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Bile reflux gastritis cystica profunda

A case report and literature review

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Abstract

Rationale: Gastritis cystica profunda (GCP) is a rare gastric lesion involving cystic dilation of the gastric glands extending into the submucosa. It is usually observed at anastomotic sites in the stomach of patients who have undergone gastric procedures. Bile reflux GCP is rare in patients who have not undergone gastric surgery. Here, we report a rare case of a patient with GCP associated with bile reflux, who had no history of gastric surgery.

Patient concerns: A 50-year-old man presented with intermittent abdominal fullness for 2 years, along with nausea. He had never undergone gastric surgery. Endoscopic ultrasonography (EUS) showed a thickened gastric wall and an echo-poor submucosal layer of the gastric fundus. A 3 cm × 2 cm × 1.5 cm lesion was noted.

Diagnosis: Bile reflux GCP

Interventions: Endoscopic retrograde cholangiopancreatography and endoscopic submucosal dissection (ESD) were performed, and the lesion was removed. Conventional pathological examination revealed GCP with glands hyperplasia and a yellow-brown deposit, which was considered bile. The findings were consistent with a diagnosis of GCP without malignancy.

Outcomes: Upper gastrointestinal barium meal revealed postoperative changes at the gastric fundus. Gastroscopy performed at 6 months after surgical resection showed superficial gastritis with bile reflux.

Lessons: The findings suggest that GCP etiology varies and that GCP can be caused by bile reflux but without malignancy. Additionally, GCP is not limited to patients who have previously undergone gastric surgery. Moreover, it is difficult to identify. EUS and ESD might be good approaches for the diagnosis and treatment of GCP.

Abbreviations: ESD = endoscopic submucosal dissection, EUS = endoscopic ultrasonography, GCP = gastritis cystica profunda, IHP = inverted hyperplastic polyp.

Keywords: bile reflux, endoscopic submucosal dissection, gastritis, gastritis cystica profunda

1. Introduction

The incidence of gastritis cystica profunda (GCP) in the general population has been reported and has been discussed in several comprehensive studies.[1–3] GCP is a rare gastric lesion involving cystic dilation of the gastric glands extending into the submucosa and is likely under-reported.[1] Most GCP cases involve secondary changes caused by prolonged chronic inflammation, ischemia, gastric surgery or suturing material, and injury to the muscularis mucosa, which can trigger the ectopic entrapment of gastric glands in the submucosa.[2] The pathological characteristic features might be polypoid hyperplasia and cystic dilatation of the gastric glands extending into the submucosa of the stomach. GCP can show upper gastrointestinal symptoms, such as upper abdominal pain, acid reflux, nausea, and anorexia, and some patients might not experience any symptoms.[3,4] It can also cause severe upper gastrointestinal bleeding and gastric outlet obstruction and can mimic cancer in some cases.[5–7] Although GCP has been identified more frequently in the setting of previous gastric surgery, it can develop in patients who have not undergone previous surgery.[8]

The disease is often misdiagnosed, and most patients are confirmed to have the condition through surgery. This involves not only great patient suffering but also high cost. Bile reflux GCP is a disease of the digestive system, and its etiology and pathogenesis are still unclear. There are many diagnostic methods, but a consensus on diagnosis is still unclear. Most current treatments are symptomatic treatments, but the overall efficacy is poor.

Here, we report a rare case of a patient with GCP associated with bile reflux, who had no history of gastric surgery and present a literature review.

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2. Case presentation

2.1. Case report

A 50-year-old man presented with intermittent abdominal fullness for 2 years, along with nausea. The symptoms often occurred after consuming food that could cause gastric irritation, and the condition improved without intervention after 10 minutes. He had no history of gastrointestinal surgery. Gastroscopy revealed a protrusion lesion on the gastric fundus. A physical examination showed normal findings. Laboratory investigations noted a total bilirubin level of 34.9 μmol/L, direct bilirubin level of 14.6 μmol/L, and aspartate aminotransferase level of 178.6 U/L. Abdominal computed tomography revealed limited gastric fundus dilatation, cholecystolithiasis, and choledocholith. Endoscopic ultrasonography (EUS) showed a thickened gastric wall and an echo-poor submucosal layer of the gastric fundus (Fig. 1).

