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Gastric xanthalesmas: Report of five cases and review of the literature

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ABSTRACT

Xanthalesmas are incidental lesions that are rarely encountered during upper gastrointestinal (GI) endoscopy. The most frequent location of xanthelasma in the upper GI tract is the stomach. The reported incidence of gastric xanthelasma is quite variable: It rangs from 0.018% to 0.8%. Upper GI xanthelasmas have a typical endoscopic appearance of yellow-white well-demarcated single or multiple nodules or plaques, with a size varying from 1 to 10 mm in diameter. Xanthelasmas are composed of large foamy cells containing lipids. In this report; five patients who attended hospital with nonspesific symptoms and xanthelasma-like lesions were incidentally found on their endoscopic examination.

1. Introduction

Xanthelasmas, also known as "xanthomas" and "lipid islands" are incidental lesions that are rarely encountered during upper gastrointestinal (GI) endoscopy. The most frequent location of xanthelasma in the upper GI tract is the stomach (Kaiserling et al., 1996). The reported incidence of gastric xanthelasma is quite variable: It ranged from 0.018% to 0.8% in endoscopy series (Chen et al., 1989; Petrov et al., 1999).

Upper GI xanthelasmas have a typical endoscopic appearance of yellow-white well-demarcated single or multiple nodules or plaques, with a size varying from 1 to 10 mm in diameter (Khachaturian et al., 1998; Oviedo et al., 2001). Xanthelasmas are generally asymptomatic, and the complaints of symptomatic patients are unlikely to be related to xanthelasma. It is a benign condition but its appearance mimics malignancy and it is found to be associated with some premalignant conditions, so histological confirmation is necessary. Gastric xanthelasmas occur more frequently in gastric mucosa in which there are pathologic changes such as chronic gastritis, intestinal metaplasia, atrophic gastritis, gastric ulcer, and changes due to excess bile reflux (Oviedo et al., 2001). Although the etiology of xanthelasmas still remains unclear (Sekikawa et al., 2013), they are likely to be the result of an inflammatory response to mucosal damage.

This report include five patients who attended hospital with gastroesophageal reflux symptoms, abdominal pain or dyspepsia. Xanthelasma-like lesions were incidentally found on their endoscopic examination and histopathological examination of the lesions revealed gastric xanthelasma.

2. Case 1

A 47 year-old man presented with gastroesophageal reflux symptoms. His personal history was significant for Behcet's disease, hyperlipidemia and nonalcoholic steatohepatitis. He was receiving steroids and colchicum intermittently for Behcet's disease and atorvastatin for hyperlipidemia. Obesity (body mass index 34.8 kg/m^2) was found on physical examination. Upper GI endoscopy revealed grade B esophagitis, erythematous gastritis and a 10x10 mm white-cream colored polypoid lesion in the cardia. Histopathological examination of the lesion showed gastric xanthelasma.

Case 2

A 65 year-old man presented with abdominal pain. He had hypertension, diabetes mellitus (for 7 years) and autoimmune hemolytic anemia. He was receiving fenofibrate for hyperlipidemia. Upper GI endoscopy revealed erythematous gastritis and 5-7 mm white-cream colored polypoid lesion at the fundus. Histopathological examination of the lesion confirmed gastric xanthelasma. At the same time, lichen planus was present.

Case 3

A 52 year-old man was under follow up for tubular adenoma and antral gastritis. Allergic rhinitis and chronic psoriasiform dermatitis were present in his personal history. Upper GI endoscopy revealed yellow-white colored milimetric lesions in the corpus and antrum. Histopathological examination of the lesion demonstrated gastric xanthelasma.

Case 4

A 62 year-old man presented with abdominal pain. He did not have any disease in his personal history. The esophagogastroduodenoscopy revealed erosive gastritis, slightly elevated multiple diffuse green-white nodular lesions in the fundus, corpus and antrum. In histological examination, histiocytes aggregats with foamy cytoplasm were determined (Fig. 1) and these lesions were diagnosed as gastric xanthelasma. He had normal lipid profile and there was not any remarkable finding in cutaneous examination.

