



## Gastritis Cystica Profunda: A Case Report and Literature Review

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### Abstract

Gastric Cystica Polyposa (GCP), a rare disease characterized by multiple cystic lesions in mucosa and/or sub mucosal layer, usually occurs in previously operated stomachs. The non-specific clinical symptoms and radiographic appearance make diagnosis difficult without postoperative pathological results. This report aims at providing a comprehensive overview on all GCP cases reported to date. A comprehensive literature search (1972-2014) was conducted for all reported GCP cases, including one case from our group retrospectively. Keywords searched included gastritis cystica profunda, submucosal cysts of the stomach, and heterotopic submucosal gastric glands. A total of 52 cases was found, including 37 (71.2%) men and 15 (28.8%) women (M/F ratio =2.5). The overall mean age was 59.9 (range 39-91) years. Among them, 58.8% (n=30) were located in the body, 25.5% (n=13) in the fundus, 19.6% (n=9) in the antrum, 3.9% (n=2) in the cardia and occasionally one case in the prepyloric lesion and one case in anastomotic site. 52% (n=26) of cases had prior gastric surgery. The main clinical symptoms included abdominal pain (n=14, 36.8%) and gastrointestinal bleeding (including hematemesis and melena, n=7, 18.4%). Among overall 52 cases, only 7.7% (4) were diagnosed before surgery, and the rest were diagnosed during postoperative histopathologic examination. In conclusion, GCP is difficult to be preoperatively correctly diagnosed due to being relatively rare and lack of typical clinical symptoms. The correct diagnosis should depend on histopathological examination. Complete surgical removal of the GCP is widely considered as the best treatment option.

**Keywords:** Gastritis cystica profunda; Cystic lesion; Submucosal cysts; Heterotopic submucosal gastric

### Introduction

GCP, a peculiar hyper plastic cystic lesion, was first described by Scott and Payne in 1947 [1]; nevertheless, until 1972 littler and Glibermann [2] coined the term “gastritis cystica polyposa” and suggested that the presence of cystically dilated gastric glands in the sub mucosa was a reactive, postsurgical condition. Subsequently, “gastritis cystica profunda” became a preferred term because it resembled similar condition in the colon [3].

Very few GCP cases have been reported over half a century. It is well known that the lesion is related to several factors working in concert: something that predisposes to mucosal defects (e.g. surgery, biopsy, and polypectomy) with chronic ischemia and inflammation [4]. Although it was commonly considered as a benign lesion, several studies have reported the correlation between GCP and gastric adenocarcinoma [5-7]. The differentials for GCP should include GIST (Gastro Intestinal Stromal Tumor) [8], Ménétrier’s disease [9,10], inverted hyperplastic polyps [11] and other polypoid lesions. Here, we report a case of GCP in an un-operated stomach and compare its clinical feature, diagnosis and treatment with other 51 published cases.

### Case Presentation

A 43-year-old woman, suffered from intermittent epigastric discomfort for almost a year, underwent an Endoscopic Ultra Sonography (EUS), indicating that there was a huge sub mucosal mass in the anterior wall of gastric antrum and it was diagnosed as antrum deep cyst (Figure 1 and 2). Results of her physical examination showed nothing abnormal, and laboratory findings including blood routine and tumor markers tests were all within the normal range. Also, her past surgical and family history was unremarkable. An abdominal Computed Tomography (CT) showed a 1.3 cm × 2.2 cm irregular hypodense mass in the greater curvature of the stomach and enhanced scanning showed mild to moderate enhancement central in the lesion, which was suspicious of GIST (Figure

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3). To further study the lesion, a Magnetic Resonance Imaging (MRI) of the stomach was performed, revealing the gastric wall on the greater curvature of antrum markedly irregularly thickened, also suggesting of GIST (Figure 4).

