

Gastric Xanthelasma: Innocent impersonator

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Abstract

Gastric xanthelasma also known as gastric xanthoma is a benign asymptomatic condition that can mimic malignancy and is associated with a few other conditions of the stomach. A careful examination of the gastrointestinal tract for other co-existing conditions and histopathological confirmation of the diagnosis is needed. Gastric xanthomas are comparatively rare their incidence ranges from 0.018-0.8%, which is more frequent when compared to esophageal and duodenal xanthomas. The most common location of xanthelasmas of the gastrointestinal tract was the stomach (76%), followed by the esophagus (12%) and duodenum (12%). Here we report two patients who presented with symptoms of dyspepsia for 2 months and 3 months respectively. An endoscopy was done to find the cause of dyspepsia. Histopathological diagnosis of gastric xanthelasma was made for both patients. Gastric xanthelasma is now viewed as a warning sign of the presence of gastric malignancy. Here we report these 2 cases to emphasize that gastric xanthoma should not be overlooked when encountered endoscopically and histopathological examination is essential for diagnosis.

Keywords: Gastric Xanthelasma, Lipid-laden macrophages, Endoscopy, Helicobacter pylori.

Introduction

Gastric Xanthelasmas, also known as xanthomas, was first defined by Orth in 1887 as lipid-laden macrophages in the gastric mucosa 1,2. Though the incidence of gastric xanthelasmas is rare, the stomach is still the most common location of xanthelasmas in the gastrointestinal tract. The incidence of upper GI xanthelasma ranges from 0.018-0.8% ³. Gastric xanthelasma incidence increases with age and there is a slight male preponderance. The lesion was seen in people of age 21 -60 years with a peak in age distribution in 40-60 years ⁴. The most common site is the antrum and pyloric region of the stomach followed by the esophagus and duodenum to a much lesser extent. Gastric xanthomas occur more often in a mucosa with chronic gastritis, intestinal metaplasia, atrophic gastritis, and alterations induced by bile reflux or partial gastrectomy, than in a normal mucosa ^{5,6}. There are very few reported cases of xanthelasma in children. There are few published reports on gastric xanthelasma, which is a mimicker prone to an incorrect diagnosis. The lesion itself is somewhat less significant but

ruling out malignancies and arriving at an accurate diagnosis are of utmost importance. So, an endoscopic biopsy becomes mandatory for diagnosis³.

Case 1

A 70-year-old male, presented with dyspepsia for 2 months. Patient was treated with proton pump inhibitor for 15 days. As there was no improvement in symptoms, endoscopy guided biopsy was taken and sent for histopathological examination. Microscopic examination of the tissue showed superficial fragments of gastric mucosa with expanded lamina propria showing sheets of foamy histiocytes and scattered lymphocytes. Another fragment appeared polypoidal with few elongated and distorted gastric foveolae with minimal lymphoplasmacytic infiltrate in the lamina propria. There was co-existing gastric xanthelasma and gastric hyperplastic polyp. No evidence of atypia, intestinal metaplasia, or activity was seen in the submitted sections. Special stains to rule out the differential diagnoses were done. Giemsa staining was done and was negative for *Helicobacter pylori*. Acid-fast bacilli (AFB) staining was done and the lesion turned out to be negative for mycobacteria. Periodic acid-Schiff (PAS) staining showed that the foamy histiocytes did not take up PAS, indicating no mucin content to rule out signet ring cell carcinoma. Hence a final diagnosis of gastric xanthelasma was made.

