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Gastric adenocarcinoma mimicking a submucosal tumor: A case report

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Abstract

BACKGROUND

Submucosal tumor (SMT)-like early-stage gastric cancer (GC) has rarely been reported. It is difficult to consider the possibility of GC and differentiate it from other submucosal lesions.

CASE SUMMARY

We present the case of a 50-year-old male patient with a 1.6 cm SMT-like flat elevated lesion covered by congested mucosa on the gastric angle. Magnifying endoscopy with narrow-band imaging, endoscopic biopsy, endoscopic ultrasound, and computed tomography were performed for diagnosis. Endoscopic submucosal dissection and gastrectomy with lymph node dissection were performed. The post-resection pathological analysis led to a final diagnosis of GC (Bormann type I, T1bN2M0).

CONCLUSION

GC should be considered when detecting an SMT-like lesion in the stomach.

Key words: Subepithelial lesion; Early-stage gastric adenocarcinoma; Endoscopic submucosal dissection; Case report

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Core tip: Gastric adenocarcinoma showing features of a submucosal tumor is unusual. Preoperative diagnosis is difficult due to the generally deep location of the tumor and non-specific and overlapping features on imaging studies. In this case, esophagogastroduodenoscopy revealed a 1.6 cm type 0-Is lesion covered by congested mucosa on the gastric angle. Endoscopic ultrasound and computed tomography reveal no

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swollen lymph nodes and the usual biopsy cannot give a definite diagnosis. After endoscopic submucosal dissection and gastrectomy with lymph node dissection, this patient was diagnosed with GC (Bormann type I, T1bN2M0).

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INTRODUCTION

Gastric cancer (GC) remains the second leading cause of cancer-related mortality worldwide and the most prevalent cancer in Eastern Asia (including China)^[1] Approximately 90% of GCs are adenocarcinomas. However, an adenocarcinoma showing features of a submucosal tumor (SMT) is unusual, and its prevalence has been reported to be 0.2%-0.62%^[2].

Here, we report a rare case of SMT-like GC, which is easily ignored and misdiagnosed.

CASE PRESENTATION

Chief complaints and history of present illness

A 50-year-old Chinese male patient presented for evaluation and treatment of an indeterminate lesion on the gastric angle, which was discovered on esophagogastroduodenoscopy (EGD) during a routine health examination 15 d previously. He had no abdominal pain or other discomfort.

History of past illness

He had a history of hypertension for half a month and was regularly taking oral agents including nifedipine controlled-release tablets and valsartan dispersible tablets once a day. The blood pressure can be well controlled.

Personal and family history

He had been smoking for 30 years.

Physical examination upon admission

On physical examination, he was 71 kg in weight and 178 cm in height. He had a blood pressure of 120/72 mmHg and pulse rate of 68 beats per minute. Other physical examination on admission revealed no abnormalities.

Laboratory examinations

After admission, the patient underwent evaluations including routine blood tests, routine urine tests, routine fecal tests and occult blood test, blood biochemistry, and some serum tumor markers including carcinoembryonic antigen, carbohydrate antigen 199, alpha-fetoprotein, serum pro-gastrin-releasing peptide, neuron specific enolase, squamous cell carcinoma antigen, and carbohydrate antigen 724. No significant abnormal results were recorded.

Imaging examinations

EGD revealed a 1.6 cm type 0-Is lesion covered by congested mucosa on the gastric angle (Figure 1A and B). Magnifying endoscopy with narrow-band imaging revealed a regular microvascular pattern, presence of a demarcation line, irregular and smaller crypt opening, and widened intervening part (Figure 1C).

Endoscopic ultrasound (EUS; GF-UM2000, Olympus, Tokyo, Japan) revealed a 15.3 mm × 9 mm hypoechoic mass within the submucosa, thickened mucosal and submucosal layers (Figure 1D), and no swollen lymph nodes.

Endoscopic biopsy specimens revealed moderately chronic super gastritis with little intestinal metaplasia.

Computed tomography of the upper abdomen revealed a 15 mm × 12 mm nodule protruding on the lesser curvature of the stomach and no evidence of swollen lymph nodes or distant metastasis (Figure 2).

