WHAT IS THE CLINICAL IMPORTANCE OF WHITE SPOTS IN THE DUODENUM?

DUODENUMDA GORULEN BEYAZ NOKTALANMALARIN KLINIK ONEMI NEDIR?

CLINICAL IMPORTANCE OF WHITE SPOTS IN THE DUODENUM

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Öz

Amaç: Bu çalışmanın amacı duodenumdaki beyaz noktalanmaların sıklığını, etiyolojisini ve klinik önemini belirlemektir. Gereç ve Yöntem: Üst gastrointestinal endoskopi sırasında duodenumda beyaz noktalanmalar tespit edilen 127 hasta çalışmaya dahil edildi. Duodenum 2.kısımda beyaz noktalanmalardan ikişer biyopsi alındı. Tüm biyopsiler tek bir uzman patolog tarafından değerlendirildi. Bulgular: Hastaların 57'si erkek, 70 'i kadındı. Ortalama yaş 43.27 ± 16.7 idi. Patolojik inceleme sonucunda, azalan sıra ile; %73 nonspesifik duodenit, %13.3 intestinal lenfanjiektazi, %11 intraepitelyal lenfositoz(IEL) ve %2,3 villus atrofisi(VA) olarak değerlendirildi. Sonuç olarak, spesifik semptomu ve endoskopik bulgusu olmayan ve IEL ve VA ile prezente olan 6 hastaya çölyak tanısı konuldu. Tartışma: Bu çalışma duodenumdaki beyaz noktalanmaların prevelansını %4.8 olarak bulmuştur. Bunların 37'nde spesifik bulgular tespit edilmiştir. Duodenum 2.kısımın dikkatli incelenmesi ciddi hastalıkların tanısını koymayı sağlayabilir.

Anahtar Kelimeler

Gastroskopi; Duodneum; İntestinal Lenfanjiektazi; Çölyak Hastalığı

Abstract

Aim: The aim of this study was to evaluate the incidence, etiological factors, and clinical importance of white spots in the duodenum. Material and Method: In total, 127 patients who were diagnosed as having white spots in the duodenum during an upper gastrointestinal endoscopic examination were included. Two duodenal biopsies were conducted from the second portion of the duodenum that contained the white spots. All biopsy samples were evaluated by a single expert pathologist. Results: Of the 127 patients, 57 (44.9%) were men and 70 (55.1%) were women. The mean age was 43.27 ± 16.7 years (range: 18–72 years). The histological examinations revealed the following pathologies in decreasing order: nonspecific chronic duodenitis (73.2%), intestinal lymphangiectasia (13.3%), intraepithelial lymphocytosis (11%), and villus atrophy (2.3%). Finally, celiac disease was diagnosed in six patients who presented with intraepithelial lymphocytosis or villus atrophy but who had no specific feature of celiac disease upon an endoscopic examination. Discussion: This study showed that the prevalence of white spots in the duodenum is 4.8%. Specific disorders were diagnosed in thirty-seven of the cases studied. A careful examination of the second part of the duodenum could provide for a better diagnosis of a serious disease.

Keywords

Gastroscopy; Duodenum; Intestinal Lymphangiectasia; Celiac Disease

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Introduction

Several factors, such as acidic gastric content, Helicobacter pylori (HP), intestinal lymphangiectasia (IL), medications, infections, celiac disease (CD), eosinophilic gastroenteritis, autoimmune enteritis, Crohn's disease, tropical sprue, and malignancies affect the duodenum. Each of these conditions is associated with endoscopic and histopathological changes in the duodenum [1,2].

The endoscopic finding of white spots in the descending duodenum (WSD) is not commonly seen and its clinical importance has not yet been investigated. In reviewing the literature, there have been only two studies on white spot appearances in the duodenum. They showed that the prevalence of WSD was 3.2% and 1%, respectively [3,4]. No other studies have aimed to investigate the incidence, endoscopic course, and clinical importance of WSD. This study aimed to evaluate the incidence, etiological factors, and significance of WSD.

Material and Method

This prospective, single-center study was performed at the Gastroenterology Department of Siirt State Hospital in Turkey from October 2013 to August 2015.

