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Case Report

Gastric Xanthomatous Hyperplastic Polyps – Just an Incidental Endoscopic Finding?

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ABSTRACT

Background: Laparoscopic sleeve gastrectomy (LSG) progressively became the preferred procedure worldwide for the treatment of morbid obesity. Occasionally, unknown gastrointestinal diseases may be incidentally discovered during the procedure or on the histologic gastric specimen. Gastric xanthomas are uncommon lesions of the lamina propria, composed by foamy macrophages and mixed inflammatory infiltrate. Rarely, xanthoma cells develop within a gastric hyperplastic polyp. Although usually benign, they may be associated with pre-malignant conditions or even gastric cancer, making advisable an appropriate workup.

Case Presentation: A hyperplastic polyp with xanthomatous proliferation was discovered in the gastric specimen of a young man, suffering from severe obesity and metabolic syndrome. The patient had been treated with proton pump inhibitors for gastric discomfort for years. After the surgical procedure, the gastric discomfort rapidly disappeared.

Conclusion: Obesity is often complicated by gastrointestinal abnormalities discovered during ultrasound or endoscopic procedures. Incidental findings of unknown gastric lesions are common occurrences during sleeve gastrectomy. Although xanthelasmas per se are harmless, they might coexist with pre-malignant/malignant lesions, especially when associated with gastric polyps. Thus, prompt intra-operative recognition and adequate work-up are mandatory. Although cases of gastric polyps or xanthomas are not a novelty, to our knowledge, this is the first case reporting about the discovery of a gastric hyperplastic polyp with xanthomatous proliferation on gastric histological piece. From the discussion of this case and of similar reports in the literature, we advocated for the importance of endoscopic screening in obese patients admitted for bariatric surgery to address the proper surgical approach and follow-up.

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Background

I Histological Findings during Laparoscopic Sleeve Gastrectomy

Obesity is a pro-inflammatory and pro-carcinogenic condition and often coexists with gastrointestinal diseases such as esophageal reflux disease,

Barrett's esophagus, gastritis, gallstone and neoplastic tumors of the esophagus, stomach, colon and pancreas [1, 2]. Undoubtedly, bariatric surgery is an effective treatment for morbid obesity. However, being a surgical and irreversible procedure, an accurate pre-operative study is advisable to limit the risk of complications and patient discomfort. Nowadays, LSG represents more than 50% of surgical procedures for obesity [3]. Poor histological data on bariatric surgery are available. A

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recent retrospective study of 248 bariatric cases revealed abnormal histological findings in more than half of the patients [4]. Unexpected findings such as *Helicobacter pylori* gastritis, autoimmune gastritis, micro carcinoid formations, metaplasia, and vasculitis, warranting clinical follow-up, emerged in 8.4% of cases [5-8].

II Gastric Hyperplastic Polyps and Xanthomatous Hyperplastic Polyps

Gastric xanthomas are characterized by the recruitment of fat-laden histocytes in the lamina propria, with destruction and effacement of the gastric mucosa [9-12]. Although the discovery during LGS is uncommon (0.02-0.3%), the stomach is the most frequent localization of intestinal xanthomas, whose incidence varies between 0.2 and 7%. For years, gastric xanthomas have been considered benign lesions with little clinical implications, however, retrospective studies recently demonstrated a correlation with early gastric cancer [13]. Gastric

hyperplastic polyps, the most frequent polyps in the stomach, derived excessive proliferation and exfoliation of foveolar cells. They are commonly associated with *Helicobacter pylori* infection, which should be eradicated to avoid the development of intestinal metaplasia [14]. Due to the risk of malignant transformation, resection of the lesion and endoscopic surveillance is recommended [14].

While gastric hyperplastic polyps and gastric xanthoma are frequently encountered, polyps with xanthomatous degeneration, called “gastric xanthomatous hyperplastic polyps” (XHP), are rare. Up to now, just a few cases have been described (Table 1) [11, 15-24]. According to the few cases reported, gastric xanthelasmas might predict the development of early gastric cancer [11, 15-24]. Therefore, a biopsy of the surrounding area is recommended [11, 15]. Herein, the incidental discovery of xanthomatous gastric polyp in the gastric specimen from bariatric surgery was discussed.

Table 1: Demographic and clinical features of thirteen cases of gastro-enteric xanthomatous hyperplastic polyps.

