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Case report

Case Series: The Gastric Face of Lipid Deposits

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Abstract

Xanthoma is a benign lesion associated with lipid metabolism, commonly manifesting in various areas of the body. Gastric xanthomas, often incidentally identified during endoscopic procedures, are histopathologically characterized by the presence of foamy histiocytes in the gastric mucosa. Their prevalence ranges from 0.23% to 7%, with the antrum being the most frequently affected site and a clear association with increasing age.

This study presents 20 cases of patients diagnosed with gastric xanthoma between 2016 and early 2024. Chronic gastritis was observed in 90% of patients, intestinal metaplasia in 20%, mild atrophy in 25%, and low-grade dysplasia in only one case (5%). In addition, *Helicobacter pylori* infection was detected in 30% of the cases. The importance of conducting prospective research is emphasized to better understand the relationship between gastric mucosal alterations and gastric xanthomas, with a particular focus on early detection of gastric cancer.

Keywords

Xanthoma, *Helicobacter pylori*, atrophic gastritis, metaplasia.

INTRODUCTION

A *xanthoma* is defined as a benign, localized lesion of cholesterol deposits. First described in the early 20th century following histological studies in patients with these lesions in various body regions, it is associated with lipid metabolism[(1)]. These deposits frequently appear in periarticular areas, such as the trunk or extremities, as a result of hyperlipidemia (primary or secondary diabetes, hypothyroidism, myeloma, lymphoma, leukemia, and obstructive liver diseases)[(2)]. Xanthelasmas, also linked to hyperlipidemia, manifest subcutaneously, most commonly on the eyelids, presenting as yellowish plaques and papules[(3,4)].

The pathogenic mechanism of xanthoma formation begins with localized increased filtration of low-density lipoproteins (LDL) from the vascular network into underlying tissues. As these lipid aggregates accumulate, monocytes and macrophages phagocytize the lipoproteins, giving rise to foam cells[(5)]. Gastric xanthomas are incidentally found in the gastrointestinal tract during upper endoscopies[(6,7)]. The most significant histopathological finding is foam-laden histiocytes in the lamina propria of the gastric mucosa,

occasionally accompanied by plasma cells, smooth muscle cells, and Schwann cells[5]. Their incidence ranges from 0.23% to 7%[6,8]). According to Gómez Martín et al., most are located in the antrum (53%), body (32%), antrum and body (10%), and fundus (5%). Additionally, xanthomas appeared as solitary lesions in 72% of cases[7].

In a study by Wei Na Shen et al. involving 47,736 patients who underwent endoscopy between January 2020 and December 2021, gastric xanthoma was detected in 2.85% (1,360 patients). Of these, 62.06% had a single lesion, while 37.94% had multiple lesions. The most common location was the antrum (52.50%), followed by the body (18.16%), with nonspecific locations accounting for 18.31%[9].

The etiology remains poorly defined, though two theories exist: the first focuses on hyperlipidemia (metabolic disorders such as type 2 diabetes and obesity), independent of gastric conditions; the second centers on prior gastric mucosal alterations, regardless of metabolic disorders. Key mucosal changes include chronic atrophic gastritis, complete intestinal metaplasia, gastric ulcer, *Helicobacter pylori* infection, bile reflux lesions, and partial Billroth gastrectomies[10]. Similarly, studies have established a significant association between gastric xanthomas and mucosal lesions such as chronic gastritis, atrophy, gastric cancer, and *H. pylori* infection[11-13].

METHODOLOGY

A retrospective search was conducted using endoscopic data and images from patients treated at Instituto de Gastroenterología y Hepatología del Oriente (IGHO S.A.S.) between 2016 and 2024, whose histopathological findings confirmed gastric xanthoma. Prior to inclusion, patients signed informed consent permitting the use of their anonymized data and images for research purposes.

RESULTS

A total of 20 cases of gastric xanthoma were identified, with detailed characteristics presented in **Table 1**. The mean age of these patients was 55.5 years (standard deviation: 13.3), with a minimum age of 37 and a maximum of 81. Sex distribution was equal, with 50% male and 50% female.