All patients undergoing an upper gastrointestinal endoscopy (UGE) were included. In total, 2,635 consecutive adult patients were surveyed who were referred for an endoscopy from several departments and outpatient clinics for upper gastrointestinal system symptoms. Demographic and clinical information and presenting complaints were collected via a questionnaire administered by trained interviewers upon study entry. Data collection about WSD was performed using information from endoscopy and pathology reports. In total, 127 patients who had been diagnosed as having WSD were included.

All patients had presented after a 12-hour overnight fast. Written informed consent was obtained from all patients before the endoscopic procedures. The UGE was performed by a single endoscopist using a videogastroscope with forward viewing (Video Gastroscope EG-2985K with the Pentax EPK-i5000 video processor, Tokyo, Japan, 2011). Special attention was paid to the duodenum.

Two duodenal biopsies from the second portion of the duodenum containing white spots (Figure 1), as well as gastric antrum and corpus biopsy specimens from all patients, were taken for histological investigation. The biopsy samples were put into a 10% formalin solution before being embedded in paraffin. Hematoxylin and eosin (H&E)-stained sections from all biopsies from each patient were evaluated for pathogens (e.g. HP and giardia lamblia), lamina propria inflammation, intraepithelial lymphocytes, and villous architecture, and they were evaluated by a single expert pathologist. Nonspecific chronic duodenitis (NCD) was described as inflammation with edema and the infiltration of leukocytes; intraepithelial lymphocytosis (IEL) was described as more than 40 IELs/100 epithelial cells in the small intestine; and IL was described as dilatation of the lymphatic channels (Figure 2).

Data analysis was performed using the SPSS package (IBM SPSS software for Windows; version 19.1; SPSS Inc., Chicago, IL, USA). Intergroup comparisons of categorical variables were conducted using a Chi-square test and continuous variables were compared using the Student's t-test. Categorical variables were presented as percentages or counts, and continuous variables were presented as mean and standard deviation in a descriptive analysis. Differences in the presenting symptoms of each group were identified by a Cox regression. A p-value lower than 0.05 was considered statistically significant.

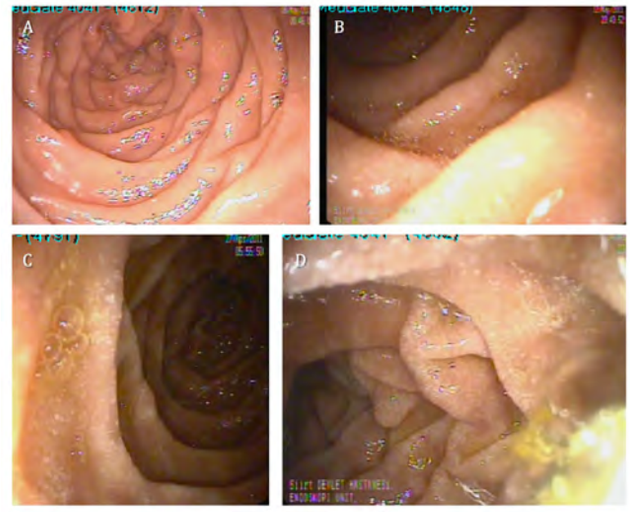


Figure 1. A, B; Rare appearance, C; Mild appearance, D; Dense appearance of white spots in the duodenum

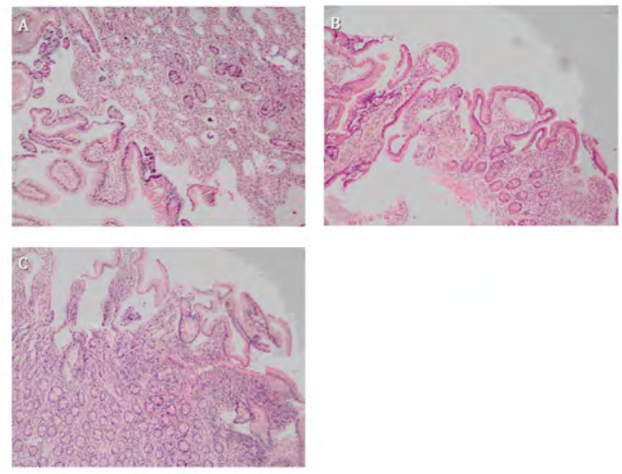


Figure 2; A, B; Dilation of the lacteals of the villi; Intestinal lymphangiectasia, C; Mild chronic inflammatory infiltration with polymorphonuclear leukocytes in lamina propria; Chronic nonspecific duodenitis

Results

Of the 127 patients, 57 (44.9%) were men and 70 (55.1%) were women. The mean age was 43.27 ±16.7 years (range: 18–72 years).

