Gastric Adenocarcinoma Presenting as a Submucosal Tumor: A Case Report

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ABSTRACT

Gastric adenocarcinoma presenting as a submucosal tumor (SMT) accounts to only 0.1% to 0.63%. A 56-year-old Filipino male presenting with new onset melena underwent magnifying endoscopy, narrow-band imaging, endoscopic ultrasound, and computed tomography revealing a 2.5 cm x 2.0 cm polypoid SMT-like lesion at the fundus. Total gastrectomy with lymph node dissection and esophagojejunostomy was performed with histopathology showing adenocarcinoma. This suggests the need for different modalities to ensure the accuracy of diagnosis and the need for subsequent invasive treatments.

Keywords: gastric adenocarcinoma, submucosal tumor, endoscopic ultrasound

BACKGROUND

Most gastric adenocarcinomas present as mucosal lesions, and are usually diagnosed by endoscopic biopsy. Gastric submucosal tumor (SMT) on the other hand poses a dilemma in endoscopic and histologic diagnosis, since normal mucosa overlies the tumor surface. A very unusual presentation of gastric adenocarcinoma with features of a SMT has a prevalence of 0.2%-0.62% only. Given differentials for SMTs are mostly benign tumors, surgical resection or close monitoring are often the options for management. However, with the non-specific and overlapping features on imaging studies of gastric SMTs, the generally deep location of such tumors makes the preoperative diagnosis of SMT-like gastric cancer challenging. Hence the need for specific modalities like endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) for tumor depth and nodal involvement characterization aside from accurate tissue diagnosis. Here, we present a rare case of SMT-like tumor which revealed gastric carcinoma after stepwise diagnostics and subsequent surgical resection histopathology report. A written and signed consent was secured prior to this writing during index case's admission.

CASE PRESENTATION

A 56-year-old Filipino male patient presenting with new onset melena was initially managed as upper gastrointestinal bleed at a local hospital. He underwent upper endoscopy which revealed a 2.5 cm x 2.0 cm polypoid submucosal mass with prominent vessels and ulcerated top with evidence of recent bleed. Colonoscopy was also done but revealed no abnormal findings. An abdominal computed tomography