The most frequent relevant medical histories were hypertension (25%) and hypothyroidism (20%). Regarding lesion quantity, gastric xanthomas ranged from 1 to 4 lesions per case, with 75% of patients presenting multiple lesions. **Figure 1** illustrates their distribution across gastric regions: most were located in the gastric antrum (60%), followed by the gastric body (25%), fundus (5%), angular notch (5%), and pylorus (5%).

Table 1. Case Characterization

Variable	Category	n: 20	%
Sex	Male	10	50
	Female	10	50
Number of Lesions	1	5	25
	2	5	25
	3	5	25
	4	5	25
Location	Antrum	12	60
	Body	5	25
	Fundus	1	5
	Angular notch	1	5
	Pylorus	1	5
Metaplasia	No	16	80
	Yes	4	20
Atrophy	No	15	75
	Yes	5	25
H. pylori	No	14	70
	Yes	6	30
Dysplasia	No	19	95
	Yes	1	5
Metaplasia percentage	0%	16	80
	20%	1	5
	40%	2	10
	60%	1	5

Table prepared by the authors.

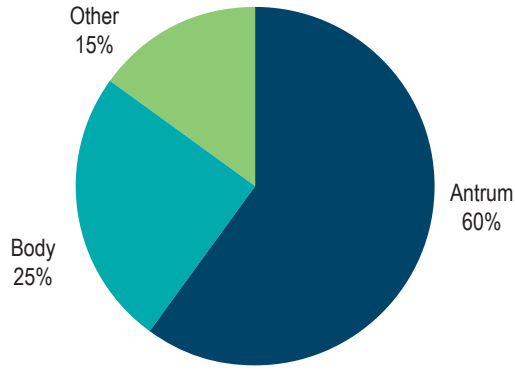

Figure 1. Distribution of gastric xanthomas by location. Image property of the authors.

Pathological analysis revealed chronic gastritis in 90% of cases. Moderately diffuse chronic gastritis was most prevalent (66.6%), followed by active follicular chronic gastritis (16%). Intestinal metaplasia was identified in four patients (20%, 40%, and 60% involvement in one, two, and one case(s), respectively). Mild gastric mucosal atrophy was observed in five patients, and low-grade dysplasia in

one case. *H. pylori* infection was detected in 30% of cases (6 patients), underscoring its relevance in gastrointestinal pathology.

Figures 2–6 provide morphological descriptions of endoscopic and histopathological findings, offering anatomical and microscopic details of the gastric xanthoma lesions.

DISCUSSION

Current literature demonstrates a significant increase in the incidence of these benign lesions among individuals over 60 years old, highlighting a correlation between advanced age and gastric xanthoma prevalence[12]. In the findings observed in the 20 patients diagnosed with this condition, the highest frequency was recorded in individuals in their fifth decade of life, accounting for 30% of cases.

Regarding sex distribution, the reviewed studies indicate that both men and women show similar incidence rates of these lesions. A study by Yi Chen et al.[15] identified 1,370 gastric xanthoma cases, distributed among 667 women and 703 men, but no significant difference in lesion incidence between sexes was demonstrated. In the cases reported in this article, we found an equal distribution between both sexes. However, it is relevant to consider that some studies postulate a higher prevalence of this lesion in men than in women[9].

Additionally, the most common location of these benign lesions tends to be predominantly in the gastric antrum[9,15,16], and these studies suggest a higher probability of finding a single gastric xanthoma lesion in the population. Regarding our case report findings, we observed agreement with the lesion location but not with the number of lesions, as 75% of cases presented with more than one lesion. This suggests the existence of particular characteristics in our population that warrant in-depth investigation.