The pathologies revealed through a histological examination are presented in Table 1.

Table 1. Overall frequencies of histological diagnoses

	Frequency	Percentage
NCD	93	73.2%
IL	17	13.3%
IEL	14	11%
VA	3	2.3%

NCD: Nonspecific Chronic Duodenit; IL: Intestinal Lymphangiectasia; IEL: Intraepithelial Lymphocytosis; VA: Villus Atrophy

A gastric histology revealed HP positivity in 87 patients in all groups, and the distribution of the groups is shown in Table 2.

Presenting complaints of the patients are shown in Table 3. Weight loss as a presenting symptom was significantly less often found in NCD patients as compared to the other groups ($p< 0.05$).

A duodenal histology revealed reduced villous atrophy (VA) in three patients (2.3%), with a histology consistent with CD. The patients did not present with either PAS-positive macrophages in duodenal biopsy samples or with a specific histology for giardiasis.

Table 2. Helicobacter pylori positivity in all groups

	Hp (+) n %	Hp (-) n %
NCD	64 68.8%	29 -31.2%
IL	11 64.7%	63 5.3%
IEL	9 64.2%	5 3 5.8%
VA	1 33.3%	2 66.7%
		p>0.05

NCD: Nonspecific chronic duodenitis; IL: Intestinal lymphangiectasia; IEL: Intraepithelial lymphocytosis; VA: Villus atrophy

Table 3. Summary of presenting symptoms of the study population

	NCD(93)		IL (17)		IEL(14)		VA (3)		p
	n	%	n	%	n	%	n	%	
Epigastric pain or discomfort	75	80	10	59	9	64	2	67	
Nausea	16	17	4	24	4	29	0	0	0.58
Vomiting	18	19	3	18	4	29	O	0	0.68
Diarrhoea	14	15	9	53	3	21	1	33	0.06
Weight loss	6	6	4	25	4	29	1	33	<0.05
Lower extremity edema	0	0	0	0	3	21	0	0	<0.001

NCD: Nonspecific chronic duodenitis; IL: Intestinal lymphangiectasia; IEL: Intraepithelial lymphocytosis; VA: villus atrophy

Discussion

Although clinicians have not placed much emphasis on WSD, a few studies on this topic have been found in the literature. Has WSD been overlooked during endoscopic investigations? Perhaps if clinicians were more alert to WSD, a higher prevalence would have been reported. This paper investigated the prevalence of WSD in our study, 4.8%, which is much higher than has been previously found. WSD may occur because of several conditions, such as NCD, IL, IEL, infectious pathologies, and CD. It was found that NCD is the most common cause of WSD. NCD is defined by the presence of inflammatory cell infiltration in the lamina propria, with or without an architectural distortion of the intestinal villi. There are different etiologies of NCD, including peptic duodenitis secondary to HP, CD, Crohn's disease, and parasitic infestation. However, HP cannot exist on the intestinal epithelium, although it may colonise in areas of gastric metaplasia in the duodenal mucosa, thereby leading to chronic active duodenitis [5]. The association of HP with WSD has not yet been investigated. In this study, while the positivity of HP was 68.8% in NCD, it was 64.7% in the IL group and 64.2% in the IEL group, with no significant statistical difference. The positivity of HP was 66.9% in all groups, lower than the overall 82.% pevelance in Turkey [6].