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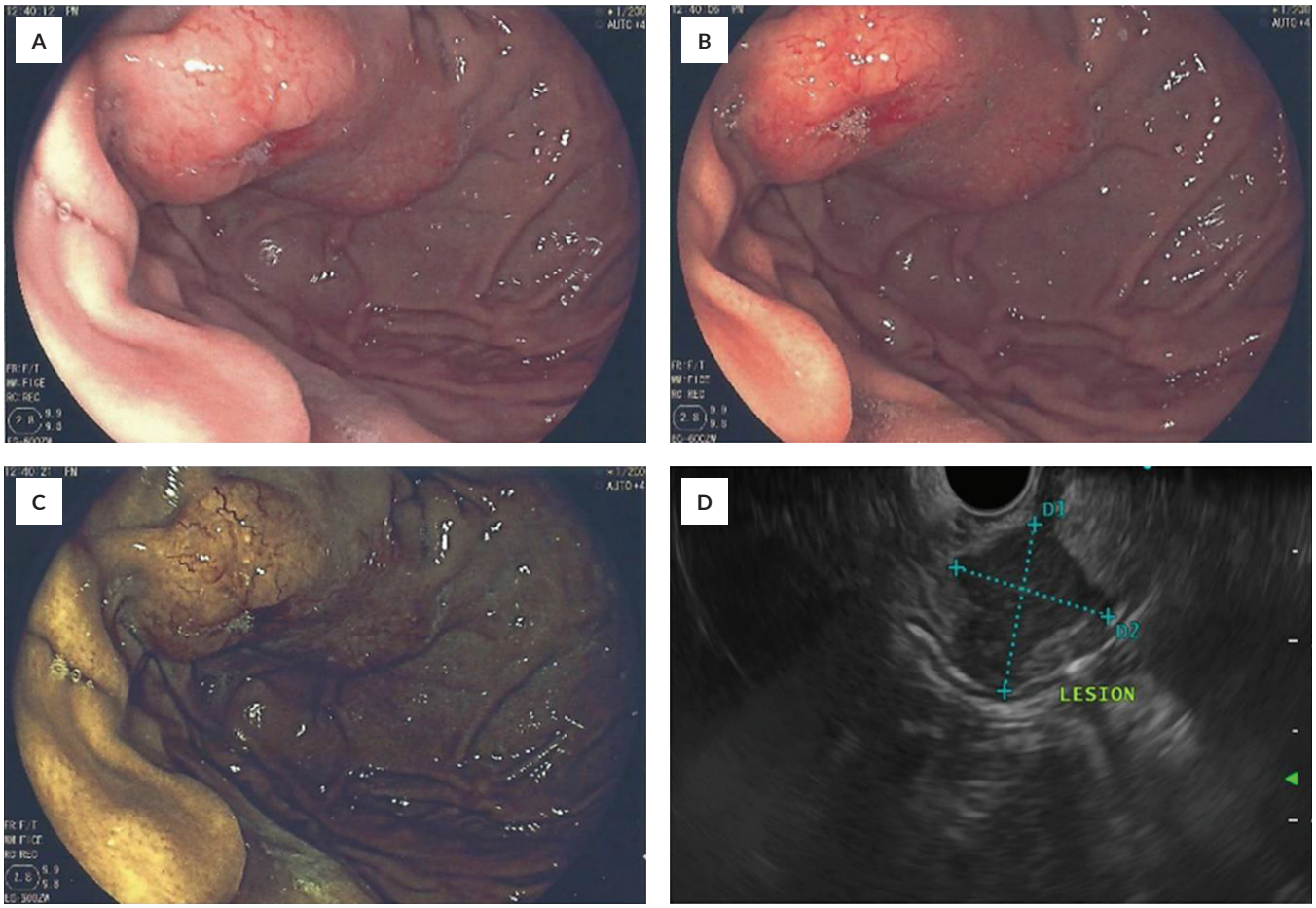

Figure 1. ***Endoscopic findings.*** **(A and B)** Regular endoscopy showed 2.5 cm x 2.0 cm Bormann type I (polypoid/protruded type) lesion covered by congested mucosa at the gastric fundus. **(C)** Narrow-band imaging revealed a regular microvascular pattern, presence of a demarcation line, irregular and smaller crypt opening, and widened intervening part. **(D)** Endoscopic ultrasound revealed a 21 mm × 19 mm hypoechoic mass with irregular borders within the 3rd layer of the gastric mucosa without invasion of lamina propria and serosa.

(CT) scan was initially requested which revealed no distant metastasis. He was eventually transferred to our institution, underwent endoscopic ultrasound (EUS), and biopsy revealed gastric adenocarcinoma. He subsequently underwent total gastrectomy and esophagojejunostomy.

He had no known comorbidities nor heredofamilial history of malignancy. He had been smoking for 30 years and occasionally drinks beer and rhum.

On physical examination, he was 70 kg in weight and 178 cm in height. He had a blood pressure of 120/70 mmHg and pulse rate of 68 beats per minute. Abdominal examination did not reveal any palpable mass, superficial vessels, succussion splash, umbilical fullness or nodules. Rest of the systemic physical examination on admission was unremarkable.

After admission, the patient underwent evaluations including routine blood tests, biochemistry, and some serum tumor markers including carcinoembryonic antigen, alpha-fetoprotein, carbohydrate antigen 199, but no significant abnormal test results were recorded.

By systematic approach, patient underwent endoscopy, narrow band imaging and subsequent endoscopic ultrasound with fine needle biopsy. He subsequently underwent total gastrectomy and esophagojejunostomy.

According to the imaging findings and the histopathologic examination, the index case was diagnosed with Gastric adenocarcinoma, moderately differentiated, Bormann type I polypoid and Pathologic staging Stage IIA, T3N0M0.