Informed written consent was obtained from the patient for the publication of this case report and accompanying images.

2.2. Surgical procedure

Endoscopic retrograde cholangiopancreatography was performed after abdominal computed tomography revealed choledocholith. Intraoperative cholangiography detected multiple filling defects. Endoscopic papillary dilation was performed, and 2 firm stones were removed. The choledochus was assessed, and endoscopic nasobiliary drainage was used to perform intraoperative cholangiography to ensure no filling defect. There were no postoperative complications.

One week later, to define the characteristics of the gastric fundus lesion and reduce gastric surgery injury, endoscopic submucosal dissection (ESD) was performed. A 3 cm × 2 cm × 1.5 cm lesion was removed, and a 1.2 cm × 0.5 cm grey region, which had an eroded mucosal surface, was noted. An intraoperative cryopathological examination revealed disordered gastric mucosal glands and single-gland dilatation in the muscularis mucosa and submucosa, without malignancy.

3. Outcome

The histological examination revealed dilated cystic glands in the submucosa and bile deposit (Fig. 2). These findings were consistent with a diagnosis of GCP without malignancy. A liquid diet was started on the morning after surgery, and the patient was discharged on the third day after surgery. There were no postoperative complications.

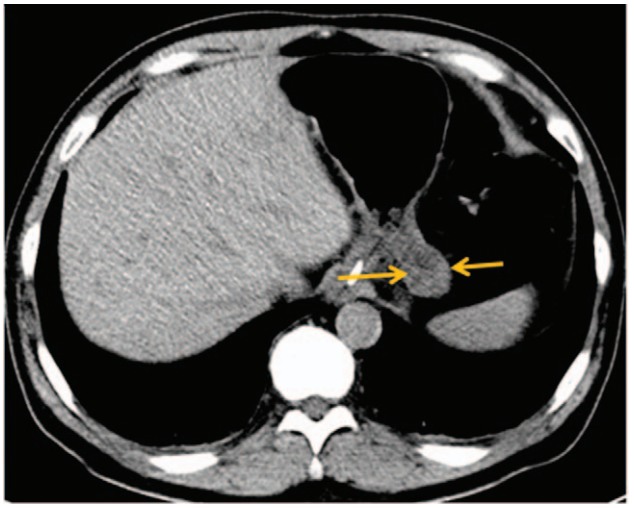

Figure 1. Abdominal compute tomography:Revealed gastric fundus dilatation was limited,cholecystolithiasis,choledocholith.

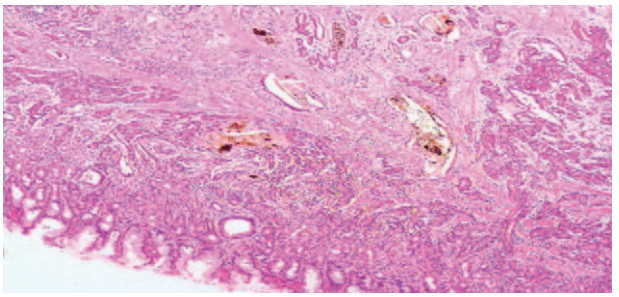

Figure 2. Tiny cysts lined by flattened epithelium within the submucosa, consistent with gastritis cystica profunda (H&E, ×40),and glands hyperplasia, yellow-brown substance deposit.

Follow-up was performed at 3 months after surgical resection. Upper gastrointestinal barium meal revealed postoperative changes at the gastric fundus. Gastroscopy performed at 6 months after surgical resection showed superficial gastritis with bile reflux.