IL is the second most common cause in these endoscopic findings. IL is a rare disorder caused by a congenital malformation or an obstruction of the intestinal lymphatic drainage system [7]. The elevated pressure of the lymph drainage system on the intestinal wall leads to dilatation and even a rupture of the lymphatic vessels, which results in a leakage of lymphatic fluid [8]. Because lymphatic fluid contains high levels of protein, fat, and lymphocytes, a leakage of lymphatic fluid will cause hypoproteinaemia, lymphocytopenia, and decreased serum levels of immunoglobulin. IL can be classified into primary or secondary IL, depending on the reason for the disease. Fewer than 200 primary intestinal lymphangiectasia (PIL) cases have been reported globally since Waldman et al. [9] reported the first case in 2010. PIL is a congenital malformation of the lymphatic system that can affect individuals of any age, but that most often affects younger patients [10]. Secondary causes include conditions that involve protein loss associated with impaired intestinal lymphatic drainage, such as congestive cardiac failure, constrictive pericarditis, Whipple's disease, Crohn's disease, intestinal tuberculosis, radiation and/or chemotherapy with retroperitoneal fibrosis and portal hypertension, or hepatic venous outflow obstruction [11-15]. Evidence of lymphangiectasia in the duodenum without the presence of malabsorption has been observed [16]. Consistent with these results, three of the patients in this study with IL had hypoalbumenia, lymphopenia, or chronic diarrhoea. Short- and medium-chain fatty acids are absorbed directly into the portal system without contributing to the formation of chylomicrons, thus providing energy and lessening lacteal engorgement and lymph loss [17]. A low-fat diet reduces lymphatic flow and pressure, preventing the lacteal dilatation and lymph leakage resulting from their rupture. Patients who had hypoalbumenia, lower extremity edema, and were diagnosed with IL were put on a low-fat diet for a period of eight weeks, after which a control endoscopy indicated improved WSD appearance and resolved peripheral edema.

The early diagnosis and treatment of IL is of great importance for effective diet therapy and for protection from malignant transformation. Edema is the main clinical manifestation due to hypoalbumenia. The patient may present with ascites, pleural effusion, and pericarditis. Lymphedema, abdominal pain, fatigue, moderate diarrhoea, weight loss, and a deficiency of fat-soluble vitamins may also be present and could be resolved by a specific diet. It is noteworthy that PIL may have a high malignancy grade potential for a long time after the first onset [18]. Therefore, clinicians should keep in mind this rare condition and should treat it urgently.

IEL forms the first line of the host immune defence system and plays an essential role in fighting infections caused by certain microorganisms and parasites [19]. IEL is thought to be an early lesion in the development of CD. Many investigators have demonstrated that IEL is the first abnormality seen after gluten challenge and that IEL alone may be a form of gluten sensitivity as type 1 CD, according to the Marsh Classification [20]. Otherwise, IEL in a normal small bowel biopsy is a somewhat nonspecific histological finding. Increased IEL counts have also been described in patients without CD, such as in cases of allergic enteritis, autoimmune disorders, tropical sprue, HP-associated gastritis, viral infections, and enteropathy-associated

T-cell lymphoma [21-25]. In this study, the HP-positive rates of all groups were 68.8%, 64.7%, and 64.2% in the NCD, IL, and IEL groups, respectively. These differences were not statistically significant.

Anti-tissue transglutaminase IgA was conducted in all patients with IEL or with VA. Three patients in the IEL group and three in the VA group had positive levels and they were diagnosed with CD. Importantly, CD was diagnosed in six patients who presented with IEL or VA and in whom an endoscopic examination had not indicated specific features of CD.

This study has a limitation in that an endoscopic evaluation was not performed after the specific treatment in all patients. The reason for not performing a second endoscopy is that the aim of the study was to investigate the clinical importance of WSD. This study has underlined the clinical importance of the use of WSD in diagnosing a serious clinical condition in cases without a specific symptom. Six patients were diagnosed with celiac disease and seventeen patients were diagnosed with IL because follow up was initiated, based on a suspicion because WSD had been observed. In our study, a few, but not all of, the patients had presented with specific symptoms.

Conclusion

WSD could be a valuable marker in the diagnosis of several diseases that are treated by diet and that require early treatment, such as CD and IL. To avoid overlooking these diagnoses, endoscopists should be alert to the appearance of WSD in the second part of the duodenum, and, if found, at least two biopsies should be obtained from this region.

Competing interests

The authors declare that they have no competing interests.

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