Because of highly suspected GIST, the patient underwent a distal gastric resection (Billroth I). Gross pathologic examination revealed that the tumor was 2.5 cm × 1.5 cm in size and had normal mucosal surface. Microscopic pathologic examination showed thickening of the muscularis and cystic down-growth of gastric glands into the submucosa of the stomach with low grade dysplasia, which is compatible with gastritis cystica profunda (Figure 5). The patient was discharged after 12 days' hospitalization and after 3-month follow-up the patient was healthy and had no sign of recurrence.

## Clinical Features

A total of 57 GCP cases were collected retrospectively, with one case from Shengzhou People's Hospital and 51 cases from 32 reports during 1972-2014. The lesion was significantly associated with older age and male gender (71.1%, M:F ratio, 2.5:1). It is known that GCP occurred most commonly in patients who had undergone gastric surgery. However, in our study, we found that there was no much difference in percentage for patients with or without gastric surgery history (52% vs. 48%).

Clinically, GCP patients have abdominal pain, followed by gastrointestinal bleeding, weight loss, anemia and other rare symptoms such as nausea, epigastric discomfort, vomiting, belching and mild dysphagia, anorexia, fatigue, fullness and hypoalbuminemia. Additionally, it was incidentally found in more than a quarter of cases and sometimes, the lesion could be found in an emergency situation as it could lead to hematemesis [12,13].

## Diagnosis

GCP is a rare condition with non-specific symptoms and radiographic images, making its diagnosis difficult without definitive surgical resection. Physical examinations and laboratory studies are commonly not significant. Imaging tests included CT and MRI. GCP presents as a polypoid mass, unspecific circumferential thickening of the gastric wall with cystic changes in CT scan and MRI appearance hasn't been reported before. In current study, a MRI scan was also performed, demonstrating that the gastric wall on the greater curvature of the antrum markedly irregularly thickened, with high signals on Diffusion Weighted Imaging (DWI), and without identified perigastric or periesophageal lymph nodes. Both CT and MRI findings were not diagnostic since they mimic other hyper proliferative conditions. But Wu et al. [14] once reported a case that the features of GCP were preoperatively evaluated by CT. The differential diagnosis of GCP should include GIST, gastric adenocarcinoma and other submucosal lesions. Compared to gastric adenocarcinoma, GCP rarely presents with weight loss, cachexia and highly enhancement in CT performances. Radio graphically, GIST and GCP all appear as hypo echoic, intramural polypoid masses with cystic changes [8]. EUS examination should be conducted to provide more information to further investigate the mucosal pathology. The most frequent EUS feature of GCP was multiple anechoic cystic spaces/cysts in the sub mucosal of those cases [15]. Additionally, the diagnosis can be improved by EUS Fine Needle Aspiration (FNA). Chung et al. [16] considered EUS as an effective diagnostic tool to evaluate and differentiate GCP from the protruding and elevated gastric lesion, with 88.9% sensitivity and 100% positive rate. Four

patients were preoperatively diagnosed by Endoscopic Mucosal Resection (EMR) or Endoscopic Mucosal Resection (ESD) along with the development of endoscopic technique in recent years.

Pathological examination is a monopolistic diagnostic procedure to evaluate GCP. Histologically, GCP is characterized by elongation of the gastric foveolae with hyperplasia and cystic dilatation of the gastric glands, extending in the sub mucosal layer and sometimes mild dysplasia could be discovered, similar to current case.

