XANTHELASMAS OF THE UPPER GASTROINTESTINAL TRACT: THEIR SIGNIFICANCE AND ASSOCIATION WITH DYSLIPIDEMI

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ABSTRACT

Objective: *The significance of gastrointestinal xanthelasmas (GX) is unclear, although sometimes lesions they may be confused with malignant lesions. The aim of this study is to investigate the relationship between GX, atrophic gastritis, Helicobacter pylori (HP), and dyslipidemia.*

Material and Method: *Upper gastrointestinal endoscopy reports of 8040 patients were evaluated retrospectively. Among them, 20 patients with GX were included into the study and evaluated for endoscopic characteristics, atrophic gastritis, HP infection and serum lipid profiles. The findings were compared with 20 age- and gender-matched control subjects.*

Results: *The prevalence of GX was 0.24% with no gender difference. As compared with the control group, lipid profiles of GX group showed significantly lower HDL-cholesterol (38.50±9.59 vs 48.80±14.80, p=0.01) and total serum-cholesterol levels (mg/dL) (171.70±26.21 vs 194.25±34.84, p=0.032). LDL- cholesterol and triglyceride levels were not related to the presence of GX. GX showed a close relationship with endoscopically determined atrophic gastritis (30.0% vs 5.0%, p=0.03). HP infection and intestinal metaplasia were not significantly related with GX.*

Conclusion: *In our serial endoscopy, the prevalence of GX was 0.24% and it showed an increase with age. Dyslipidemia and atrophic gastritis were found to be related to GX. This relation was not observed with HP infection.*

Key Words: *Xanthelasma, dyslipidemia, Helicobacter pylori, atrophic gastritis* **Nobel Med 2014; 10(1): 53-57**

ÜST GASTROİNTESTİNAL SİSTEM KSANTELEZMALARI: ÖNEMİ VE DİSLİPİDEMİ İLE İLİŞKİLERİ

ÖZET

Amaç: Gastrointestinal ksantelezmaların önemi net olarak bilinmemektedir ancak bazen premalign ve malign lezyonlarla karışabilmektedir. Bu çalışmanın amacı gastrointestinal ksantelezma ile atrofik gastrit, Helicobacter pylori (HP) ve dislipidemi arasındaki ilişkinin araştırılmasıdır.

Materyal ve Metod: 8040 hastanın üst gastrointestinal sistem endoskopisi raporu retrospektif olarak incelendi. Bunlar arasından gastrointestinal ksantelezma saptanmış olan 20 hasta çalışmaya dahil edilerek, endoskopik özellikler, atrofik gastrit, HP infeksiyonu ve dislipidemi açısından değerlendirildi. Bulgular yaş ve cinsiyet açısından uyumlu 20 vakalık kontrol grubu ile karşılaştırıldı.

Bulgular: Gastrointestinal ksantelezma prevalansı %0,24 olarak bulundu ve cinsiyet açısından farklılık yoktu. Kontrol grubu ile karşılaştırıldığında, ksantelezma grubunda HDL-kolesterol (38,50±9,59 vs 48,80±14,80, p=0,01) ve total kolesterol seviyeleri (mg/dL) (171,70±26,21 vs 194,25±34,84, p=0,032) anlamlı olarak daha düşük bulundu. LDL-kolesterol ve trigliserid seviyeleri açısından ise farklılık saptanmadı. Gastrointestinal ksantelezma ile atrofik gastrit varlığı arasında anlamlı bir ilişki mevcuttu (%30 vs %5, p=0,03). HP infeksiyonu ve intestinal metaplazi varlığı ile ksantelezma arasında ise anlamlı ilişki bulunmadı.

Sonuç: Endoscopy serimizde gastrointestinal ksantelezma prevalansı %0,24 olarak bulundu ve yaşla artış göstermekteydi. Ksantelezma ile dislipidemi ve atrofik gastrit varlığı arasında anlamlı ilişki tespit edilmişken HP infeksiyonu ile benzer bir ilişki gözlenmedi.