First Author, year	Sex	Age	Diameter	Localization	Gastritis	H. py	Cancer	Lipid profile
Ginsbach <i>et al.</i> , 1988 **	-	-	-	multiple	-	-	-	-
Hirasaki <i>et al.</i> , 2009	M	69 yrs	7 mm	antrum, multiple	metaplasia	yes	-	normal
Lin Py <i>et al.</i> , 1989**	-	-	-	multiple	erosive	-	-	-
Vazquez <i>et al.</i> , 2009 *	F	82 yrs	8 mm	greater curvature	-	-	-	-
Ashwini <i>et al.</i> , 2013**	M	70 yrs	-	-	yes	-	-	-
Tezcan E <i>et al.</i> , 2017**	M	46 yrs	3 mm	fundus	no	no	no	-
Tezcan E <i>et al.</i> , 2017 **	F	56 yrs	4 mm	antrum	no	no	no	-
Rey <i>et al.</i> , 2014 *	F	44 yrs	-	multiple	no	no	no	normal
Fukuda <i>et al.</i> , 2015 **	M	73 yrs	-	antrum	no	no	gastric	-
Basullo <i>et al.</i> , 2013	F	78 yrs	2 mm	cardia	inactive	no	-	normal
Basullo <i>et al.</i> , 2013	F	68 yrs	5-6 mm	fundus, multifocal	no	no	colonrectal	normal
Basullo <i>et al.</i> , 2013	M	68 yrs	4 mm	fundus	no	no	-	normal
Basullo <i>et al.</i> , 2013	M	45 yrs	3 mm	antrum	inactive	No	-	normal
Basullo <i>et al.</i> , 2013	M	48 yrs	6 mm	fundus	inactive	-	-	normal
Present case	M	32 yrs	7 mm	greater curvature	non atrophic	No	-	dyslipidaemia

Gastritis: presence of pathological changes suggestive of gastritis (active, chronic, atrophic, non-atrophic) in the surrounding mucosa; H. py: concomitant presence of *Helicobacter pylori* infection. yes: present; no: absent; -: not available. *not in English; **only abstract available.

Case Presentation

A 32-year-old Caucasian man was referred to the Obesity Outpatient Clinic, Endocrine Unit in Varese, for clinical evaluation of morbid obesity condition. He had a family history of hypertension and dyslipidemia. Smoker from the age of 15 years, he was unmarried and was working as a barman. Suffering from overweight from childhood, he had been declared unfit for military service at the age of 20. He had been previously admitted to the Surgery Department for acute diverticulitis, treated with urgent left hemicolectomy. After the diagnosis of chronic gastritis in 2015, he had been treated with daily proton pump inhibitors. At the age of 27, the patient's weight was 115 kg, height 169 cm (BMI 40.3 Kg/m²). After unsuccessful weight loss attempts, he underwent the application of an adjustable gastric bandage, managing to lose 55 kg. In the following years, he succeeded in stabilizing his body weight. In 2012, due to the patient's discomfort, the gastric bandage was removed, with consequent rapid weight regain. When he was admitted

at the Obesity Outpatient Clinic, he had reached the weight of 125 Kg (anthropometric measures: BMI 43.8 kg/m², waist circumference 124 cm; estimation of abdominal fat by bioelectrical impedance: trunk fat 56%, visceral fat 35%). He suffered from fatty liver disease, hiatal hernia and severe obstructive sleep apnea syndrome. Metabolic syndrome, defined by the coexistence of hypertension, dyslipidemia and fasting hyperglycemia, was diagnosed.

According to guidelines, endocrine disorders as contributory causes of excess body weight were ruled out (serum TSH levels 0.96 mcU/ml - normal range 0.31-4.5 mcU/ml; blood cortisol secretion after Nugent suppression test was 6.4 ng/ml - normal range < 18 ng/ml) [2]. The interview revealed the habit of picking and nibbling food during the day, often being unable to plan a complete meal until midnight. He was given dietary counseling by the dietitian (1800 Kcal daily, 55% carbohydrates, 28% lipids, 17% proteins), and he managed to modify his dietary style. In February 2017, due to his young age, the degree of morbid obesity

and the absence of organic or psychological contraindications, the patient underwent LSG at the Bariatric Surgery Centre. The procedure lasted 165 minutes and was uneventful. A residual scar from the previous gastric bandage, determining the adherence of gastric fundus to the spleen, was removed. The macroscopic analysis of the large surgical specimen from LSG revealed a gastric polyp of 0.7 cm arising from the greater curvature. Histopathologic slides stained with hematoxylin and eosin showed foamy histiocytes, inflammatory cells, fibrous tissue, and multinucleated giant cells, suggesting the diagnosis of hyperplastic polyp associated with gastric xanthelasma (Figure 1). The surrounding mucosa showed chronic inflammatory changes, suggestive of non-atrophic inactive chronic gastritis. Giemsa staining excluded the presence of *Helicobacter pylori* infection. There was no evidence of malignancy. The postoperative course was regular. The gastro-duodenal transit study was normal. He was prescribed pantoprazole 40 mg/day and was advised to report if dyspeptic symptoms relapsed. He restored a significant clinical improvement of the gastrointestinal symptoms. In the following 10 months he managed to lose 29 Kg (weight 96.4 Kg, BMI 33.7 Kg/m², waist circumference 110 cm, trunk fat 37% and visceral fat 21%) achieving normal glycemic, hepatic and lipid profiles.