## Treatment and Prognosis

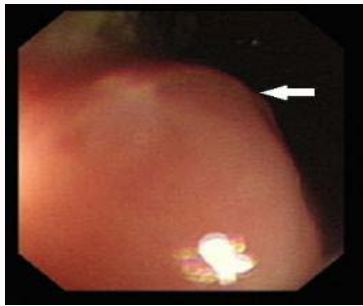
Given the rarity of the lesions and the difficulty in diagnosing them preoperatively, a defined treatment strategy on GCP has not been well described. To date, among the 37 cases providing specific treatment plans, only four patients were without surgical treatment, one with medication with proton pump inhibitor and the other three were in surveillance. Nearly 89.2% patients underwent surgical resection, similar to our current case. The most popular surgical treatment is partial gastrectomy, followed by complete removal of stomach, endoscopic mucosal resection and polypectomy. It is well known that the location of GCP determines surgery approach. In current study, distal gastrectomy with a Billroth I gastrojejunostomy was performed because the lesion was located in the antrum. Currently, since increasing reports tend to approve the potential malignance of GCP, gastrectomy or total gastrectomy is regarded as the most recommended approach to relieve the symptoms and cure the disease. However, the reflux after surgery, foreign bodies (sutures) and gastric mucosa damage may lead to the development of GCP, which requires an appropriate surgical plan and close follow-up. In addition, ESD and EMR have become new options for treatment along with the advantage in minimally invasive approaches. But it is noteworthy that these surgical procedures may facilitate the deep misplacement of gastric glands into the muscularis propria according to a report published in 2011, which found that after three attempts of endoscopic removal of the polyp, GCP recurred within short period and a gastric sleeve resection was performed eventually [17].

In general, the prognosis of this condition is not bad if not coexists with gastric adenocarcinoma, Menetrier disease, gastric lymphoma and other malignant diseases. The possibility of recurrence is not well studied. To date, two cases have been reported of the GCP recurrences after surgical resections [17,18]. And a 10-year follow-up for a case with GCP in an unoperated patient revealed low grade dysplasia, and the sizes of both the GCP and the adenoma overlying increased during the follow-up period [19].

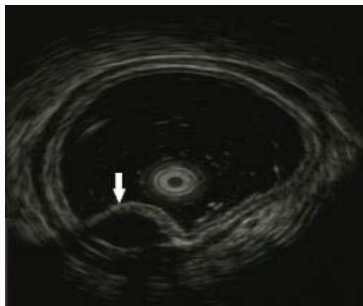
## Results

Fifty-two cases of GCP have been documented, including the case reported here. Clinical and treatment data are detailed in below.

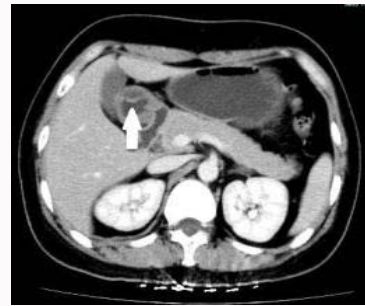
Among these 52 patients, 37 were men and 15 were women (M:F ratio, 2.5:1), with an overall mean age of 59.9 years (range: 39-91 years). The ones who were older than 50 years old accounted for 74%. The mean age among women was 60.2 years (range: 39-79 years), and the mean age among men was 60.3 years (range: 44-91 years). Only 52% of patients had previous stomach surgery history. Among the 38 cases presenting symptoms, GCP was an incidental finding in 28.9% (n=11) of patients, and the main clinical manifestation is abdominal pain (n=14, 36.8%), followed by gastrointestinal bleeding (n=7, 18.4%), weight loss (n=4, 10.5%) and anemia (n=4, 10.5%). It is occasional to find the patient with nausea (n=1, 2.6%), epigastric



**Figure 1:** Gastroscopy revealed a subepithelial protruding mass (arrow) covered by normal mucosa in the anterior portion of the gastric antrum.



**Figure 2:** Endoscopic ultrasonography showed a homogeneous and hypoechoic mass measuring 1.0 cm × 1.6 cm in size with irregularly thickened wall in the submucosal layer of the stomach.



**Figure 3:** Contrast-enhanced CT scan of stomach revealed the gastric wall on the greater curvature of the antrum markedly thickened irregularly (arrow), with mild to moderate enhancement.