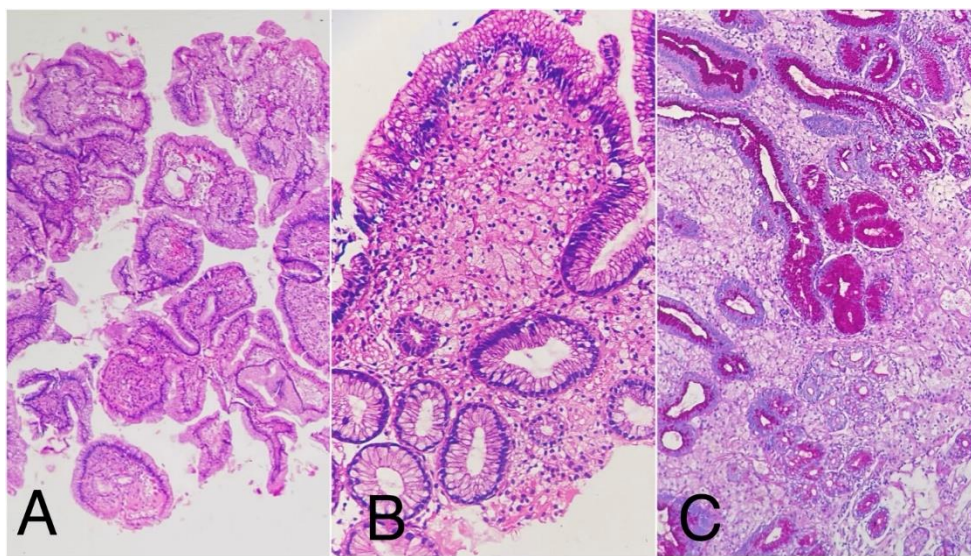


Figure 1: Shows superficial fragments of gastric mucosa with expanded lamina propria showing sheets of foamy histiocytes and scattered lymphocytes (A and B). Foamy histiocytes are negative for PAS stain (C).

Case 2

A 60-year-old male, presented with indigestion and loss of appetite for 3 months. An endoscopy was done that showed a polypoid growth in the body of the stomach. Endoscopy-guided biopsy from the polypoidal lesion was taken. Microscopic examination of the biopsied fragments of gastric corporal mucosa showed a polypoidal fragment with expanded lamina propria packed with sheets of foamy histiocytes with abundant bubbly cytoplasm. The focal area showed intestinal-type metaplasia. No dysplasia, activity, or atrophy was noted. Special

stains were done to confirm the diagnosis. Giemsa staining was done and was negative for *Helicobacter pylori*. AFB stain was negative for acid-fast bacilli and the PAS stain was not taken up by the foamy macrophages. Final diagnosis of gastric xanthelasma was made.

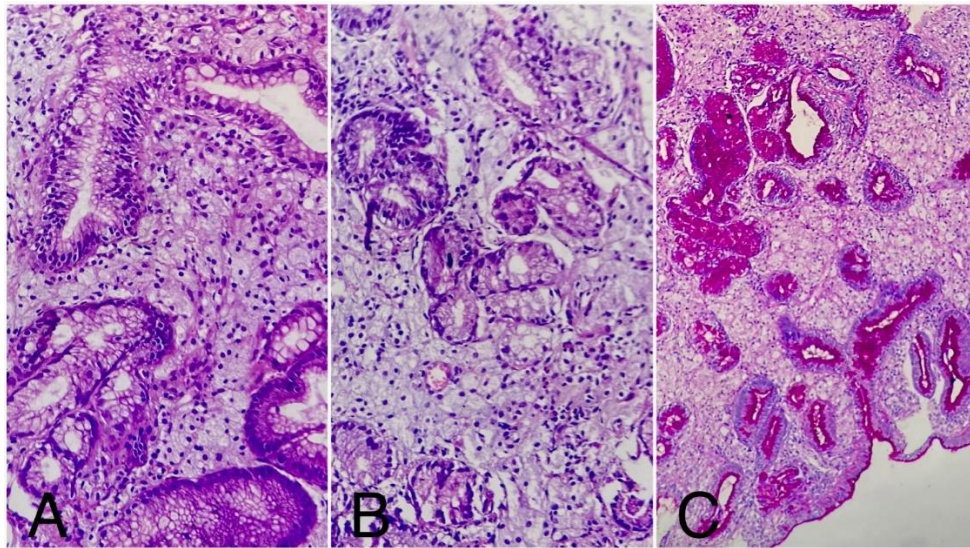


Figure 2: Showed a polypoidal fragment with expanded lamina propria packed with sheets of foamy histiocytes with abundant bubbly cytoplasm (A and B). Foamy histiocytes are negative for PAS stain (C).