It is crucial to note that chronic gastritis diagnosis is based on histopathological findings, with potential progression to atrophy and metaplasia over time[17]. When reviewing studies linking chronic gastritis to gastric xanthomas, we found limited evidence on this subject, with the few available studies suggesting a low incidence, representing a small percentage (2.29%) in patients with gastric xanthomas[9]. In our analysis, we found that 90% of the 20 cases presented with this condition, a discrepancy that may correspond to the coexistence of both conditions in our population.

Previous studies have demonstrated a strong association between gastric xanthomas and the presence of gastric mucosal atrophy[18,19]. In our case series, 30% presented with this association, similar to the findings of the study by Dinghong Xiao et al., where 30.1% of the studied population showed gastric mucosal atrophy[16]. Thus, this reinfor-

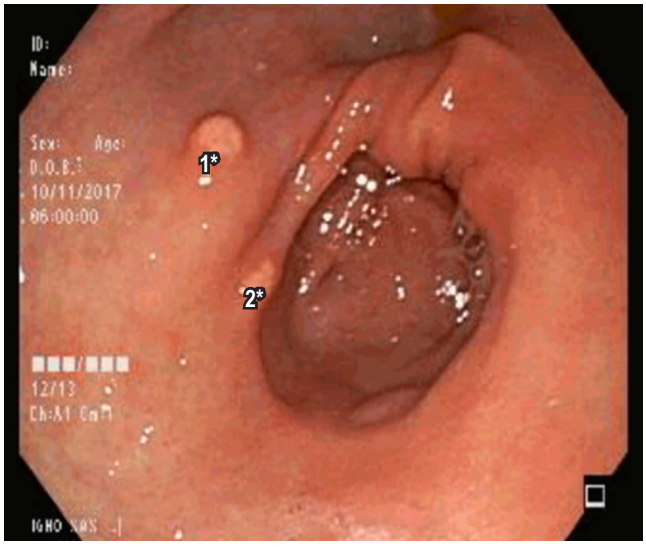

Figure 2. The gastric antrum is observed between the anterior wall and lesser curvature, classified as Paris 0-1s[14]. The lesion (1*) measures approximately 8 mm in diameter, with a yellowish, speckled, xanthomatous appearance and irregular borders. A second lesion (2*), approximately 5 mm, is located on the more proximal anterior wall near the pylorus, exhibiting similar yellowish speckling. Image property of the authors.

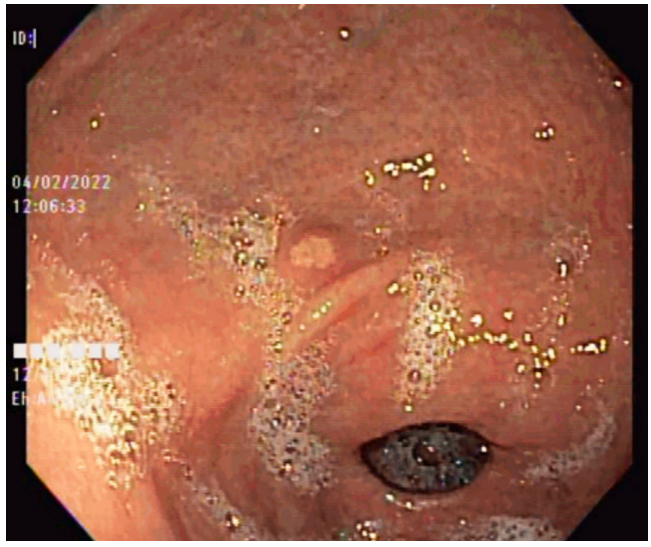

Figure 3. A yellowish, mottled lesion measuring ~4 mm in diameter (Paris 0-1s classification)[14] is observed in the antral region along the curvature and anterior wall. Image property of the authors.