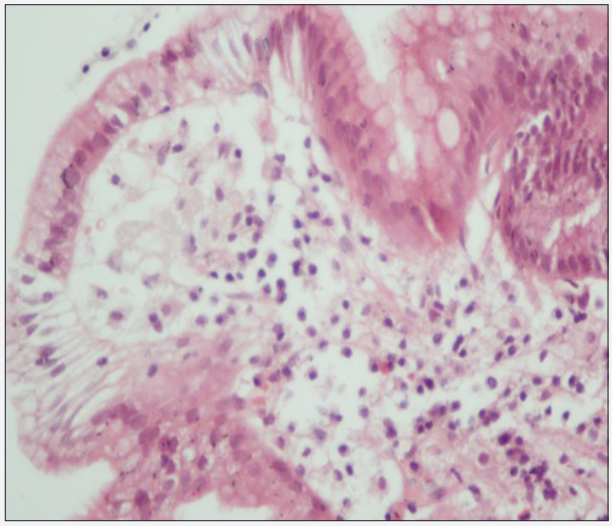

Fig. 1. Histiocytes aggregats with foamy cytoplasm in histological examination

Case 5

A 58 year-old man presented with right upper quadrant pain. His medical history was unremarkable, and he was not on any medication. Physical examination showed normal findings. The esophagogastroduodenoscopy revealed grade A esophagitis, sliding hiatal hernia, atrophic gastritis and duodenitis. There were three slightly elevated, white nodular lesions in the fundus (Fig. 2) and one similar lesion each in the corpus and antrum. Histopathological examination of the lesions revealed xanthelasma. Cutaneous lesions were absent.

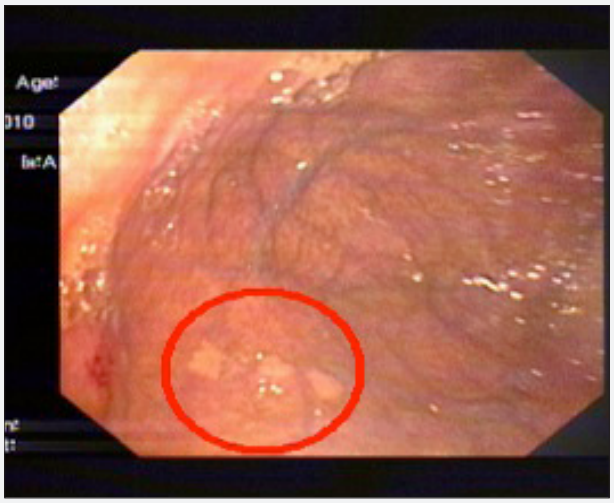

Fig. 2. Yellow-white coloured lesions at fundus

3. Discussion

The incidence of upper-GI xanthelasmas was reported as 0.23-7% in different populations (Gencosmanoglu et al., 2004; Sekikawa et al., 2013). About 76% of the lesions are located in the stomach, particularly at the antrum and the pyloric region (70%) and to a much lesser extent in the esophagus (12%) and duodenum (12%) (Scheiman et al., 1988; Naito et al., 1991; Gencosmanoglu et al., 2004). We did not identify any xanthelasma-like lesions in the esophagus or duodenum in our upper-GI endoscopy series and two out of five patients had xanthelasma in the antrum. In literature, it was reported that the incidence of gastric xanthelasma increases with age and the mean age of our patients was 57 years. A male predominance was present in a large study (Sekikawa et al., 2013). Similarly all of the patients in our series were male. The lesions had generally a yellowish-white appearance and varied between 0.5 and 10 mm in size. In Oviedo's (2001) study, multiple lesions were determined in 13 to 24% of the cases and 17% of the patients had more than five lesions (Oviedo et al., 2001). In our study, the size of the lesions was consistent with those reported in the literature and all patients had multiple lesions. The characteristics of these patients in comparison to other cases in literature are shown in Table 1.

