Case Report

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Leiomyosarcoma of stomach extending to gastroesophageal junction and distal esophagus as a rare cause of dysphagia: a case report

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Introduction and importance: Gastric leiomyosarcoma is a rare malignant tumor among the primary gastric carcinomas. Among the different common presentations, dysphagia is an uncommon presentation of gastric leiomyosarcoma.

Case presentation: A 29-year-old female presented with complaints of progressive dysphagia for 1 year associated with vomiting, significant weight loss, and anorexia for 6 months. On blood investigations, she had anemia, hypokalemia, prerenal acute kidney injury, and unconjugated hyperbilirubinemia. Upper gastrointestinal endoscopy and contrast-enhanced computed tomography (CECT) were initially suggestive of carcinoma of stomach. Immunohistochemistry was diagnostic of leiomyosarcoma of stomach extending to the gastroesophageal junction and distal esophagus. She underwent total gastrectomy with distal esophagectomy with lateral segmentectomy of liver (nonanatomical) with Roux-en-Y esophago-jejunal anastomosis (end-to-side and retro-colic) through thoracoabdominal approach. After 6 weeks, she received four cycles of doxorubicin therapy. Follow-up at 18 months after surgery revealed no recurrence of malignancy.

Clinical discussion: Leiomyosarcoma, a rare malignant tumor arising from stomach involves commonly gastric body followed by antrum and fundus. Imaging including CECT and tissue diagnosis including immunohistochemistry (positive for α-SMA, desmin, calponin, h-caldesmon, or smoothelin) have been mainstay for definitive diagnosis. The standard treatment for leiomyosarcoma of stomach is complete surgical resection of tumor because it has malignant potential and does not respond to targeted treatment with a tyrosine kinase inhibitor. The type of surgery depends on the size and localization of the tumor.

Conclusions: Early diagnosis with proper imaging, immunohistochemistry, and biopsy play important role in differentiating gastric leiomyosarcoma from gastrointestinal stromal tumor. Surgical resection is the mainstay of treatment.

Keywords: gastrointestinal stromal tumor, leiomyosarcoma, proto-oncogene KIT, stomach

Introduction

Primary gastric leiomyosarcoma is an extremely rare entity that incorporates less than one percent of gastrointestinal malignancy[1]. It was misdiagnosed as gastric gastrointestinal stromal tumor (GIST) before the late 1990s as there was no clear distinction between gastric stromal tumors[2]. Although common presentation includes anorexia, vomiting, and upper gastrointestinal bleeding; patients rarely present with dysphagia[1].

HIGHLIGHTS

- Leiomyosarcoma is a rare malignant tumor among primary gastric carcinoma.
- Symptom of dysphagia in primary gastric leiomyosarcomas can be presenting complaint due to infiltration of gastroesophageal junction and distal esophagus.
- Leiomyosarcoma are generally positive for α-SMA, desmin, calponin, h-caldesmon or smoothelin, and negative for KIT or DOG-1.
- The standard treatment for gastric leiomyosarcoma is complete surgical resection of the tumor.

Herein, we report a case of a young female who primarily presented with dysphagia secondary to gastric leiomyosarcoma extending to the gastroesophageal junction and distal esophagus; a rare tumor with a rarer symptom.

This case has been reported in line with the Surgical CAse REport (SCARE) 2020 criteria[3].

Case presentation

A 29-year-old female presented to the surgery outpatient department with a complaint of insidious onset dysphagia gradually progressive for 1 year. Dysphagia was predominantly on solid diet, which later advanced to liquid diet as well. It was

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associated with occasional nonprojectile, nonblood mixed vomiting. She had a history of significant weight loss, and anorexia for 6 months. However, she had no history of odynophagia, chest pain, foreign body sensation, hoarseness of voice, or symptoms suggestive of gastroesophageal reflux disease. There was no history of pain abdomen, abdominal distension, melena, or hematochezia. She had no surgical intervention in the past. She had no known history of allergy or intake of long-term medication. She never smoked or consumed alcohol. There was no history of malignancy running in her family. On examination, she was cachectic. She had pallor and dehydration; however, her vital parameters were normal. Abdominal examinations revealed normal findings and left supraclavicular lymph nodes were not palpable. Her chest and cardiovascular examinations were normal.