Endoscopy revealed a 2.5 x 2.0 cm Bormann type I (polypoid/protruded type) mass with overlying congested mucosa at the gastric fundus (Figures 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 21 mm × 19 mm hypoechoic mass with irregular borders within the 3rd layer of the gastric mucosa without invasion of lamina propria and serosa (Figure 1D), and no perilesional lymph

nodes noted. The descending aorta, celiac axis and superior mesenteric artery were patent and free of tumor. No celiac lymph nodes noted.

Computed tomography of the upper abdomen was requested by the referring hospital which revealed an 18 mm × 11 mm broad based nodular density at the posteromedial aspect of the gastric fundus and no evidence of swollen lymph nodes or distant metastasis (Figure 2).

As endoscopic ultrasound biopsy showed gastric adenocarcinoma, without lamina propria and lymph node invasion, a total gastrectomy and esophagojejunostomy were performed. Pathology of the resected specimen revealed a polypoid mass occupying an area measuring 2.5 x 2.0 cm at the gastric cardia, grossly infiltrating beyond the muscularis propria of the stomach, with a depth of invasion measuring up to 1.5 cm (Figure 3). Accordingly, the final diagnosis was verified as moderately differentiated adenocarcinoma. The final histopathologic examination revealed no lymphovascular invasion, no perigastric lymph node invasion including those in the hepatoduodenal ligament, the periphery of the hepatic artery, the greater curvature, and the left gastric area. The resection margins and omental tissue are free of tumor cells.

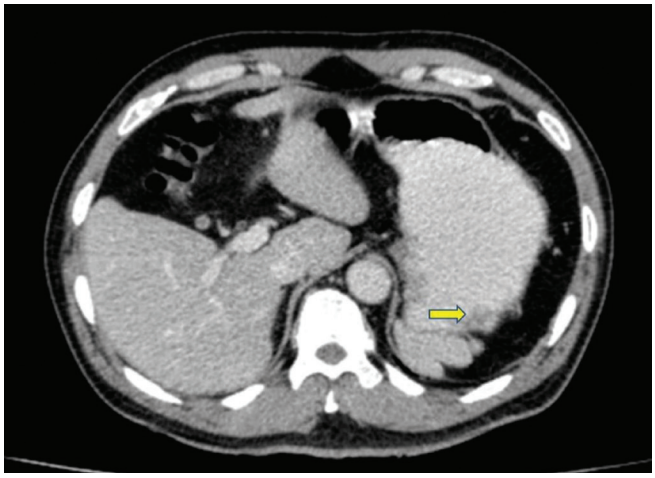

Figure 2. ***Abdominal computed tomography.*** An 18 mm × 11 mm broad based nodular density at the posteromedial aspect of the gastric fundus *(yellow arrow)*.

Differential Diagnosis

A patient presenting with overt gastrointestinal bleed must be worked up with upper endoscopy as in this case with melena. Usual etiologies of which include ulcer, erosions, bleeding vessel or masses. In the evaluation of the index case, it was noted on standard gastroscopy, a subepithelial lesion. Hence, the need for further evaluation with CT scan and endoscopic ultrasound. The latter modality ensures evaluation of the layer of origin of a submucosal tumor, ascertain presence of regional lymph nodes, and facilitate fine needle biopsy for histopathology. Gastric adenocarcinoma rarely presents as submucosal mass. Differentials of which varies per location. At the third layer of stomach wall, leiomyoma is usually a homogenous hypoechoic well-defined mass. Lipoma on the other hand is usually diffusely hyperechoic. Varices which arise at this layer as well are usually anechoic, serpiginous with positive Doppler for blood flow. In our case, the submucosal lesion was a hypoechoic heterogenous mass with irregular borders suspicious of malignancy. Histopathology has proven then it was a gastric adenocarcinoma.