**Figure 4:** MRI images show the gastric wall on the greater curvature of the antrum markedly irregularly thickened (arrow).

discomfort (n=2, 5.3%), vomiting (n=2, 5.3%), belching and mild dysphagia (n=1, 2.6%), anorexia (n=2, 5.3%), fatigue (n=1, 2.6%), fullness (n=1, 2.6%) and hypoalbuminemia (n=1, 2.6%). The most common anatomic GCP location was the gastric body (n=30, 58.8%), followed by the fundus (n=13, 25.5%), antrum (n=9, 19.6%), and cardia (n=2, 3.9%); some lesions were located at the anastomotic site, in the prepyloric lesion and junction of body and antrum or fundus. According to the documented cases, 37 cases provided treatment plans, including partial gastrectomy (n=20, 54.1%), complete removal of stomach (n=5, 13.5%), endoscopic mucosal resection (n=5, 13.5%), polypectomy (n=2, 5.4%), medication with proton pump inhibitor (n=1, 2.7%), surveillance (n=3, 8.1%) and one case without detailed surgical approach.

## Discussion

The etiology and pathogenesis of GCP are not fully elaborated at present. Chakravorty and Schatzki [20] considered GCP as a congenital disease in 1975 because it was found in some patients without gastric ulcer and previous gastric surgery history. However, more researchers supported that acquired factors played a leading role in the development of GCP. In 1981, by studying a particular case, Franzin and Novelli [3] concluded that the presence of cystically dilated gastric glands in the submucosa was a reactive, postsurgical condition and was caused by disruption of the integrity of gastric mucosal. Furthermore, Fonde and Rodning [4] in 1986 pointed out that GCP developed secondary to ischemia, chronic inflammation and foreign body (surgical suture) stimulation. Kcne2 is short for potassium voltage-gated channel subfamily E member 2, which is one of the important subunits of apical potassium channels in parietal cells [21]. In 2010, Torsten et al. [22] demonstrated a breakthrough finding, i.e. all of the eleven Kcne2 gene knockout mice exhibit a severe gastric preneoplastic phenotype comprising GCP, while none of the five mice

in control group developed GCP, suggesting that Kcne2 disruption was associated with the development of GCP and gastric neoplasia. Additionally, a recent study [5] showed Kcne2 expression was reduced in human gastric cancer tissues, in line with Torsten finding that Kcne2 expression was negatively correlated with gastric cancer formation. In 2012, Kim et al. [23] reported a case of GCP associated with gastric carcinoma with lymphoid stroma, and the Epstein-Barr virus (EBV) in situ hybridization revealed positive reaction at the dysplastic area as well as carcinoma area, suggesting that GCP is a precancerous lesion and EBV infection plays an important role in dysplastic change. In addition, a review by Choi et al. [24] on 10,728 patients with gastric cancer who underwent gastric cancer surgery found that the EBV-positive rate was significantly higher in the GCP group (31.1%) than that in the non-GCP group (5.8%), suggesting that GCP was strongly associated with EBV-positive gastric cancers, and it was highly suspected as the premalignant lesion. Finally, experiments [25] have shown that animals predisposed to *Helicobacter* infection develop not only secondary GCP but also subsequent primary gastric carcinoma.

Whether or not GCP is malignant is still controversial. Historically, the performance of submucosal glands in GCP was not thought to represent cancer. However, it has been reported that GCP coexisted with gastric adenocarcinoma [5,7], Ménétrier disease [9,10] and gastric carcinoma with lymphoid stroma [23]. A Japanese study [26] performed an immunohistochemical analysis on a GCP gross specimen and described elevated expression of Ki-67, p53, and p21 in GCP lesions, which was indicative of increased epithelial proliferation and increased DNA repair, and thus might explain the etiology of GCP as the precursor of gastric cancer [27-40].

Although complete removal of the GCP using established surgical oncology principles is widely recommended as the most



perfect treatment, there is no much difference in GCP treatment whether with or without prior surgery. GCP is always confused with other submucosal gastric lesions without typical manifestations. The most common presenting symptom is abdominal pain, and EUS appears as the most effective approach to investigate the condition while imaging examinations as CT and MRI can provide limited information. Future studies need to elucidate the natural history of this disease process, and malignant potential, thus more evidence-based treatment strategies are warranted.

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