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DOUBLE THE TROUBLE: A RARE FINDING OF GASTRITIS CYSTICA PROFUNDA IN A PREVIOUSLY UNOPERATED YOUNG FEMALE WITH CONCOMITANT *HELICOBACTER PYLORI* INFECTION

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ABSTRACT

Gastritis cystica profunda (GCP) is a rare lesion of the stomach. It is characterised by hyperplasia and cystic dilation of the gastric gland in the submucosal layer. It is usually believed to occur at the site of previous gastric surgeries, as the anastomotic remnants act as a foundation for the development of the lesion. We present a case of a 39-year-old female, previously healthy with no history of gastric surgeries, who sought medical care for melena and lethargy of one month's duration. Her complete blood count showed a significant drop in haemoglobin (from 13 to 9 g/dl). Upper endoscopy revealed a submucosal lesion in the pre-pyloric region; biopsies showed the characteristic findings of GCP. The latter is a rare cause of upper gastrointestinal (GI) bleeding and its diagnosis and treatment remain challenging. Medical literature has not unveiled its association with chronic inflammation and *Helicobacter pylori* infection as many cases are being found in previously unoperated individuals. Even though GCP remains a rare entity, it should be incorporated in the differential diagnoses of upper GI bleeding and further prospective studies should highlight other contributing factors.

KEYWORDS

Gastritis cystica profunda, submucosal lesion, upper gastrointestinal bleeding

LEARNING POINTS

- Gastritis cystica profunda (GCP) is a rare lesion of the stomach.
- GCP is seldom included in the differential diagnosis of an upper GI bleed.
- GCP can be considered as a premalignant lesion or can portend an underlying malignancy.

INTRODUCTION

Gastritis cystica profunda (GCP) is a rare benign lesion of the stomach characterised by cystic dilation of gastric glands in the submucosal layer[1]. It is distinct from more common types of gastritis that involve inflammation of the gastric lining without cystic formation. GCP is usually found in male

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patients who had previously undergone gastric surgeries at the site of gastric anastomosis[2].

The pathogenesis of GCP involves a combination of ischaemia, mucosal injury, altered gastric secretion and chronic inflammation of the gastric mucosa. Together, these factors distort the normal architecture of the gastric mucosa resulting in hyperplasia of gastric glands and subsequent cyst formation[3]. In many individuals, GCP is found incidentally on routine endoscopy. When symptoms occur, they are non-specific and can be mistaken for other gastric conditions[4,5]. Endoscopic modality is the best choice to diagnose and treat GCP as opposed to traditional surgical resection, as it is less invasive and causes minimal trauma to the stomach[6]. Despite being benign, several studies have reported a correlation between GCP and the development of gastric adenocarcinoma[7]. However, concomitant *Helicobacter pylori* infection and GCP formation is still not well highlighted. We present a rare case of a young female patient, with no known gastric surgeries, who was found to have GCP in the unusual pre-pyloric area while being co-infected with *H. pylori*.

CASE DESCRIPTION

A 39-year-old female patient, non-smoker with no known drug allergies and previously healthy, was hospitalised due to anaemia, fatigue and dizziness of one month's duration. On admission, complete blood count showed a severe drop in haemoglobin (from 13 to 9 g/dl) and a positive faecal occult blood test.

She was scheduled for an upper endoscopy as part of medical workup. The patient has no pertinent past medical history and is not on any chronic medication. She denied any family history of GI disorders and has not undergone any previous abdominal surgeries. Upon physical examination, there was no pathological findings in the abdomen, and the patient denied any weight loss, nausea, vomiting or abdominal pain.

An upper endoscopy showed a 25 mm pedunculated polypoid mass *(Fig. 1)* with central umbilication *(Fig. 2)* situated at the pre-pyloric area, which was immediately removed by snare-assisted polypectomy. Biopsies of the lesion revealed characteristic pseudo-invasion of benign cystically dilated gastric glands into the muscularis propria but without dysplastic changes and no evidence of mitoses, corroborating a diagnosis of GCP *(Fig. 3)*. In addition, *H. pylori* colonisation was noted.