Treatment

After recovery from total gastrectomy and esophagojejunostomy, feeding per orem was progressed successfully. Index patient subsequently underwent chemotherapy for gastric

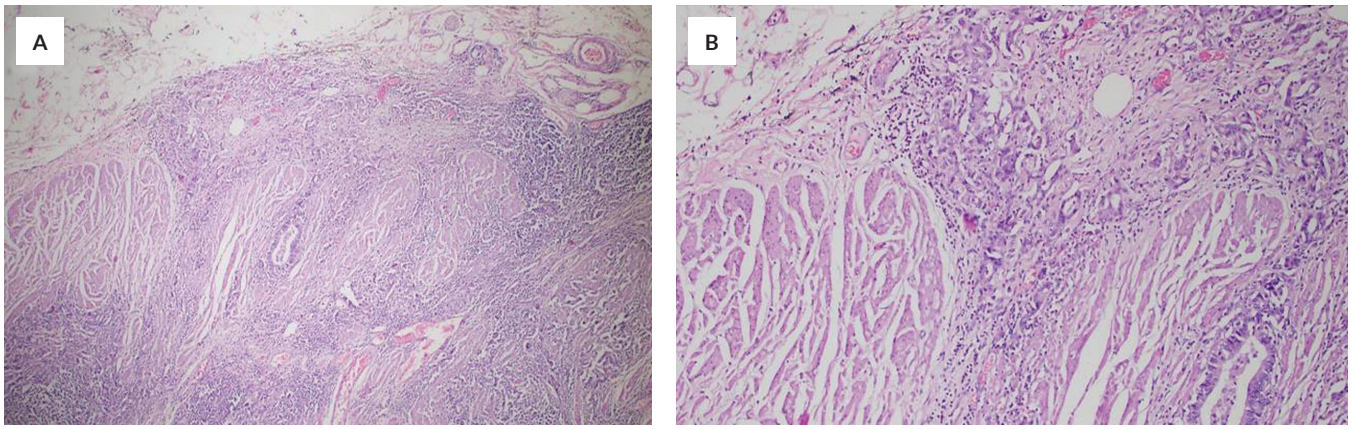

Figure 3. ***Histopathological findings (Hematoxylin and eosin staining).*** Adenocarcinoma, moderately differentiated, 2.5 cm in greatest tumor dimension, gastric cardia. **(A)** Representative section of the tumor revealed neoplastic glandular cells invading through the muscularis propria of the stomach, into the perigastric soft tissue. **(B)** An accompanying desmoplastic response is seen as the tumor cells interface with the adipose and fibrovascular tissue that comprise the perigastric soft tissue. Invasion beyond the visceral peritoneum was not seen in the specimen. Magnification: **(A)** Scanning 40x; **(B)** High Power Objective 400x.

adenocarcinoma Stage II with Folinic acid, 5-Fluorouracil and Oxaliplatin (FOLFOX).

Outcome and Follow-Up

Patient has been on regular follow-up with medical oncologist, nutritionist, and gastroenterologist. Patient has been feeding per orem since discharged and has reportedly regained weight and appetite.

DISCUSSION

As per GLOBOCAN 2018 data, gastric cancer, accounting for 8% of all cancers, is the third leading cause of cancer mortality, following only lung and colorectal cancer in overall mortality worldwide. About 8.3% or 1 in 12 of all oncological deaths are attributable to gastric cancer.[1] Adenocarcinomas account for 95% of all gastric malignancies and are usually derived from the lamina propria layer with fused neoplastic glands of various sizes.[2]