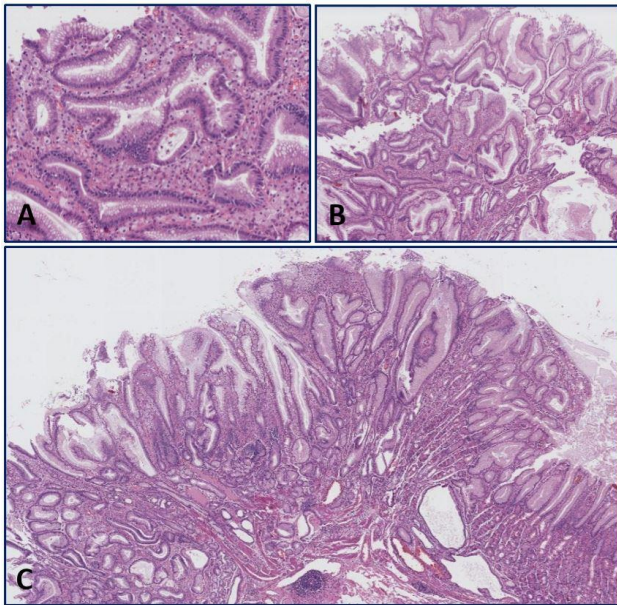


Figure 1: Gastric hyperplastic polyp with xanthomatous cells. **A & B)** foveolar epithelium with elongated and distorted architecture and cystic dilatations (H&E stain). **C)** Numerous foamy histiocytes in the lamina propria (H&E stain).

Conclusion

Obesity is often associated with gastrointestinal disorders. Remarkably, recent studies stressed a causative effect of obesity in the development of several types of cancers, like esophageal and gastric cancers [1]. Large retrospective studies stated that multifocal atrophic gastritis and intestinal metaplasia were significantly more common in patients with gastric xanthelasma, especially if multiple [13]. Therefore, gastric xanthelasma are warning endoscopic signs for the presence of pre-malignant lesions. Proper endoscopic diagnosis, treatment and follow-up are warranted. The etiology of xanthomas and xanthomatous hyperplastic polyps remains unclear. They are likely the result of the inflammatory response to mucosal damage, or the consequence of

gastric mucosa aging. A relation with coexisting gastric diseases such as chronic gastritis and *Helicobacter pylori* infection was speculated [11, 15]. Fasting blood glucose, neutrophil and carcinoembryonic antigen (CEA) have been significantly associated with gastric xanthelasma in a recent large retrospective endoscopic series among the Chinese population, but no consistent data are available on HPX [11-23]. The association with hyperlipidemia is unclear [11]. Two Korean studies on gastric xanthelasma found an inverse association with HDL-cholesterol levels and a direct association with LDL-cholesterol [11, 12]. Nevertheless, lipid accumulation has been ascribed as the cause of hyperplasia in the overlying mucosa [11].

Investigation on scientific databases using PubMed, Google Scholar and ResearchGate revealed a total of 15 cases of gastric hyperplastic polyps with xanthomatous proliferation (Table 1) [11, 15-24]. To our knowledge, only 13 of them had an English abstract and were considered for discussion [11, 15-24]. In this case series, the mean age was 63.4±13 years, 7 out of 15 cases were men. Lesions were < 1 cm of diameter (4.7 ± 2 mm). The smallest XHP was found at cardia in an old woman. Gastric discomfort, pain, bloating and heartburn were the main complaints. Apart from the case reported by Rey no data on BMI, glycemic profile, and concomitant treatment were available [22]. In that case, BMI was 29 Kg/m², and metabolic profile was normal [22]. No data were obtained on the previous treatment with proton pump inhibitor therapy. *Helicobacter pylori* infection did not appear as a major risk factor, while half of patients had gastritis. In two cases gastric XHP coexisted with gastrointestinal cancer (respectively gastric and colorectal) and in one case with intestinal metaplasia [15, 23, 24]. No data on follow-up after excision were available.

To our knowledge, our case is the first one reporting the discovery of gastric hyperplastic polyp with xanthomatous proliferation discovered during bariatric surgery. Indeed, we suggest an expansion of case reporting to improve scientific knowledge on its pathogenesis, clinical outcome, and appropriate workup. The correct clinical workup is mandatory, especially for patients suggested elective surgery. Bariatric surgeons and clinicians should be aware of the existence of benign and malignant tumors associated with obesity as well as of the optimal management of different conditions at the time of evaluation, during the surgical procedure and the postoperative period. In accordance with guidelines, we suggest that restrictive procedures may be preferred in those patients presenting with suspicious endoscopic signs.

Abbreviations

BMI: Body Mass Index

Ca: Cancer

CEA: Carcinoembryonic antigen

H. py: *Helicobacter pylori*

LSG: Laparoscopic Sleeve Gastrectomy

XHP: Gastric Xanthomatous Hyperplastic Polyps

Author Contributions

All the authors were directly involved in patient clinical work-up and took part in manuscript editing. DG and EP conceived the manuscript. LB supervised the final version of the manuscript. FF performed specimen analysis and drafted the description of Figure.

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DG received a scholarship for the management of obesity by the University of Insubria.

Consent for Publication

Written informed consent was obtained by the patient. All procedures described were part of the clinical workup of patients admitted for bariatric surgery. Thus, the description of this case report did not require specific Ethical Committee permission.

Conflicts of Interest

None.

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