4. Discussion

We reported a rare case of a patient with GCP associated with bile reflux, who was treated with ESD. Because of the low incidence of this disease, a literature search was systematically performed using the PubMed database and Cochrane Library with the following keywords:

"Bile reflux AND gastritis cystica profunda" or "gastritis cystica profunda." Relevant abstracts were selected and reviewed, and reports were identified. Specific information of the identified reports is presented in Table 1.

Although GCP is generally benign, it is considered precancerous,[3] and there have been some reports of GCP associated with cancer.[13,22] The etiology and pathogenesis of GCP remain unclear, and the mechanisms of GCP involve chronic inflammation, ischemia, and presence of a foreign body.[2] It is believed that inflammation causes erosion of the muscularis mucosa, consequently leading to the formation of submucosal cysts.[3] Littler and Gleibermann[5] proposed that mucosal prolapse and subsequent inflammation play roles in the development of GCP. GCP is often associated with gastric adenocarcinoma, and loss of the potassium voltage-gated channel subfamily E member 2 (KCNE2) subunit from potassium channel complexes is considered as a common primary factor associated with both GCP and malignancy.[9] There is evidence that infection with the Epstein–Barr virus might result in GCP and is negatively correlated with gastric cancer formation. In a previous report, in situ hybridization for Epstein–Barr virus revealed that the Epstein–Barr virus-positive rate was significantly greater in cancer patients with GCP (37 of 119 patients; 31.1%) than in those without GCP (29 of 503 patients; 5.8%; $P < .001$).[8] The etiology varies, and the most important factor appears to be previous gastric surgery. Our patient did not have previous stomach surgery, and his GCP was associated with bile reflux.

GCP remains a rare diagnosis, and it is difficult to identify. The differential diagnosis of a submucosal tumor includes gastric adenocarcinoma, gastrointestinal stromal tumors, inflammatory myofibroblastic tumors, neuroendocrine tumors, schwannomas,

Table 1

Profiles of reported cases of Gastritis cystica profunda.

No.	Refs.	sex	Age, yr	Symptom	Auxiliary examination, outcome	diagnosis	Treatment	pathology	Follow-up	Previous history of gastric surgery
1	McCurdy et al[10]	F	55	Persistent nausea	Endoscopy:SMT CT: normal EUS: cystic lesion	GCP	EMR	Dilated cystic gland	Normal	NG
2	Yu, X F et al[3]	F	43	No symptom	Endoscopy:mass-like lesion EUS: sessile polyp	GCP	Billroth I	GCP without malignancy	NG	No
3	Butt et al[7]	F	38	Epigastric pain	Endoscopy:HP infection,distal duodenal folds	GCP	Billroth II	Irregular proliferation	Normal	No
4	Wang L, et al[18]	M	63	Epigastric discomfort	Endoscopy:nodular lesion EUS: cystic lesion	GCP	Exploratory laparotomy	Dilated cystic gland	NG	No
5	Lee, TH et al[4]	F	48	No symptom	EUS: anechoic lesion	GCP	ESD	Polypoid lesion and Long stalk	NG	NG
6	Xu, G et al[16]	F	48	Recurrent Nausea, diarrhea	Endoscopy:submucosal with irregular mucosal EUS: anechoic lesion	GCP	Billroth II	GCP with dysplasia	Recurrence	NG
7	Moon,SY, et al[21]	M	76	Anorexia	Endoscopy:irregular mucosal lesion CT:Perigastric lesion	GCP	ESD	Dilated cystic gland	NG	NG
8	Itte V et al[5]	F	50	Epigastric pain	Endoscopy:Lesser curvature bleeding in anterior wall	GCP	Exploratory laparotomy	Intestinal metaplasia,dilation cystic gland	NG	Yes
9	TomizukaT, et al[20]	M	78	Weight loss	Endoscopy:submucosal mass with small stalk EUS: low-density mass	GCP	Total-gastrectomy	dilation cystic gland	Normal	Yes
10	BechadeD, et al[19]	F	79	Epigastric pain	Endoscopy:Giant gastric folds CT: polypoid mass EUS:submucosal cysts	GCP	No surgery	No	The tumor size remained unchanged	No
11	Kurland et al[6]	M	78	Anemia	CT: normal EUS:multiple small anechoic	GCP	Partial gastrectomy	dilation cystic gland	NG	Yes