Majority of gastric adenocarcinomas present as mucosal lesions, and are usually diagnosed by endoscopic biopsy. On the other hand, gastric submucosal tumor (SMT) is often difficult to diagnose histologically by standard endoscopy and biopsy forceps, since the tumor surface is covered with normal mucosa. Submucosal tumors are usually benign. A gastric carcinoma with the endoscopic features resembling SMT is rare, and reportedly account for only 0.1% to 0.63% of all resected gastric carcinomas reported.[3] Aside from the non-specific and overlapping features on imaging studies, the generally deep location of such tumors makes preoperative diagnosis of SMT-like gastric cancer challenging. The wide array of SMT differentials including gastric neuroendocrine tumors (GI-NETs), stromal and smooth muscle tumor, and lipoma; heterotopic pancreas; and other uncommon cases, such as metastatic carcinoma, gastric glomus tumor, and gastric hamartomatous inverted polyp, makes adenocarcinoma a least likely considered etiology. In the advent of multiple modalities for early gastric cancer detection and diagnosis, some available reported cases of GC manifesting as SMT have further broadened the pathologic etiologies including gastric adenocarcinoma,[4] gastric mucinous adenocarcinoma,[5,6] and lymphoepithelioma-like carcinoma.[7]

The pathogenesis of SMT-like adenocarcinoma is still unclear. It is believed that unwarranted infiltration of lymphocytes in gastric cancer, intensive mucus secretion by mucous adenocarcinoma, and excessive fibrosis around gastric cancer may be accountable for gastric adenocarcinoma without mucosal lesion.[2] The upper and middle third of the stomach are the usual location of gastric adenocarcinomas without mucosal lesions. Oftentimes, they appear with central depression of mucosa and invasion of the muscular layer.[8] With repetitive erosion and regeneration from chronic inflammatory processes (Epstein-Barr virus infection, chemical irritation as in ethanol and cigarette smoking), the lamina propria becomes aberrant and heterotropic gastric glands become abundant. The latter being linked then to carcinogenesis.[9]

The American Gastroenterological Association (AGA) has recently published its clinical practice guideline update on the management of subepithelial lesions during endoscopy. When an SMT evaluation is indeterminate and/or if non-diagnostic tissue by forceps biopsies on standard esophago-gastroduodenoscopy (EGD), an endoscopic ultrasound (EUS) serves as the modality of choice. If arising from the submucosa, it can be sampled using tunnel biopsies (or deep-well biopsies), EUS-guided fine-needle aspiration (FNA), EUS-guided fine-needle biopsy (FNB), or advanced endoscopic techniques (unroofing or endoscopic submucosal resection). Subepithelial lesions discovered to be ulcerated, presented with bleeding, or causing obstructive symptoms should be considered for resection especially when proven malignant. Tumor size >2 cm, malignant features on endoscopy (malignant border or tumorous ulcer) and high risk features on EUS (anechoic area with echogenic foci, irregular border with lymph node swelling) may be resected endoscopically by ESD or EMR unless it has invaded beyond submucosa where surgical resection is warranted.[10]

EGD has become the standard procedure for the investigation of upper gastrointestinal cancer. In a retrospective cohort study by Raftopoulos, up to 6.7% of GCs may be concealed when endoscopy shows no initial cancer findings,[11] particularly when early gastric malignancy mimics a submucosal tumor. In this case, EGD revealed a type 0-Ip lesion, covered by nearly normal mucosa on the gastric angle, very much like typical submucosal tumors. At the time, clinician was suspicious of underlying malignancy hence an EUS was subsequently planned instead of EGD biopsy. The neoplastic cells exposed on the surface accounted for less than 20%-30% only of the whole tumor in gastric cancer cases imitating an SMT as in previous reports. Hence, multiple biopsies may improve the yield of confirmed diagnosis but the authors decided to proceed with EUS biopsy instead.