The patient was reassured and discharged on bismuth-based quadruple therapy as an eradication regimen for *H. pylori*. A repeat endoscopy was scheduled in 6 months, which revealed complete resolution of GCP with normal biopsies and absence of *H. pylori*. The patient's symptoms had abated and her haemoglobin level normalised (13 g/dl).

DISCUSSION

We present a rare case of a benign submucosal lesion known as GCP; the term was first described by Littler et al. in 1972[1]. It has been theorised that GCP arises secondary to prior gastric trauma and chronic inflammation. It is characterised

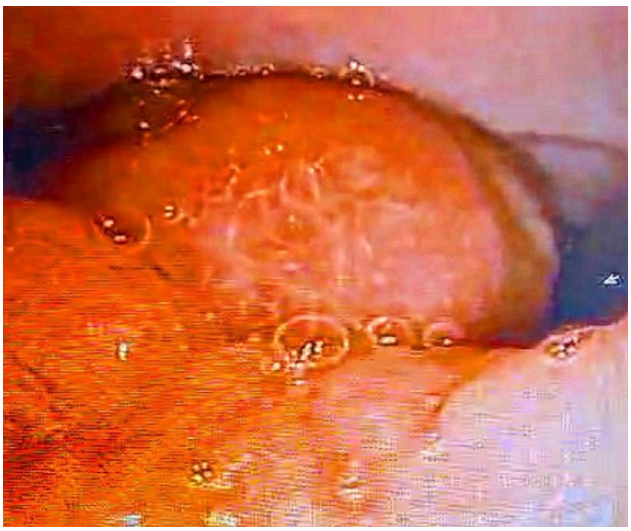

Figure 1. Upper GI endoscopy showing a 25 mm pedunculated polypoid lesion in the pre-pyloric region.

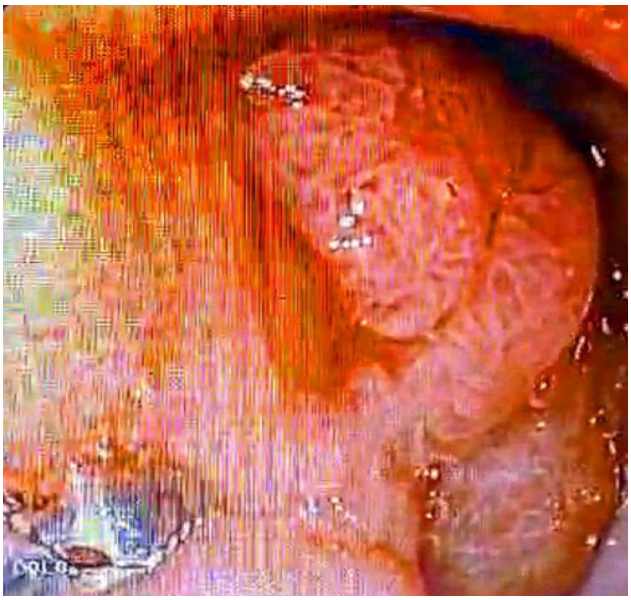

Figure 2. Upper endoscopy demonstrating umbilication of the pyloric polypoid lesion.