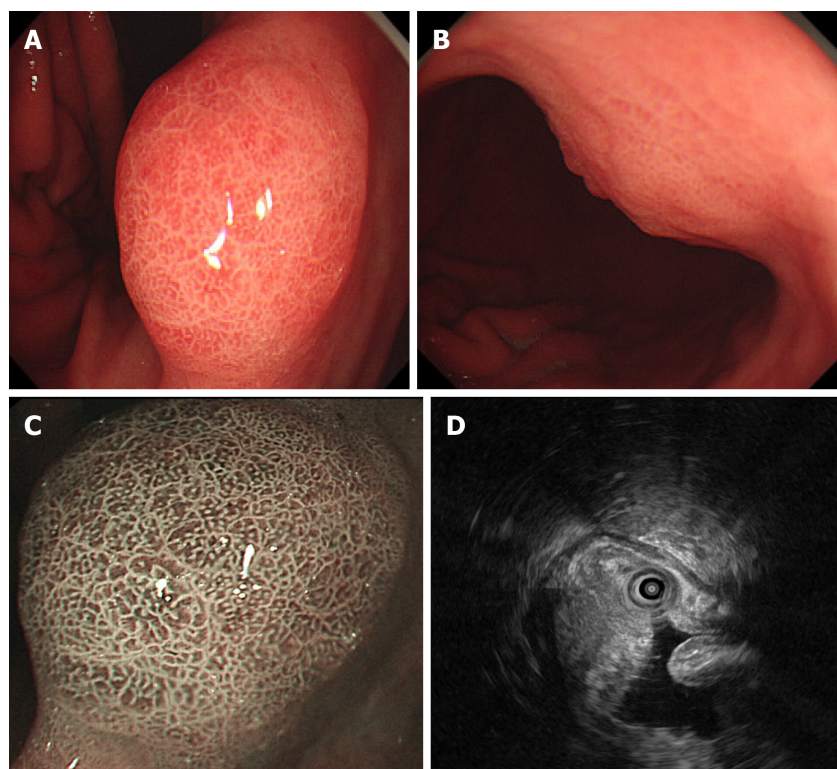


Figure 1 Endoscopic findings. A and B: A 1.6-cm type 0-Ia lesion covered by congested mucosa on gastric angle was observed by white light endoscopy; C: Regular microvascular pattern, presence of a demarcation line, irregular and smaller crypt opening, and widened intervening part were observed by magnifying endoscopy with narrow-band imaging. Magnification: 40×; D: Endoscopic ultrasound showed a 15.3 mm × 9 mm hypoechoic mass within the submucosal layer and thickened mucosal and submucosal layers.

FINAL DIAGNOSIS

According to the imaging findings and the histopathologic examination, this patient was diagnosed with GC (Bormann type I, T1bN2M0).

TREATMENTS

According to the examination results, an initial diagnosis of an SMT-like lesion was made and endoscopic submucosal dissection (ESD) was performed to confirm the diagnosis. Based on the pathology of the resected specimen, we suspected moderately to poorly differentiated adenocarcinoma (Figure 3). Consequently, immunostaining was performed. The lesion was positive for cytokeratin, partly positive for Villin, and weakly positive for CDX-2, but negative for Syn, CgA, CD56, CD3, and CD20. Ki-67 was positive in 30% cells. Accordingly, the final diagnosis was confirmed as poorly-differentiated adenocarcinoma. Because the basal cutting edge was involved, subsequent gastrectomy with lymph node dissection was performed. The final histopathologic examination revealed positive metastasis in 5 of 25 lymph nodes of the lesser curvature and negative results for not only other lymph nodes including those in the hepatoduodenal ligament, the periphery of the hepatic artery, the left gastric artery, and the large curvature but also, the resection margin and omentum tissue. Residual cancer was not observed on parallel mucosal biopsy examination.

OUTCOME AND FOLLOW-UP

After surgery, he was cured. Six months later, the follow-up upper gastrointestinal endoscopy and the biopsies showed no abnormalities.

DISCUSSION

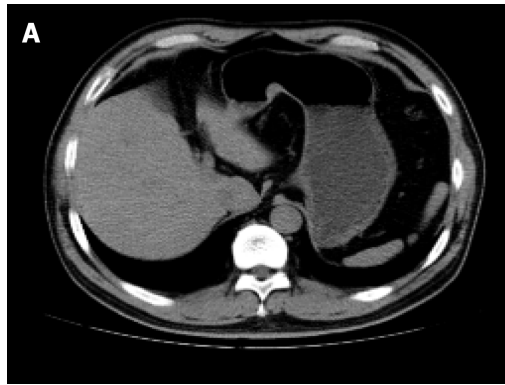


Figure 2 Abdominal computed tomography findings. A 15 mm × 12 mm protruding nodule was shown on the lesser curvature of the stomach.

GC usually derives from the lamina propria layer, accounting for 8% of all cancers^[3] and adenocarcinomas account for 95% of all GCs^[4]. But adenocarcinoma showing features of an SMT is unusual with a prevalence of 0.2%-0.62%^[2]. Preoperative diagnosis of SMT-like GC is difficult due to the generally deep location of the tumor and the non-specific and overlapping features on imaging studies.