On investigation, she had anemia (hemoglobin: 5.6 gm/dl) which was corrected with blood transfusions. In addition, she had prerenal acute kidney injury (creatinine: 141 μmol/l) which was corrected with fluid resuscitation. Furthermore, she had hypokalemia (serum potassium:3.4 mEq/l) and hypoalbuminemia (serum albumin: 3.3 gm/dl). Total bilirubin was raised (63.27 μmol/l) while direct bilirubin was normal. Liver enzymes and PT/INR were under normal range (Table 1). Upper gastrointestinal endoscopy showed narrowing of the lumen at 36 cm for upper incisor due to protrusion of normal mucosa intraluminally, suggestive of intramural or extraesophageal mass, and scope could not be negotiated further (Fig. 1). Multiple biopsies were taken, which showed spindle cell proliferation and chronic inflammation with negative for dysplastic change. Contrast-enhanced computed tomography (CECT) abdomen and pelvis [Figures 2(A), (B), 3(A) and (B)] showed diffuse heterogeneously enhancing wall thickening involving distal esophagus (up to 2.9 cm proximal to gastroesophageal junction), gastroesophageal junction, cardia, and lesser curvature of the stomach with a maximal thickness of 26 mm with gross luminal narrowing of the distal esophagus. There were multiple ill-defined heterogeneously enhancing intramural and exophytic nodular lesions along the thickened wall, most showing coarse calcification with evidence of fat stranding around the lesion. The lesion was abutting the left lobe of the liver with an indistinct fat plane and abutting the pancreas posteriorly. There were multiple enlarged perigastric lymph nodes along the greater curvature and gastroesophageal junction, few in the periportal and lower para-esophageal region. In addition, there was incomplete occlusion of the right branch of the portal vein with chronic thrombosis. There was no evidence of liver metastasis and chest findings was normal. Considering GIST, leiomyoma or carcinoid tumor as differential diagnoses, she underwent repeat biopsy with immunohistochemistry (IHC) since previous biopsy report was inconclusive and did not correlate with imaging findings. In IHC, spindle shaped cells with moderate pleomorphism were seen which was diagnostic of leiomyosarcoma. Specimen was positive for alpha smooth muscle actin (SMA), caldesmon, and muscle specific antigen (MSA) (focal) while negative for ALK, PANCK, and KIT (CD117). Ki67 proliferation index was 30%.

Table 1

Baseline investigations of the patient.

Investigation	Value
Hemoglobin	5.6 gm/dl
Total leukocytic count	3900/cc
Differential leukocytic count	Neutrohphil:76%, Lymphocytes:23%
Platelets	558 000/cc
Blood grouping	B Positive
Random blood sugar	8.6 mmol/l
Sodium	136 mEq/l
Potassium	3.4 mEq/l
Creatinine	141.44 μmol/l
Total Bilirubin	63.27 μmol/l
Direct Bilirubin	5.13 μmol/l
SGPT	14 U/l
SGOT	4 U/l
ALP	53 U/l
Total serum albumin	6.7 gm/dl
Serum albumin	3.3 gm/dl

With the diagnosis of dysphagia secondary to leiomyosarcoma of stomach extending to distal esophagus, she underwent feeding jejunostomy for nutritional optimization. After 6 weeks of adequate nutritional build up, she underwent definitive surgery. Tumor was accessed with upper midline incision followed by left thoracotomy, extending the midline incision to left sided chest. Left hemi-diaphragm was divided up to esophageal hiatus. Intra operative finding was a hard mass infiltrating gastroesophageal junction to cardia of stomach and extending to segment II and III of liver, with the approximate size of 6 cm × 8 cm (Fig. 4). The patient underwent total gastrectomy with distal esophagectomy with left lateral segmentectomy. As segment II and III of liver were adherent to the tumor, nonanatomical liver resection was performed. Roux-en-Y esophago-jejunal anastomosis was done with end to side and retro-colic fashion with circular stapler. Free abdominal drain and a water seal drain were placed in left subphrenic space and left hemithorax, respectively.

Histological evaluation revealed leiomyosarcoma involving distal esophagus, stomach, and liver with maximum tumor diameter of 13 cm and all the margins were free of tumor. All seven lymph nodes were negative for malignancy and the TNM staging of the tumor was pT3pN0. Lympho-vascular and perineural invasions were not identified. Postoperatively, patient was managed in surgical intensive care unit (SICU) with mechanical ventilation and inotropic support. Otherwise, the postoperative period was uneventful.

After 6 weeks of surgery, she was followed up in oncology department for adjuvant chemotherapy. There were no new symptoms and dysphasia was resolved. She received four cycles of doxorubicin-based chemotherapy. Repeat CECT abdomen and pelvis was done which showed no residual or recurrent lesion. Follow-up to 18 months after surgery revealed no recurrence of malignancy.