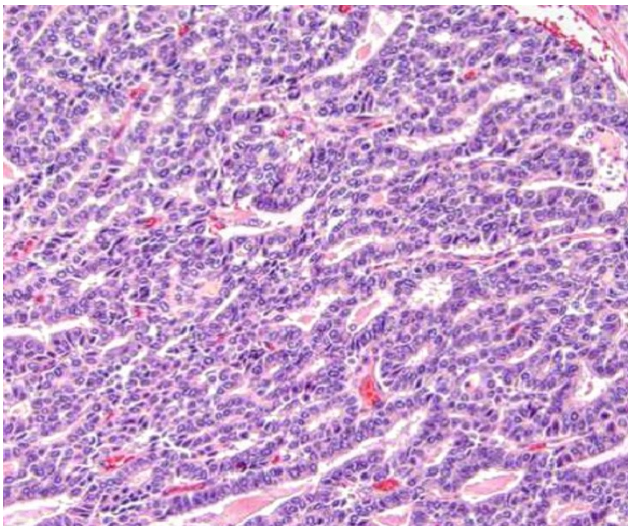

Figure 3. A histological view revealing multiple cystically dilated glands extending beyond the muscularis mucosa into the submucosa, corroborating a diagnosis of GCP.

by the presence of benign cysts within the gastric mucosa[2]. Patients with GCP may present with a variety of symptoms, ranging from being completely asymptomatic to full-blown symptoms. When symptoms do occur, they can be quite non-specific and may overlap with other gastric disorders[8]. Common symptoms may include abdominal pain (ranging from mild discomfort to more significant pain, often located in the upper abdominal region), nausea, vomiting, abdominal fullness, loss of appetite, weight loss and chronic upper GI bleeding[8]. Our patient presented to the emergency department due to severe lethargy and dizziness of one month's duration. The patient was found to have a significant drop in haemoglobin and anaemia workup was sought accordingly (from 13 to 9 g/dl). Presenting symptoms may represent a wide variety of differential diagnosis including peptic ulcer disease, variceal bleeding, angiodysplasias and Mallory Weiss syndrome. Given its low prevalence in the population, GCP was not in our differential diagnosis. In our experience, the first examination performed to identify the cause of upper GI bleed was an upper GI endoscopy, which revealed a submucosal broad-based lesion in the stomach[1]. These endoscopic features were compatible with GCP and later confirmed by biopsy.

As for the location of GCP, Xu et al. performed endoscopic resection in 34 patients from a single centre in China and reported the location of every specimen[6]. It was found that 15 lesions were dissected from the cardia (41.1%), 12 from the antrum (35.3%), 4 from the corpus (11.8%), 2 from the angularis (5.9%) and 1 from the stomach fundus (2.9%). None of the specimens were found in the pre-pyloric region[6]. In our case, GCP was isolated from the pylorus. Hence, GCP should be suspected and included in the differential diagnosis of every gastric submucosal tumour independently of its location.

GCP is believed to occur at the site of previous surgical anastomosis as a result of mucosal injury and disruption of the normal gastric architecture, leading to the invagination of the gastric glands in the submucosal layer[1,2]. However, in our case and among other cases found in the literature, patients had no prior history of gastric surgery, suggesting the need to look for other potential contributing factors. Medical literature has still not offered a clear pathological process for previously unoperated cases; however, it is believed that chronic gastric inflammation plays a major role in the development of GCP[5,9]. Both mucosal damage and ischaemia manifesting in gastritis promote a suitable environment for the emergence of GCP[10].

In the 11 articles reviewed later, we stratified patients based on their *H. pylori* status. *H. pylori* is the most common cause of acute and chronic gastritis and might be considered as the major contributor for GCP formation in previously unoperated patients *(Table 1)*. Moreover, most cases of GCP