Anahtar Kelimeler: Ksantelezma, dislipidemi, Helicobacter pylori, atrofik gastrit **Nobel Med 2014; 10(1): 53-57**

INTRODUCTION

Gastrointestinal xanthelasmas (GX) are uncommon benign lesions. The etiology and clinical significance of GX is unknown. Chronic gastritis, Helicobacter pylori (HP) infection, diabetes mellitus and hyperlipidemia have been implicated in the etiopathogenesis. The most frequent location of xanthelasma in the upper gastrointestinal (GI) tract is the stomach.[1] The incidence of GX is reported as ranged from 0.018% to 0.8% in endoscopy series and approximately 58% in autopsy series.[2,3] Its frequency increases with age, and highest in the seventies.[4,5] Endoscopic appearance of upper GX is typical. They appear as yellow-white, well-demarcated, single or multiple nodules or plaques, with a size varying from 1 to 10 mm in diameter (Figure 1, 2).[3,6,7] Xanthelasmas are composed of large foamy cells containing mixture of lipids, including cholesterol, neutral fat, low-density lipoprotein, and oxidized low-density lipoprotein (Figure 3).[1]

Although the clinical significance of GX is unclear and they are not uncommon, there are few reports about GX in the literature. They may be confused with malignant lesions.[5,8]

In this study, we aimed to determine the prevalance of upper GX and their association with HP infection, gastric mucosal changes, atrophic gastritis, intestinal metaplasia and dyslipidemia.

MATERIAL and METHOD

A retrospective analysis of 8040 upper GI endoscopy reports, done at the gastroenterology department of Süleyman Demirel University between January 2007 and December 2009, was performed. Patients with diagnoses of xanthalesma on upper GI endoscopy and confirmed by histopatologic examination of biopsy specimen, were included into the study. Demographic, clinical, endoscopic and histopathologic features and serum lipid profiles of patients were recorded. Blood samples were taken following 10-12 hours of fasting. Total cholesterol, triglyceride and HDL levels were analyzed with spectrophotometric method using Olympus AV 2700 autoanalyzer. HP infection was detected by rapid urease test and histopathologic examination. The diagnosis of atrophic gastritis was made by endoscopic appearance and histologic examination of mucosa.

The color, shape, size, and location of the lesions, and the presence of associated upper GI conditions, such as esophagitis, gastritis, or peptic ulcer disease were assessed. All lesions suspected to be xanthelasma were totally removed by resection. The surrounding gastric mucosa was evaluated for associated pathologic changes, such as atrophic gastritis, presence of HP infection, or intestinal metaplasia, by sampling biopsy. Histopathologic slides stained with periodic acid-Schiff (PAS) and toluidin blue were evaluated by a single pathologist.

Statistical analysis was performed using the Chi-square test, Student's *t* test, and Mann-Whitney *U* test, when appropriate. A p value less than 0.05 was considered statistically significant. Data were expressed as mean±SD. SPSS 15.0 version (SPSS Inc., Chicago, IL, USA) software was used to analyze the data.

RESULTS

GX was detected in 20 of 8040 patients (0.24%). Age and gender-matched 20 individuals without GX were included in the control group.

The mean ages of patients in the GX and control groups were 57.25±12.81 (28-79) years and 48.90 ±11.13 (25-68) years, respectively. There were 9 (45%) women and 11 (55%) men in the GX group and 8 (40%) women and 12 (60%) men in the control group. There was no difference between the groups in terms of age and gender (p=0.13, p=0.74).

The mean size of lesion was 3.05±1.09 mm in patients with GX. Lesion was located in the stomach in 19 (95.0%) patients, and in the duodenum in 1 patient (5.0%). 11 (57.89%), 6 (31.57%) and 2 (10.52%) of the gastric lesions were located in the corpus, antrum and cardia, respectiveley. Lesion was single in 11 (55.0%) patients, 2 in six patients, 3 in two patients and 4 in one patient. In patients with multiple lesions, lesions were located in the corpus in 4 patients, in the antrum in 4 patients and in the duodenum in 1 patient (Table 1). Serum HDL (38.50±9.59 and 48.80±14.80, p=0.01) and total cholesterol (171.70±26.21 and 194.25±34.84, p=0.03) levels (mg/dL) were low in the xanthalesma group compared to control group, and this difference was statistically significant. There was no association between GX and serum triglyceride and LDL cholesterole levels.

Atrophic gastritis was detected in 6 (30%) patients of GX group while in only one patient (5%) of control group (p=0.03). Intestinal metaplasia was detected in 5 (25%) patients of GX group and in 4 (20%) patients of control group (p=0,7). H. pylori infection was detected in 16 (80%) patients of GX group and in 13 (65%) patients of control group (p=0.28). Atrophic gastritis was detected significantly higher in GX group while there was no difference between the groups in terms of H. pylori infection and intestinal metaplasia.→

Demographic features, serum lipid profiles and histopathologic features of GX and control groups were showed in Table 2.

