only been 43 cases of adenocarcinoma [33-35] in association with HGM reported in the literature to date. Based on two studies, it can be estimated that the incidence of malignancies among patients with HGM ranges between 0 and 1.56% [36,37].

There is no standardized treatment strategy for inlet patch. Treatment is not required for asymptomatic patients. For symptomatic patients, H2-receptor antagonists or proton pump inhibitors can be used. Dilatation may be performed for strictures and webs. Furthermore, laser or radiofrequency ablation of inlet patches has been shown to relieve globus and has been used to successfully treat inlet patch dysplasia although its routine use in this context has not been determined [21,38].

In conclusion, the incidence of this disease, which is generally diagnosed incidentally, differs greatly from publication to publication. Careful examination of the esophageal proximal contributes to a significant increase in the diagnosis rate of inlet patch. With the diagnosis of inlet patch, the etiology of symptoms such as sore throat, globus sensation and dysphagia, which have become uncomfortable and chronic in some patients, can be detected and this may help to prevent many examinations in such patients. Acid secretion blockers can relieve symptoms. Inlet patch will become more clear with the increase in the diagnosis rate of this typically-overlooked disease and the publications on the subject.

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TABLES

Table 1. Demographic characteristics of patients.

<u>Variables</u>	
Age, year, mean\pmSD (min-max)	37.73 \pm 13.01 (16-77)
Female, n (%)	106 (%43.4)
Male, n (%)	138 (%56.6)
Number of pathces, n (%)	
<1	204 (% 83.6)
>1	40 (% 16.4)
Size of patch , n (%)	
<1 cm	102(% 41.8)
>1 cm	142 (% 58.2)

SD; standart deviation, n;number

Table 2. Clinical features of patients.

<u>Supra esophageal/ upper esophageal symptoms, n (%)</u>	<u>54 (%22.1)</u>
Globus sensation	35(% 64.8)
Hoarseness	3 (% 5.5)
Disfaji	7 (% 12.9)
Sore throat	0
Chronic cough	5 (% 11.1)
Odynophagia	3 (% 5.5)

n;number

FIGURE

Figure 1. Endoscopic images of heterotopic gastric mucosa of the proximal esophagus. Flat, round inlet patches in (A) white light endoscopy vs (B) optical chromoendoscopy (narrow band imaging), in a middle age man.