Xanthelasmas are composed of large foamy cells containing a mixture of lipids, including cholesterol, neutral fat, low-density lipoprotein, and oxidized low-density lipoprotein (Kaiserling et al., 1996). These foamy cells are mostly histiocytes, although plasma cells, smooth muscle cells, and Schwann cells may also be involved (Boger and Hort., 1977). Since histochemical characteristics resemble those of skin lesions, a possible relationship with lipid

Table 1. Summary of our cases compared with the literature

	Age, gender	Admitting symptoms	History	Endoscopic findings	Plaque size	Plaque location	Helicobacter pylori	Lipid profile	Cutaneous findings
Case 1 (Gürsoy et al., 2005)	59, M	Abdominal pain, weight loss	Bilateral truncal vagotomy and pyloroplasty for gastric ulcer	Decreased gastric peristalsis, erythema and edema on the gastric mucosa, yellowish-white plaque, a 6x7 mm ulcer on the incisura angularis	10x10 mm	Anterior wall of the distal corpus	Negative	Normal	Unknown
Case 2 (Gürsoy et al., 2005)	35, M	Epigastric pain,burning and occasional diarrhea with yellowish stools	Unknown	Stage A peptic esophagitis (Los Angeles classification), and three slightly elevated, yellowish white plaques, a 5x5 mm ulcer on the anterior wall of the bulbus	7x8 mm	Cardia near the Z-line	Negative	Normal	Unknown
Case 3 (Gürsoy et al., 2005)	70, F	Abdominal pain radiating to the back	Hypertension and Billroth II operation	Yellowish-white plaque	15x15 mm	Just near the gastrointestinal anastomosis	Negative	Normal	Unknown
Case 4 (Gürsoy et al., 2005)	80, F	Abdominal pain and fatigue	Type 2 diabetes mellitus	Two slightly elevated, irregularly-edged, yellowish white lesions, the remaining mucosa was atrophic	7-8 mm	Posterior wall of the distal corpus and incisura angularis	Unknown	Normal	Unknown
Case 5 (De Roberto et al., 2009)	49, F	Asymptomatic	Pulmonary B-cell lymphoma	Soft, white/yellowish, isolated, and confluent multiple nodules	3-8 mm	Corpus	Unknown	Normal	Unknown
Case 6 (Gravina et al., 2009)	56, M	Dyspepsia	No disease	Numerous slightly elevated yellowish-white mucosal lesions, focal intestinal metaplasia	0.5-1.5 cm	Corpus	Negative	Normal	Psoriatic-like dermatitis with perivascular infiltrate of eosinophils and lymphocytes
Case 7 (Oviedo et al., 2001)	34, F	Dyspepsia	No disease	Flat, yellow plaque	1 cm	Antrum	Negative	Mildly hyperlipidemic	No
Present case 1	47, M	Reflux symptoms	Behçet disease, nonalcholic steatohepatitis, obesity	Grade B esophagitis, erythematousgastritis, white polipoid lesion	10x10 mm	Cardia	Negative	Hyperlipidemic	No
Present case 2	65, M	Abdominal pain	HT, DM, autoimmun hemolytic anemia	Erythematous pangastritis, white polipoid lesions	3-7 mm	Fundus	Negative	Hyperlipidemic	Liken planus
Present case 3	52, M	Asymptomatic	Alerjic rinitis	Chronic gastritis, tubuler adenoma, white polipoid lesions	2x2 mm	Corpus	Unknown	Normal	Chronic psoriasiform dermatitis
Present case 4	62, M	Abdominal pain	No disease	Erosive gastritis, slightly elevated diffuse green-white nodular lesions	10 mm	Fundus, corpus, antrum	Negative	Normal	No
Present case 5	58, M	Right upper quadrant pain	No disease	Grade A esophagitis, sliding hiatal herni, atrofic gastritis, duodenitis, slightly elevated white nodular lesions	5 mm	Fundus, corpus, antrum	Negative	Normal	No

M: Male; **F:** Female; **HT:** Hypertension; **DM:** Diabetes mellitus

metabolism has been investigated, but in contrast to cutaneous xanthelasmas, no obvious association with lipid metabolism disorders or hypercholesterolemia was found for gastric xanthelasmas (Naito et al., 1991; Covotta et al., 1994; Owen, 1999). Our cases had also no systemic signs of xanthomatosis and only two of our five patients had hyperlipidemia. Fasting blood glucose levels of the patients were within normal limits; only one patient had mild diabetes mellitus. Furthermore, we have examined the patients for skin lesions. Even though some cutaneous lesions that accompany gastric xanthelasma were observed in a small number of our cases and in literature, we did not determine any specific lesion. These findings are in agreement with those of Isomoto's study who also reported no association of gastric xanthelasma with diabetes, hypercholesterolemia, or skin xanthomas (Isomoto et al., 1999).