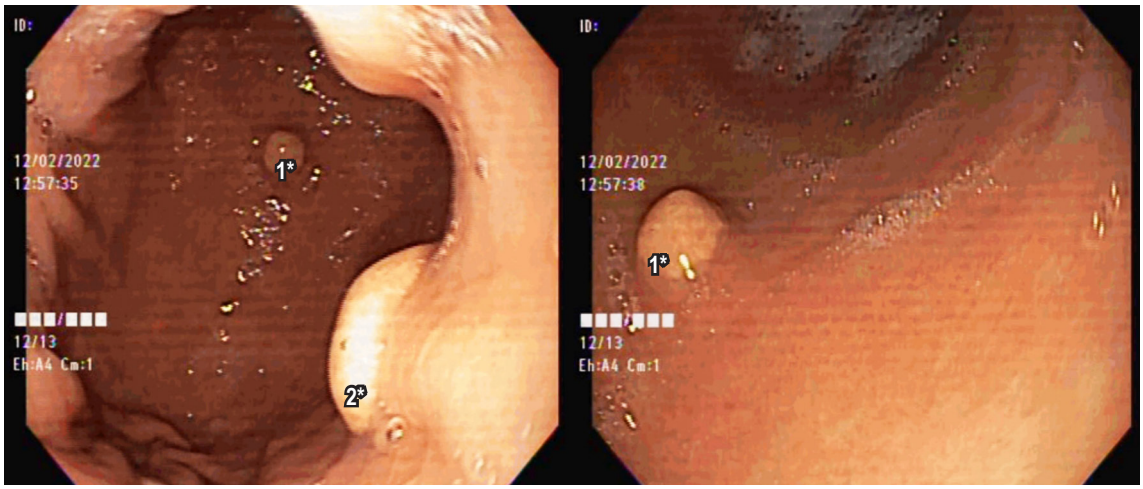

Figure 4. Endoscopic images of two lesions: The first (1*), located at the antral-body junction between the greater curvature and anterior wall, measures 7 mm with a yellowish surface (Paris 0-1s)[14]. The second (2*), ~10 mm in diameter, is positioned in the proximal body near the posterior wall along the lesser curvature. Images property of the authors.

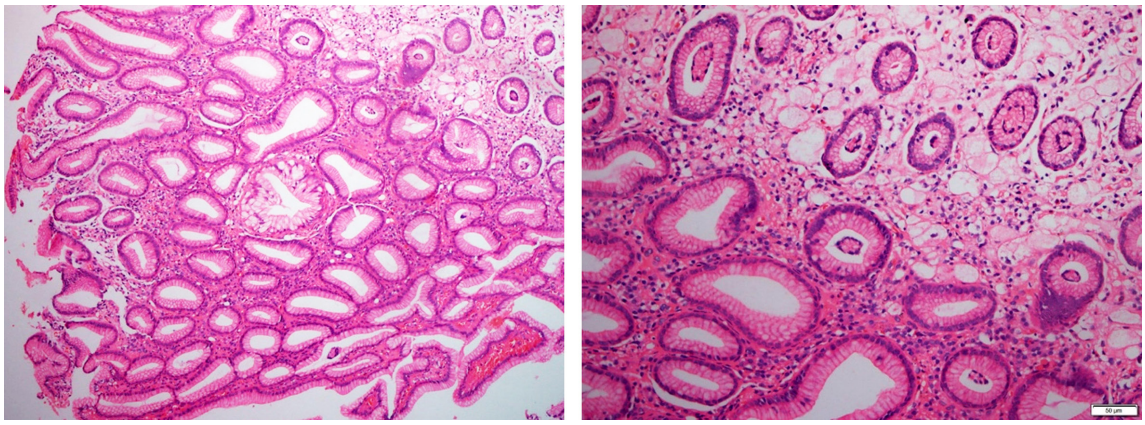

Figure 5. Histopathological images (20× and 40×, H&E staining). Gastric mucosa shows numerous foam-laden histiocytes in the lamina propria, with abundant globular, clear cytoplasm and round-to-oval, occasionally eccentric nuclei. Images property of the authors.