CT = computerized tomography, EMR = endoscopic mucosal resection, ESD = endoscopic submucosal dissection, EUS = endoscopic ultrasonography, GCP = gastritis cystica profunda, NG = no given, SMT = submucosal tumor.

heterotopic pancreas, lipomas, sarcomas, cysts, lymphomas, and leiomyomas.[10] Particularly, hypertrophic folds of the stomach should be differentiated from Menetrier's disease, malignant lymphoma and gastric carcinoma of the linitis plastica type, and GCP.[11,12] In addition, gastric inverted hyperplastic polyp (IHP) is characterized by marked submucosal glandular proliferation associated with cystic dilation, leading to a polypoid lesion, and it might be difficult to distinguish between IHP and GCP.[13] IHP might be an exaggerated hyperplastic state of GCP.[14] EUS can be helpful in differentiating these entities.[15] EUS-fine needle aspiration (FNA) and EUS-guided trucut biopsy have been proven to be very valuable in the diagnostic evaluation of submucosal lesions of the gastrointestinal tract and adjacent organs.[16] Endoscopic forceps biopsy is usually limited to the mucosa; thus, information regarding the state of the submucosa is seldom available.[17] By reviewing the literature and treatment experience, we believe that EUS can be an effective diagnostic method.

ESD appears to be useful for the diagnosis of submucosal tumors, including GCP.[2,16] The combination of EUS and ESD appears to be very effective for the diagnosis of GCP, and this makes an open surgical procedure unnecessary.[1] Some reports have mentioned treatment with other surgical methods, such as endoscopic mucosal resection, Billroth I, Billroth II, and gastrojejunostomy, as well as regular re-examination (Table 1). In our case, we performed ESD. The advantage of performing ESD is that the use of an endoscopic technique combined with laparoscopy can allow better diagnosis and treatment.

It has been reported that GCP can recur after surgery,[18] and GCP can lead to upper gastrointestinal bleeding and gastric outlet obstruction. Thus, we suggest that patients who are diagnosed with GCP should be regularly followed-up. The findings of the present case indicate that GCP is not limited to patients who have previously undergone gastric surgery and that it might be associated with bile reflux, without malignancy. Clinically, we should be cautious about patients who have GCP, because GCP might be associated with malignancy or might have a potential role as a premalignant lesion. We recommend that patients with non-malignant GCP should be monitored. Further studies are needed to clarify the pathogenesis of GCP along with its possible link in the development of gastric carcinoma and to determine whether bile reflux is a risk factor of GCP. To our knowledge, bile reflux GCP is rare. We believe that our report provides important information for the diagnosis and treatment of this disease.

4. Conclusion

Bile reflux GCP is a rare gastric lesion. The findings suggest that GCP etiology varies and that GCP can be caused by bile reflux but without malignancy. Additionally, GCP is not limited to patients who have previously undergone gastric surgery. Moreover, it is difficult to identify. EUS and ESD might be good approaches for the diagnosis and treatment of GCP.

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Author contributions

Shenghe Deng, Yinghao Cao contributed equally to this work. Shenghe Deng, Jiang Li,Yinghao Cao, Liming Shen contributed to the study design and literature search.Shenghe Deng,Yinghao Cao contributed to the literature search and the writing of the manuscript. Kailin Cai contributed to the review and revise of the manuscript.