When an SMT-like lesion is encountered in clinical practice, we should consider the possibility of GC and carefully differentiate it from other submucosal lesions, such as gastric neuroendocrine tumors (GI-NETs)^[5], smooth muscle tumor, stromal tumor, and lipoma; heterotopic pancreas; and other unusual cases, such as metastatic carcinoma^[6], gastric glomus tumor^[7], and gastric hamartomatous inverted polyp^[8]. According to available reported cases of GC presenting as SMT, the pathologic diagnosis varies including gastric adenocarcinoma^[9], gastric mucinous adenocarcinoma^[10,11], and gastric lymphoepithelioma-like carcinoma^[12].

The mechanism of SMT-like adenocarcinoma is obscure. Heterotopic gastric glands (HGGs) are gastric glands observed in the submucosa, which have been recognized as aberrant lamina propria components associated with repeated erosion and regeneration, which is inferred to develop to a wide variety of adenocarcinomas^[9]. Gastritis cystica profunda (GCP), also related to repeated erosion and regeneration induced by chronic inflammation, causes an aberration of the gastric glands and may be related to carcinogenesis as well^[13]. In this case, we did not find any submucosal heterotopic gastric gland or gastritis cystica profunda. Moreover, Epstein-Barr virus-positive GC is associated with Epstein-Barr virus infection and severe lymphocytic infiltration in the submucosa^[14]; mucinous gastric carcinoma is due to abundant mucin pools in the submucosa^[10,11], and they all show the features of SMT-like cancer. Gastric adenocarcinoma of fundic gland type (GA-FG) has been recognized as a tumor typically arising from the normal gastric mucosa of the fundic gland region without atrophic changes or intestinal metaplasia^[9,11]. There is no conclusion if SMT-like GC is the earlier stage of Bormann type IV GC or of linitis plastica.

Upper gastrointestinal endoscopy has become an important tool in the diagnosis of patients with GC. However, up to 6.7% of GCs may be missed when endoscopy shows no initial cancer findings^[15], especially when early GC (EGC) mimicks an SMT. In this case, EGD revealed a type 0-Is lesion, covered by nearly normal mucosa on the gastric angle, which is distinguished from that of a past report which appeared as small circumscribed, sometimes ulcerated thickening of the gastric wall^[16].

EGD was also performed to obtain a biopsy specimen of suspected gastric lesion. But in previous reports, the cancer cells exposed on the surface accounted for less than 20%-30% of the whole tumor in GC mimicking an SMT, and hence, a usual biopsy cannot confirm the diagnosis. In this case, a usual biopsy was performed twice and two or three pieces of tissue were taken at a time; however, a diagnosis was not confirmed. Multiple biopsies or larger forceps may improve the yield of confirmed diagnosis.

Performance of EUS is important in the initial clinical staging of GC. EGCs are identified on EUS as areas of focal thickening, irregularity, or disruption of layers^[17]. However, the diagnostic accuracy of EUS is operator-dependent, ranging from 57%-88% for T staging and 30%-90% for N staging^[18]. For T1b cancers, the coincidence rate of EUS and pathological diagnosis is only 40%. Ulcers and undifferentiated cancer are two independent factors of EUS mis-staging^[19]. In this case, EUS showed that the mucosal and submucosal layers were thickening and the hypoechoic mass was within the submucosal layer, which is consistent with the pathological result. Unfortunately,