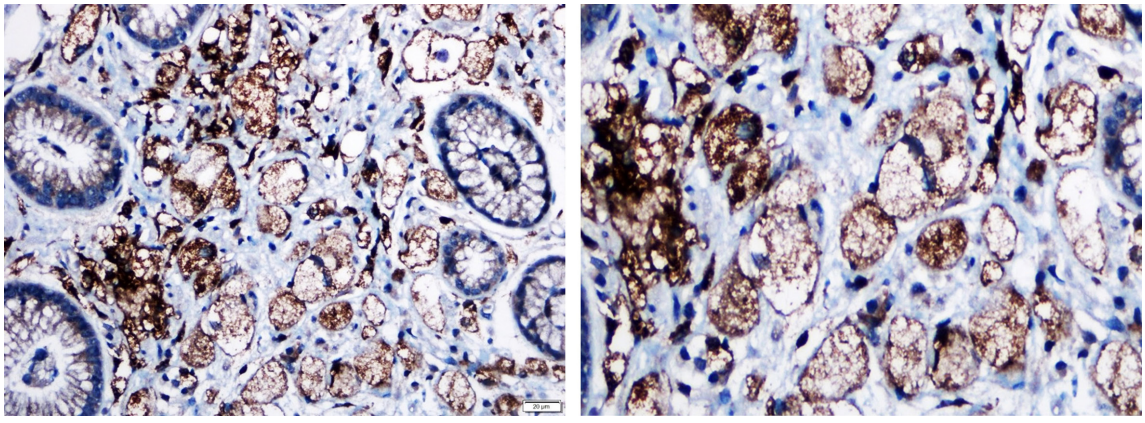

Figure 6. Immunohistochemistry was strongly positive for CD68 in all described cellular elements. Notably, these cells were negative for pan-cytokeratin and epithelial membrane antigen. Images property of the authors.

ces the idea that gastric xanthomas may be related to degenerative changes in the gastric mucosa.

A study conducted by Sekikawa et al. demonstrated that the presence of gastric xanthomas was associated with gastric cancer, with an odds ratio (OR) of 7.19 (95% confidence interval [CI]: 2.50-20.83) in the studied population[12]. Similarly, the study by Dinghong Xiao et al. revealed that gastric xanthoma was significantly associated with the presence of intestinal metaplasia (OR: 2.3; 95% CI: 1.6-3.2)[16]. In our results, no cases of gastric cancer were present, suggesting the need to expand the study sample size.

Regarding intestinal metaplasia and dysplasia in relation to gastric xanthomas, previous studies have reported a significant association with intestinal metaplasia ($p < 0.001$)[15] and a prevalence of approximately 49%[15,20]. Concerning dysplasia, the reviewed literature suggests a significant relationship ($p < 0.001$)[15]. In our study, intestinal metaplasia was evident in only 20% of cases, and intestinal dysplasia was identified in only one patient.

Regarding *H. pylori* infection, which has been the subject of numerous recent studies due to its association with gastric cancer, some research indicates a prevalence of about 94% in the relationship between the bacteria and gastric xanthomas[20]. The study conducted by Chen et al.[15] reports an *H. pylor*i prevalence of 30.8%. In our reported cases, we found that 30% of patients with gastric xanthoma had the bacteria. Finally, the immunohistochemistry results from our cases correlate exactly with what is described in the literature, highlighting intense positivity for CD68 with negativity in all cases for pan-keratins and epithelial membrane antigen[21].

CONCLUSION

Based on the above, there may be a relationship between the presence of gastric xanthomas and premalignant gastric lesions; therefore, additional studies are needed to confirm this hypothesis. Identifying this association could contribute to detecting new conditions or risk factors that facilitate the prevention and early diagnosis of malignant and premalignant gastric lesions. However, the information and data available to date are insufficient to make recommendations about modifications to clinical practice that could be included in current guidelines.

The study has certain limitations, as it is a retrospective study in which patient selection and data collection were based on existing reports. Additionally, the sample size limits the ability to establish robust associations and generalize the results. Prospective studies with more representative samples are needed to determine the relationship between premalignant gastric lesions and gastric xanthoma. This would facilitate the identification of additional predictive factors for gastric cancer prevention.

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