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References

[1] Xu G, Peng C, Li X, et al. Endoscopic resection of gastritis cystica profunda: preliminary experience with 34 patients from a single center in China. Gastrointest Endosc 2015;81:1493–8.
[2] Ogasawara N, Noda H, Kondo Y, et al. A case of early gastric cancer arising from gastritis cystica profunda treated by endoscopic submucosal dissection. Case Rep Gastroenterol 2014;8:270–5.
[3] Yu XF, Guo LW, Chen ST, et al. Gastritis cystica profunda in a previously unoperated stomach: a case report. World J Gastroenterol 2015;21:3759–62.
[4] Lee TH, Lee JS, Jin SY. Gastritis cystica profunda with a long stalk. Gastrointest Endosc 2013;77:821–2.
[5] Itte V, Mallick IH, Moore PJ, et al. Massive gastrointestinal haemorrhage due to gastritis cystica profunda. Cases J 2008;1:85doi: 10.1186/1757-1626-1-85.
[6] Kurland J, DuBois S, Behling C, et al. Severe upper-GI bleed caused by gastritis cystica profunda. Gastrointest Endosc 2006;63:716–7.
[7] Butt MO, Luck NH, Hassan SM, et al. Gastritis profunda cystica presenting as gastric outlet obstruction and mimicking cancer: a case report. J Transl Int Med 2015;3:35–7.
[8] Choi MG, Jeong JY, Kim KM, et al. Clinical significance of gastritis cystica profunda and its association with Epstein-Barr virus in gastric cancer. Cancer 2012;118:5227–33.
[9] Kuwahara N, Kitazawa R, Fujiishi K, et al. Gastric adenocarcinoma arising in gastritis cystica profunda presenting with selective loss of KCNE2 expression. World J Gastroenterol 2013;19:1314–7.
[10] McCurdy KR, Parmar K, de Melo SW, et al. Gastritis cystica profunda: a deeper problem. ACG Case Rep J 2016;3:e125.
[11] Park KH, Seong SG, Kim DK, et al. A case of Menetrier's disease association with gastritis profonda. Korean J Med 1995;48:811–5.
[12] Okada M, Iizuka Y, Oh K, et al. Gastritis cystica profunda presenting as giant gastric mucosal fold: the role of endoscopic ultrasonography and mucosectomy in the diagnostic work-up. Gastrointest Endosc 1994;40: 640–4.
[13] Lee SJ, Park JK, Seo HI, et al. A case of gastric inverted hyperplastic polyp found with gastritis cystica profunda and early gastric cancer. Clin Endosc 2013;46:568–71.
[14] Yamashita M, Hirokawa M, Nakasono M, et al. Gastric inverted hyperplastic polyp. Report of four cases and relation to gastritis cystica profunda. APMIS 2002;110:717–23.
[15] Machicado J, Shroff J, Quesada A, et al. Gastritis cystica profunda: endoscopic ultrasound findings and review of the literature. Endosc Ultrasound 2014;3:131–4.
[16] Xu G, Qian J, Ren G, et al. A case of gastritis cystica profunda. Ir J Med Sci 2011;180:929–30.
[17] Franzin G, Novelli P. Gastritis cystica profunda. Histopathology 1981;5:535–47.
[18] Wang L, Yan H, Cao DC, et al. Gastritis cystica profunda recurrence after surgical resection: 2-year follow-up. World J Surg Oncol 2014;12:133doi: 10.1186/1477-7819-12-133.
[19] Béchade D, Desramé J, Algayres JP. Gastritis cystica profunda in a patient with no history of gastric surgery. Endoscopy 2007;39(suppl 1):E80–1.
[20] Tomizuka T, Mazaki T, Mado K, et al. A case of gastritis cystica profunda. Surgery 2008;143:449–50.
[21] Moon SY, Kim KO, Park SH, et al. Gastritis cystica profunda accompanied by multiple early gastric cancers. Korean J Gastroenterol 2010;55:325–30.