Endoscopic Ultrasound (EUS) is the well-studied modality for the staging of gastric cancer. It has remained standard test of choice in evaluating tumor depth and nodal involvement.[12] EUS allows visualization of five layers of gastric wall. These lesions typically involve thickening of the submucosa and muscularis propria with accompanying irregularity or disruption of layers. According to meta-analysis by Mocellin et al. on utility of EUS for gastric cancer staging, it has a specificity of 91% and sensitivity of 86% to identify T1-2 versus T3-4 tumors.[13] It can distinguish intramucosal lesions (T1a), on the other hand, with 83% sensitivity and 79% specificity. The utility of EUS also allows subsequent planning by identifying early gastric cancer lesions amenable to advanced endoscopic therapy such as endoscopic mucosal resection (EMR) or submucosal dissection (ESD).[14] However, some factors contribute to EUS staging which include ulcers and undifferentiated cancer as two independent factors.[15] Hence, the need for FNA to

distinguish such for other more common SMT-like lesions. In our index case, EUS showed that the mucosal and submucosal layers were thickened and a hypoechoic mass within the submucosal layer was visualized and biopsied as described.

The management of gastric adenocarcinoma in general depends on the size of the lesion, depth of invasion, and presence of lymphovascular invasion and metastasis. The TNM classification is used to stratify disease into four clinical stages (I through IV) to predict prognosis in patients treated with gastrectomy. A submucosal gastric adenocarcinoma definitely requires gastrectomy. Surgical resection remains the primary curative treatment for gastric cancer. The survival after surgery alone however is not promising (20% to 50% at 5 years), hence the need for perioperative chemotherapy or postoperative (adjuvant) chemoradiotherapy as was employed in the index case.[12] An independent risk factor for the survival of patients with EGC, lymph node metastasis is influenced by tumor characteristics. The probability of EGC increases with increasing tumor size, poorly differentiated tumors, submucosal invasion, and lymphatic and vascular invasion.[16] In our case, the moderately differentiated adenocarcinoma did not show any perigastric or perilesional lymphovascular invasion. Ideally, an EUS alone can characterize the depth of invasion to aid the preoperative diagnosis and staging. This thus negates the need for computed tomography pre-operatively. This matter can be thoroughly discussed during multidisciplinary planning.

CONCLUSION

Accurate diagnosis of submucosal tumors prior to surgical management is imperative as some may resemble gastric cancer and may require different surgical approach compared to more common but benign SMT. For diminutive and typical SMT, close outpatient follow-up and monitoring suffice, and even when surgery is performed, its goal is margin-free resection rather than radical gastrectomy.[17] Thus, a postoperative diagnosis of gastric adenocarcinoma will just necessitate subsequent surgery if inadequately diagnosed preoperatively and consequently burdens both patients and clinicians. Hence, multiple modalities are employed to achieve a definitive diagnosis and assess lymphovascular involvement prior to surgery.

Learning Points

- Gastric adenocarcinoma rarely presents as submucosal tumor and requires different modalities for diagnosis.
- Endoscopic ultrasound must be employed for tumor depth and nodal involvement, staging and prognosis alongside with fine needle biopsy for histopathologic confirmation to avoid missed diagnosis of malignancy.
- An inadequate investigation preoperatively of a submucosal tumor will lead to repeated surgeries and consequently burdens both patients and clinicians.

Statement of Authorship

JMKT provided substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; participated in drafting the article and revising it critically for important intellectual content; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. TCFU reviewed the slides of histopathology and interpreted findings as part of the manuscript's analysis of data. RMM reviewed the manuscript and recommended final approval of the version to be published.

Author Disclosure

All authors declared no conflicts of interest.