The detection of Helicobacter pylori antigens in the cytoplasms of xanthelasma cells in some studies led to the hypothesis that these lesions may be precipitated by Helicobacter pylori infection (Hori and Tsutsumi., 1996). Gastric xanthelasma was also associated with atrophic gastritis, possibly secondary to chronic persistent infection by Helicobacter pylori (Isomoto et al., 1999). Similarly, we determined that two of the patients had atrophic or chronic gastritis. However, gastric xanthelasma had been reported in patients without gastritis or Helicobacter pylori. In contrast to these reports, Helicobacter pylori could not be demonstrated in our patients although one had a duodenal ulcer and the

prevalence of Helicobacter pylori infection is high in our country. In another study from our country, 76% of patients with xanthelasma had atrophic gastritis, and the presence of Helicobacter pylori was shown in 53% of these patients (Gencosmanoglu, et al., 2004). The incidence of gastric xanthelasma in a population may be associated with the prevalence of Helicobacter pylori infection and its associated atrophic gastritis

In various studies, the gastric glands around the lesions were found to exhibit moderate-to-severe atrophy (89%) and intestinal metaplasia (13%) (Chen et al., 1989; Naito et al., 1991; Isomoto et al., 1999). Xanthelasmas were also found to be associated with chronic gastritis and GI anastomoses (Chen et al., 1989). Some studies found that gastric xanthelasma was associated not only with age but also with the severity of gastric atrophy (Sekikawa et al., 2013). In patients with atrophic gastritis, Sekikawa et al. (2013) found that gastric cancer was detected more frequently in those with gastric xanthelasma than in those without. Therefore, vigilance for gastric xanthelasma in patients with atrophic gastritis may be an effective approach for surveillance of early gastric cancer. No malignant changes were detected in any of our patients.

The endoscopic appearances of gastric xanthelasmas may be confused with gastric tumors. Atrophic gastritis, intestinal metaplasia, Helicobacter pylori infection and chronic gastritis, all of which are predisposing conditions for gastric cancer, may accompany xanthelasmas. In a recent study, the presence of gastric xanthelasma, in addition to age and severe gastric atrophy, was also identified as a risk factor for gastric cancer (Sekikawa et al., 2013). However, it is still unclear whether gastric xanthelasma is a useful warning sign for the presence of early gastric cancer and further studies are needed to clarify the significance of gastric xanthelasma in relation to gastric cancer. Furthermore, there is a case description with a clear-cell carcinoid tumor of the stomach, in which the endoscopic and microscopic findings resembled a gastric xanthelasma (Luk et al., 1997). Muraoka et al. (1988)observed an association between gastric cancer and xanthoma. On histopathologic evaluation, gastric xanthelasma are characterized by the presence of numerous foamy histiocytes in the lamina propria. This microscopic appearance is reminiscent of that observed in signet ring-cell carcinoma. Thus, some studies have suggested that xanthelasma should be differentiated from signet ring cell carcinoma (Dreude et al., 1982).

Gastric xanthelasma has received little attention, as its benign nature has been considered to have little clinical significance. No treatment is necessary but histologic assessment is mandatory because some gastric malignancies may also macroscopically resemble these benign lesions. When a patient is diagnosed with upper GI tract xanthelasmas, we do not recommend routine endoscopic follow-up.

In conclusion, xanthelasmas of the upper GI tract may be rarely encountered during upper GI endoscopies and their clinical significance remains unknown. Because these lesions may have a similar appearance with some neoplasms, all endoscopists should be aware of these lesions and it seems reasonable to perform biopsies for histopathology and investigate the presence of Helicobacter pylori.

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