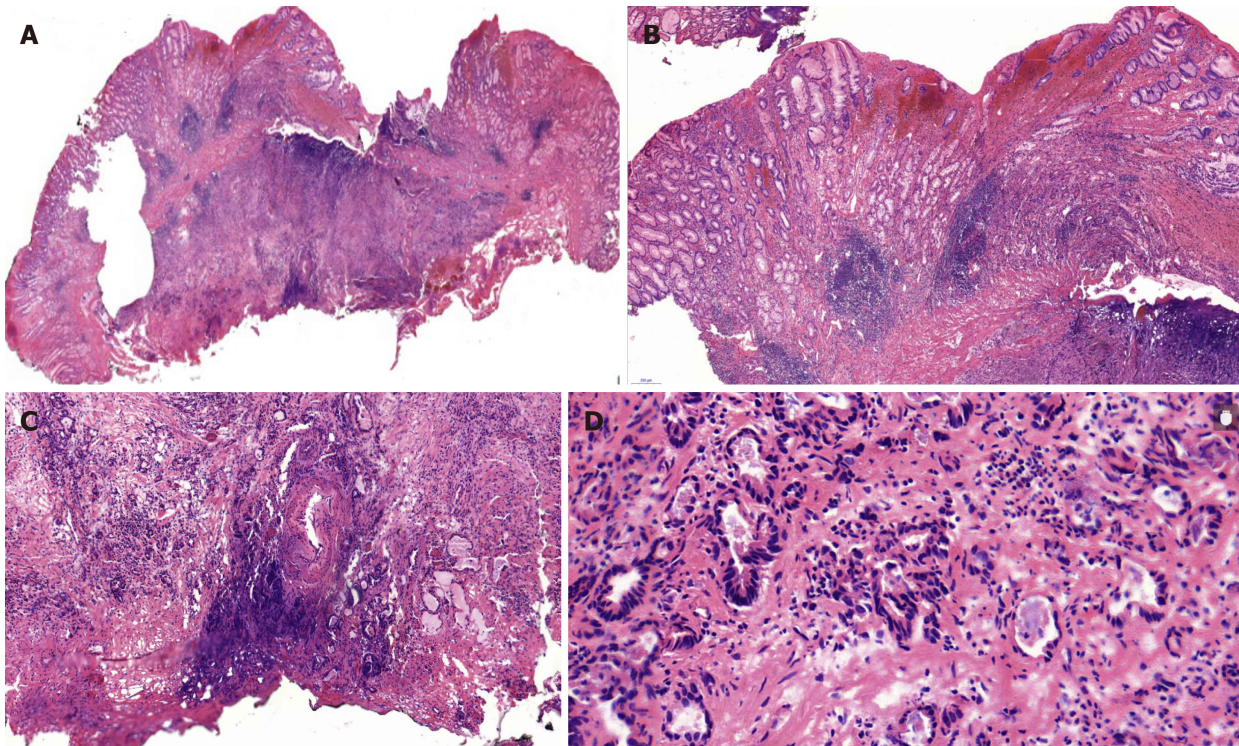


Figure 3 Histopathological findings (hematoxylin and eosin staining). A moderately and poorly differentiated adenocarcinoma was suggested. A: The submucosal layer and muscularis mucosae were invaded; B: The tumor seemed to originate from the basal layer and invade towards the submucosal layer; C: The basal cutting edge was involved; D: Glands were arranged irregularly, with hyperchromatic nuclei and pathologic mitoses visible. Magnification: A: 40×; B and C: 100×; D: 200×.

we did not perform EUS-guided fine needle aspiration (FNA), which is recommended if areas of wall thickening are seen^[20], and we were unable to distinguish it from other SMT-like lesions or provide any indications on abnormal lymph nodes. Considering the aforementioned findings, EUS diagnostic performance cannot be considered optimal, either for disease confirmation or for exclusion, especially for the ability of EUS to distinguish T1a (mucosal) *vs* T1b (submucosal) cancers and positive *vs* negative lymph node status^[21].

Lymph node metastasis is an independent risk factor for the survival of patients with EGC. In the past three reports, the rate of lymph node metastasis for submucosal EGC was 12.5%^[22], 11%-20%^[23], and 16.7%^[24], respectively. One study reported poorly differentiated adenocarcinoma, with a lymph node metastasis rate of 17.0%^[25]. In another study, T1b tumors with lymphovascular invasion had a 64.3% rate of positive LN^[26]. The probability of lymph node metastasis in EGC is influenced by tumor characteristics and increases with increasing tumor size, submucosal invasion, poorly differentiated tumors, and lymphatic and vascular invasion^[24,27]. In our case, LN metastasis in the lesser curvature (5/25) may be related with submucosal invasion and poor differentiation.

In this case, when the SMT-like lesion was found on EGD, we could not distinguish it from other SMTs and we failed to perform EUS-FNA. According to the new consensus guidelines, we directly performed the diagnostic ESD. In contrast to other methods, ESD may increase the economic burden. Subsequently, because of the positive edge, subsequent gastrectomy with lymph node dissection was performed and final histopathologic examination revealed that lymph node metastasis was positive for 5 of 25 lymph nodes in the lesser curvature. Long-term follow-up and monitoring were suggested.

CONCLUSION

From this case, we infer that some SMT-like lesions pose difficulties in distinguishing between benign tumors and cancers. Thus, during the diagnosis of a sub-mucosal tumor, if usual biopsies cannot confirm the diagnosis, multiple biopsies using larger forceps or even EUS-guided FNA or fine needle biopsy may improve the clinical diagnosis and staging. Sometimes, diagnostic ESD is the preferred method to offer

further information to a pathologist such as the degree of differentiation and the depth of infiltration^[28]. Moreover, ESD can potentially be used for therapeutic purposes^[29]. Additional therapy by gastrectomy with lymphadenectomy should be taken into consideration for lesions that are poorly differentiated, invade into the deep submucosa, and have positive lateral or deep margins with lymph node metastases.

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