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REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018 Nov;68(6):394–424. doi: 10.3322/caac.21492.
2. Umehara Y, Kimura T, Okubo T, Sano Y, Nakai K, Oi S, et al. Gastric carcinoma resembling submucosal tumor. Gastric Cancer. 1999 Nov;2(3):191–3. doi: 10.1007/s101200050045.
3. Howson CP, Hiyama T, Wynder EL. The decline in gastric cancer: epidemiology of an unplanned triumph. Epidemiol Rev. 1986;8:1–27. doi: 10.1093/oxfordjournals.epirev.a036288.
4. Manabe S, Mukaisho K-I, Yasuoka T, Usui F, Matsuyama T, Hirata I, et al. Gastric adenocarcinoma of fundic gland type spreading to heterotopic gastric glands. World J Gastroenterol. 2017 Oct;23(38):7047–53. doi: 10.3748/wjg.v23.i38.7047.
5. Yu B-C, Lee W-K. Two cases of mucinous adenocarcinoma of the stomach mistaken as submucosal tumor. J Korean Surg Soc. 2013 Feb;84(2):118–22. doi: 10.4174/jkss.2013.84.2.118.
6. Yoo CH, Park SJ, Park MI, Moon W, Kim HH, Lee JS, et al. Submucosal tumor-like early-stage mucinous gastric carcinoma: a case study. Korean J Gastroenterol. 2013 Aug;62(2):122–5. doi: 10.4166/kjg.2013.62.2.122.
7. Takahashi T, Otani Y, Yoshida M, Furukawa T, Kameyama K, Akiba Y, et al. Gastric cancer mimicking a submucosal tumor diagnosed by laparoscopic excision biopsy. J Laparoendosc Adv Surg Tech A. 2005 Feb;15(1):51–6. doi: 10.1089/lap.2005.15.51.
8. Yuki T, Sato T, Ishida K. Clinicopathological and imaging feature of gastric carcinoma resembling submucosal tumor. Stomach Intest. 2003; 38:1527–36.
9. Tsuji T, Iwahashi M, Nakamori M, Ueda K, Ishida K, Naka T, et al. Multiple early gastric cancer with gastritis cystica profunda showing various histological types. Hepatogastroenterology. 2008 May-Jun;55(84):1150–2.
10. Raftopoulos SC, Segarajasingam DS, Burke V, Ee HC, Yusoff IF. A cohort study of missed and new cancers after esophagogastroduodenoscopy. Am J Gastroenterol. 2010 Jun;105(6):1292–7. doi: 10.1038/ajg.2009.736.
11. Sharzehi K, Sethi A, Savides T. AGA Clinical practice update on management of subepithelial lesions encountered during routine endoscopy: expert review. Clin Gastroenterol Hepatol. 2022 Nov;20(11):2435–43.e4 doi: 10.1016/j.cgh.2022.05.054.
12. Feldman M, Friedman LS, Brandt LJ. Sleisenger and Fordtran's gastrointestinal and liver disease- 2 volume set: Pathophysiology, diagnosis, management. 11th ed. Philadelphia, PA: Elsevier - Health Sciences Division; 2020.

13. Mocellin S, Marchet A, Nitti D. EUS for the staging of gastric cancer: a meta-analysis. Gastrointest Endosc. 2011 Jun;73(6):1122–34. doi: 10.1016/j.gie.2011.01.030.
14. Okada K, Fujisaki J, Kasuga A, Omae M, Yoshimoto K, Hirasawa T, et al. Endoscopic ultrasonography is valuable for identifying early gastric cancers meeting expanded-indication criteria for endoscopic submucosal dissection. Surg Endosc. 2011 Mar;25(3):841–8. doi: 10.1007/s00464-010-1279-4.
15. Cheng J, Wu X, Yang A, Zou L, Yao F, Guo T, et al. Evaluation of preoperative endoscopic ultrasonography for diagnostic and therapeutic decision making in superficial gastric cancers [Internet]. 2016 [cited 2021 Sep 5]. Available from: https://www.semanticscholar.org/paper/dbec8a1d1ca1eaf8acb6eade8159bf3f949fd243
16. Jin EH, Lee DH, Jung S-A, Shim K-N, Seo JY, Kim N, et al. Clinicopathologic factors and molecular markers related to lymph node metastasis in early gastric cancer. World J Gastroenterol. 2015 Jan;21(2):571–7. doi: 10.3748/wjg.v21.i2.571.
17. Joensuu H, Fletcher C, Dimitrijevic S, Silberman S, Roberts P, Demetri G. Management of malignant gastrointestinal stromal tumours. Lancet Oncol. 2002 Nov;3(11):655–64. doi: 10.1016/s1470-2045(02)00899-9.