Discussion

Most GI xanthelasmas are incidental findings on endoscopy since xanthelasma are asymptomatic. On endoscopy, they are yellowish to white, well-demarcated nodular lesions. Xanthelasmas are composed of large foamy cells containing a mixture of lipids, including cholesterol, neutral fat, low-density lipoprotein, and oxidized low-density lipoprotein⁷. A possible relationship with lipid metabolism has been investigated, but in contrast to cutaneous xanthelasmas, no obvious association with lipid metabolism disorders or hypercholesterolemia was found for gastric xanthelasmas⁸. Xanthelasma of the gastrointestinal tract being an incidental finding does not require any treatment but only if the diagnosis is definite.

Gastric xanthelasma has many differential diagnoses such as mycobacterium avium intercellulare complex infection, Whipple's disease, signet ring cell carcinoma, granular cell tumor, and rarely neuroendocrine tumor. Xanthelasma is a diagnosis of exclusion. To make an accurate diagnosis of xanthelasma, it is essential to differentiate it from its mimickers. Some special stains are used to rule out differential diagnoses. Immunohistochemistry also plays a role in distinguishing xanthelasma from other conditions with similar microscopic features. Mycobacterium avium intercellulare complex infection in the stomach can show very similar histopathological features to Xanthelasma. This can be differentiated by doing an Acid-Fast Bacilli (AFB) stain. This stain will highlight the presence of acid-fast bacilli. Whipple's disease is a bacterial infection caused by *Tropheryma whipplei*. It is more commonly seen in the small intestine rather than stomach and is more of a clinical diagnosis

than a histopathological one. In the cases of suspected Whipple's disease, the small intestinal biopsies will show additional features like blunting of villi, fat vacuoles in the lamina propria, and scattered dilated lacteals. Microscopically, granular cell tumors have polygonal cells with granular cytoplasm round to oval hyperchromatic nuclei whereas xanthoma is composed of cells with abundant clear cytoplasm. Granular cell tumors are also positive for S-100 immunohistochemistry. Another look-alike of gastric xanthelasma is signet ring cell carcinoma. Signet ring cell carcinoma is a poorly differentiated tumor with a poor prognosis. It is characterized by the proliferation of signet ring cells that are formed due to excess production of intracellular mucin that pushes off the nucleus to a side. This appearance of the cell looks very similar to a foamy histiocyte that has a clear and bubbly cytoplasm. Also, signet ring cell carcinoma has nuclear pleomorphism which is absent in xanthoma. Periodic Acid Schiff (PAS) stain is done which will be taken up by mucin. PAS will be negative in xanthelasma as the foamy histiocytes will not take up PAS due to the absence of mucin in them. Also, there are reports of a rare clear cell variant of a gastric carcinoid tumor that was first thought to be xanthelasma then histopathological examination revealed the diagnosis⁹. It was ruled out because there was no nests or cords formation and no typical carcinoid cells were made out. Before making a diagnosis of xanthelasma, special stains and if needed IHC should be done to rule out carcinoma, as definitive treatment is needed for the latter.

Unlike cutaneous xanthomas, there is no association found between xanthelasma and hyperlipidemia⁸. Even though initially *Helicobacter pylori* was thought to be an etiological factor in the development of xanthelasma, recent studies suggest that the association of *H. pylori* with xanthelasma depends on the prevalence of the organism in that specific population¹⁰. Gastric xanthelasma was identified to be a condition associated with gastric cancer in a retrospective study⁶. Some studies show that xanthelasma are related to the rate of growth of gastric cancers and are frequently associated with rapidly growing cancers of the stomach¹¹. Xanthomas do not directly turn into a malignancy but when a gastric xanthoma is encountered, it is essential to examine the whole gastric mucosa for any co-existing lesion¹².

Conclusion

The pathogenesis of gastric xanthelasma is now considered to be a healing response to local trauma or inflammation. This chronic gastric mucosal trauma or injury is the basis for the development of gastric cancer. Gastric xanthelasma directly giving rise to gastric malignancy has not been proven but the presence of gastric xanthelasma is associated with the presence of gastric malignancy. Gastric xanthelasma is now viewed as a warning sign of the presence of gastric malignancy in a patient. Gastric cancer is still one of the leading causes of cancer-related deaths worldwide. Thus, gastric xanthelasma, even though is not so significant should not be disregarded but should be well studied to rule out other above-mentioned differential diagnoses.

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