Author	Age	Sex	Symptoms	Location	Operated stomach?	*H. pylori* Infection	Treatment
Oztruk et al.[14]	44	F	Abdominal pain, low back pain, bloating and vomiting Abdominal pain and vomiting	Antrum	Yes	-	Mass excision with laparotomy
Yu et al.[9]	43	F	Asymptomatic	Antrum	No	-	Distal gastrectomy
Wang et al.[15]	69	M	Diffuse abdominal pain and melena	Antrum	No	-	Six months surveillance
Shimizu et al.[5]	72	F	Anorexia and weight loss	Pre-pyloric	No	Yes	Submucosal dissection with open laparotomy
Düzenli et al.[16]	70	F	Mild dysphagia and resistant dyspepsia	Body	No	-	Proximal gastrectomy with extended lymphadenectomy, splenectomy and total omentectomy
De Stefano et al.[17]	61	M	General discomfort and multiple episodes of melena	Antrum	No	-	Distal gastric resection with Billroth II-type reconstruction
Du et al.[8]	43	F	Intermittent epigastric discomfort	Antrum	No	-	Distal gastrectomy
Machicado et al.[18]	61	F	Epigastric pain, nausea and vomiting	Antrum	No	-	Partial gastrectomy
Lin et al.[4]	50	M	Incidental finding on routine endoscopy	Body	No	No	No surgical intervention
Noh et al.[19]	61	M	Incidental finding on routine endoscopy	Body	No	Yes	Laparoscopic wedge resection
Our case	39	F	Severe drop in haemoglobin and melena	Pre-pyloric	No	Yes	Snare-assisted polypectomy

Table 1. Summary of clinical and pathological features of 11 cases of GCP.

in unoperated stomachs were found to be associated with the development of subsequent gastric cancer, or were found within gastric cancer specimens[5]. GCP has been recently considered as a precancerous lesion and many cases in the literature reported the association between GCP and cancer[3,11,12]. In addition, Moon et al. reported the presence of dysplasia within some GCP samples, further highlighting the correlation between GCP and gastric cancer[13]. Hence, chronic inflammation caused by *H. pylori* infection can be considered as a potential driving factor for the development of GCP, which in turn can be associated with the occurrence of gastric cancer or could be a heralding sign of present malignancy[7]. Effective detection and prompt diagnosis of GCP are required to halt the precancerous cascade and development of invasive gastric cancer. Furthermore, little is found in the literature regarding the standardised treatment of GCP and the duration of follow-up, making cancer association not well established[8]. *H. pylori* infection was detected in our case, and as discussed previously it may be associated with gastric cancer, thus there is a need to eradicate it. Bismuth quadruple therapy, which consists of a proton pump inhibitor, bismuth, tetracycline and metronidazole, was initiated.

We conducted a review of 11 cases of GCP in operated and unoperated stomachs using PUBMED as our database and included our case. The mean age was 57: four individuals were men and seven were women (women-to-male ratio 1.75). 10 out of 11 cases involved patients with a previously unoperated stomach. The symptoms reported were diffuse abdominal tenderness, loss of appetite, anorexia, vomiting, heartburn, haematemesis and melena. Notably, three cases were asymptomatic and found incidentally during routine endoscopy. The lesions were located as follows: six in the gastric antrum, three in the gastric body and two in the pre-pyloric area. As for *H. pylori* infection, it was only confirmed in two patients.

Treatment approaches varied: three patients underwent distal gastrectomy, one had a proximal gastrectomy, one underwent partial gastrectomy, one was treated with endoscopic submucosal dissection, two were monitored with observation and two had submucosal dissection with open laparotomy. In our case, we employed snare-assisted endoscopic resection. Literature has still not offered a clear and standardised treatment plan for GCP; nevertheless, our case underscores the effectiveness and sufficiency of snare polypectomy in the complete excision of GCP.

CONCLUSION

GCP is an exceedingly rare submucosal tumour of the stomach that is seldom included in the differential diagnosis of upper GI bleed. Patients typically present with non-specific symptoms and sometimes remain asymptomatic. GCP should be suspected in every submucosal tumour of the stomach irrespective of its location. The pre-pyloric region was previously deemed uncommon for the development of GCP.

GCP can occur in unoperated stomachs contrary to what was assumed previously, and chronic inflammation plays a major role in its development. Thus, further prospective studies should be conducted to evaluate the correlation between *H. pylori* and GCP as *H. pylori* remains the most common cause of chronic gastritis.

GCP can be considered as a premalignant lesion or can portend a present malignancy. Effective diagnosis and treatment modalities must be established to prevent the precancerous cascade.

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