DISCUSSION

GX is a benign lesion characterized by the presence of lipid islands in the gastrointestinal mucosa. The significance and cause of GX still remain unknown.[9] The incidence of upper GX was reported as 0.23% in our population.[3,10] In the present study, it was found to be 0.24%. However, in a Korean study by Yi, the prevelance was reported as 7%, which was much higher than previous studies.[11] Approximately 76% of the lesions are located in the stomach, particularly in the antrum and pyloric region (70%); they occur less frequently in the esophagus (12%), duodenum (12%) and colon.[3,4,12,13]

Xanthelasma is more frequent in women and its incidence shows an increase with age. Distribution of gender was almost equal (M:F=1.2:1) in our series, however this ratio was reported as 3.3:1 by Oviedo et al.[6] Symptoms in patients with GX were nonspecific and may be variable. One third of patients are asymptomatic; epigastric fullness, anorexia, nausea and precordial pain were reported in symptomatic patients but the association between the lesion and these symptoms was very suspicious.[5] The symptoms of our patients were nonspecific and considered as related to gastritis and duodenal ulcer rather than GX.

Although the clinical significance of GX is unclear, they are important because they may be confused with malignant lesions. Several studies have shown that xanthelasma is associated with gastritis, carcinoma, intestinal metaplasia of the gastric epithelium, or peptic ulcer diseases.[14] Moderate-severe atrophy (89%) and intestinal metaplasia (13%) on the gastric glands around the lesions were reported in previous studies.[4,10,15] In our series, 30% of patients had atrophic gastritis. In addition, 25% of patients had developed gastric intestinal metaplasia. Intestinal metaplasia was not frequently seen within the GX specimens as reported by Pieterse et al. and Hori et al.[16,17] Pieterse et al. observed that intestinal metaplasia was less frequent at the site of GX, but common in the mucosa near the lesion.[16] Furthermore, degree of intestinal metaplasia was lower in the GX lesion than in the adjacent mucosa. Therefore, we cannot agree with the suggestion that intestinal metaplasia is associated with active absorption of gastric lipids.

We also showed a close relationship between atrophic gastritis and GX, similar to the results reported by Yi and Gocho.[11,18] Atrophic gastritis is considered as a precursor lesion of gastric cancer.[15,19] GX may be a marker of gastric cancer, especially of the intestinal type, due to coexistence with atrophic gastritis, but to verify this relationship a large study is required.

Table 1: Distribution of patients according to the location and number of xanthelasmas

Location	n (%)	Single/Multiple
Stomach	19/20 (95%)	
Cardia	2	2/0
Corpus	11	7/4
Antrum	6	2/4
Duodenum	1/20 (5%)	0/1

Table 2: Demographic features, serum lipid profiles and histopathologic features of xanthalesma and control groups

Variable	Xanthalesma group	Control group	p
Age (years)	57.25±12.81	48.90±11.13	0.13
Sex (n) (M/F)	11/9	12/8	0.74
Serum Lipid Parameters*			
Total Cholesterol	171.70±26.21	194.25±34.84	0.03
HDL-cholesterol	38.50±9.59	48.80±14.80	0.01
LDL-cholesterol	101.55±19.55	118.50±31.24	0.053
Triglyceride	155.25±83.73	138.15±68.83	0.65
Histopathologic features			
Inflammation	16/20 (80%)	20/20 (100%)	0.03
Activation	7/20 (35%)	12/20 (60%)	0.11
H. pylori	16/20 (80%)	13/20 (65%)	0.28
Atrophy	6/20 (30%)	1/20 (5%)	0.03
Intestinal metaplasia	5/20 (25%)	4/20 (20%)	0.7

*Normal ranges of serum lipid parameters; Total cholesterol: 140-200 mg/dL, LDL-cholesterol: 0.0-130 mg/dL, Triglyceride: 40-160 mg/dL, HDL-cholesterol: 30-80 mg/dL

H. pylori antigens were detected in the cytoplasms of xanthelasma cells in some studies and it was hypothesised that these lesions may be initiated by H. pylori infection.[10,15,17] Chronic persistent H. pylori infection is considered as an important factor in the development and extent of atrophic gastritis. Turkey is an endemic country for H. pylori infection and its estimated prevalance is approximately 80%.[20,21] Some studies found a close association between H. pylori infection and GX.[15,17] However, in a study, Yi reported the prevelance of H. pylori was similar in GX and control groups and suggested no correlation between GX and H. pylori infection.[11] H. pylori was detected in 80% of our patients both with histopathologically and rapid urease test. The prevalence of H. pylori infection in GX patients and controls was similar, however atrophic gastritis was detected more frequently in GX patients. Although atrophic gastritis was highly related to H. pylori infection, there was no absolute correlation between atrophy and H. pylori in some endemic areas like Turkey. Also atrophy could be induced by some other reasons, such as autoimmune, idiopathic, reactive, drug-associated, or other gastric →

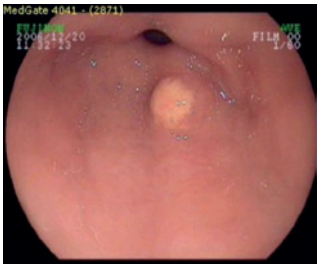

Figure 1: Endoscopic view of the xanthelasma occurring in the prepyloric antrum of stomach

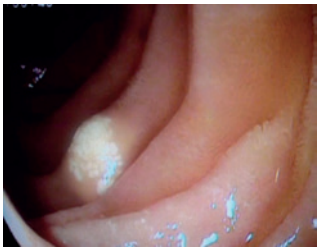

Figure 2: Endoscopic view of the xanthelasma occurring in the second part of duodenum

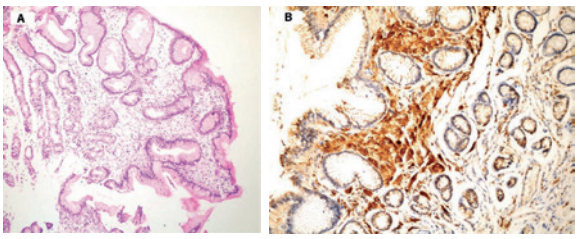

Figure 3: A. Microscopic examination of a representative gastric xanthoma stained with hematoxylin and eosin (low-power view) B. Xanthoma cells are positive for anti-CD68 antibody (low-power view)

irritant-induced causes.[11] In our cases, GXs were not associated with H. pylori infection. The prevalence of H. pylori infection is high in our country, so we think that the existence of H. pylori infection and gastric xanthelasma may be coincidental.

Although some amount of triglycerides and esterified cholesterol were detected on chemical analyses of these islands, most studies suggest that there is no correlation between GX and hypercholesterolemia.[5,22] Generalized disturbance of fat metabolism seems not to be essential for lipid islands.[5,8,22] Because of the histochemical characteristics resemble those of skin lesions, a possible relationship with lipid metabolism has been investigated, but no obvious association with lipid metabolism disorders or hypercholesterolemia was found.[4,8,23] Yi reported lower mean HDL-cholesterol and higher mean LDL-cholesterol levels and Chang et al. reported lower mean HDL-cholesterol and higher mean triglyceride levels in GX subjects in comparison with the controls.[11,24] In the present study, mean HDL-cholesterol and total serum cholesterol levels were lower in GX subjects than in controls, and this differences were statistically significant. Our investigation showed higher mean triglyceride level in GX subjects than controls, however this elevation was not statistically significant, similar to the results of Yi.[11] We concluded that, abnormalities of lipid metabolism may play a role in presence of GX.

Muraoka et al. observed an association between type IIa early gastric cancer and xanthelasma and speculated that cancer cells may have caused xanthelasma cell proliferation via an autocrine mechanism.[13] In addition, it was recommended that xanthelasma should be differentiated from signet ring cell carcinoma by histochemistry and immunohistochemistry.[10,25,26] Predisposing conditions for gastric cancer such as atrophic gastritis, intestinal metaplasia and H. pylori infection may accompany xanthelasmas.

CONCLUSION

Clinical significance of GX is not known. Our findings demonstrated that, atrophic gastritis and dyslipidemia are significantly associated with GX. This association was not detected with intestinal metaplasi and H. pylori infection. Diagnosis of xanthalesma should be confirmed with histopathologic examination of lesion. Patients with xanthalesma should be followed-up, because of increased incidence with age, association with atrophic gastritis and H. pylori infection, which could be a predisposan factor for carcinoma, and possibility of interference with malignant lesions.

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