Discussion

Leiomyosarcoma is a rare malignant tumor among primary gastric and esophageal carcinomas. The etiology of gastric leiomyosarcoma has been postulated to ionizing radiation, Epstein Barr Virus, and various chemical exposures but definitive evidence has not been established[1]. Relationship between *Helicobacter pylori* infection and gastric leiomyosarcomas have been investigated, encouraging eradication of the infection[4]. Even though a case of malignant transformation of primary gastric leiomyoma to leiomyosarcoma has been reported highlighting the presence of

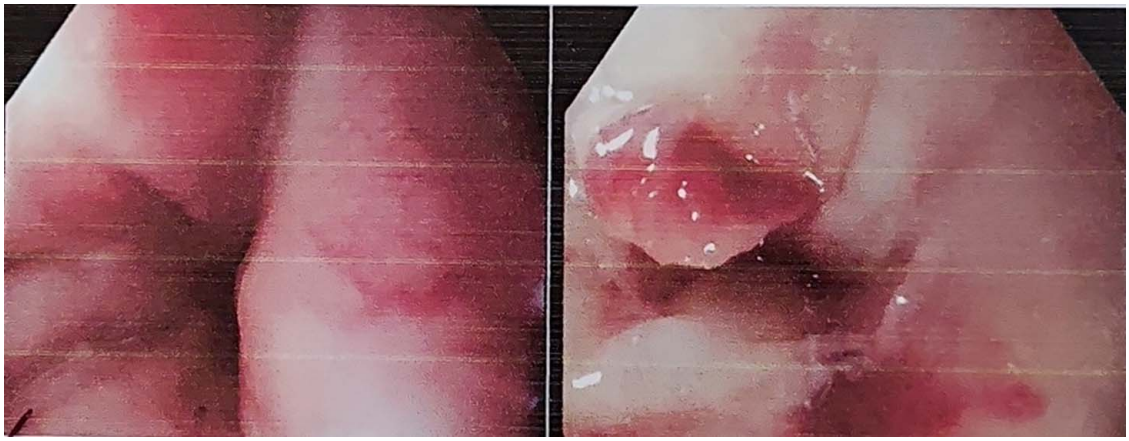

Figure 1. Upper GI endoscopy showing narrowing of esophageal lumen at 36 cm from incisor with mucosal protrusion intraluminally.

the leiomyoma- leiomyosarcoma sequence in the stomach, gastric leiomyomas are considered to have virtually no risk of progression to leiomyosarcoma[5]. Leiomyosarcoma is usually asymptomatic but can present with anorexia, weight loss, nausea, vomiting, or bleeding as hematemesis and melena[6]. In a review of 16 cases of leiomyosarcoma by Garg *et al.*[1], mean age of presentation was 52 years and mean tumor size was 4.80 cm. Gastric body followed by antrum and fundus are the mostly involved regions. Gross appearance may be exophytic, polypoid, ulcerating, or fungating mass[1]. But our case presented with huge tumor and infiltrating type of growth with diffuse wall thickening.

Esophageal leiomyosarcoma is an extremely rare malignancy accounting for 0.1 to 2.8% of all malignant lesions of esophagus and has shown slow growth and late metastasis resulting better prognosis than squamous cell carcinoma and adenocarcinoma. Rocco *et al.*[7] reported 19 cases of esophageal leiomyosarcoma out of 6359 (0.3%) patients with primary esophageal carcinoma. Average age of presentation is 50–60 years[8]. As lower third of esophagus is most commonly involved, presenting symptoms includes dysphagia (64.7–91.7%) retrosternal and back pain, weight loss, vomiting, and respiratory symptoms. Dysphagia signifies a large tumor size[8]. Approximately one-third of leiomyosarcomas may have metastasized irrespective of pathological type, size, and location of the tumor[9]. They may spread by local contiguous spread to the lungs, pleura, pericardium, diaphragm and stomach, or by distant spread to the liver, lungs, and bones. Brain and the inferior vena cava metastasis have been reported. The tumor size of ≥ 5 cm correlates significantly with poor prognosis[1].

Imaging and tissue diagnosis has been the mainstay for definitive diagnosis. Arising between the muscularis propria and muscularis mucosa layers, diagnosis relies on histological examination of deep biopsies and immunohistochemistry. Endoscopic biopsy alone usually yields superficial and normal mucosa resulting false negative reports as in the first biopsy in our case. Endoscopic ultrasonography, has great sensitivity, up to 97%, in diagnosis with exact localization in the deeper planes[10]. On computed tomography (CT) images, leiomyosarcomas are heterogeneous with enhancement of solid portions of the tumor more marked peripherally, admixed with nonenhancing areas of degeneration, hemorrhage, and necrosis. Dystrophic calcification is an uncommon finding unlike in this case. MRI has no specific findings that distinguishes leiomyosarcoma. The tumor is most often iso to hypointense relative to skeletal muscle on T1-weighted images, heterogeneously hyperintense on T2-weighted MR images, and heterogeneous contrast enhancement[11]. Recently, F-18 fluorodeoxy glucose positron emission tomography/CT (PET/CT) has proven its role in diagnosis of leiomyosarcoma[12] although,

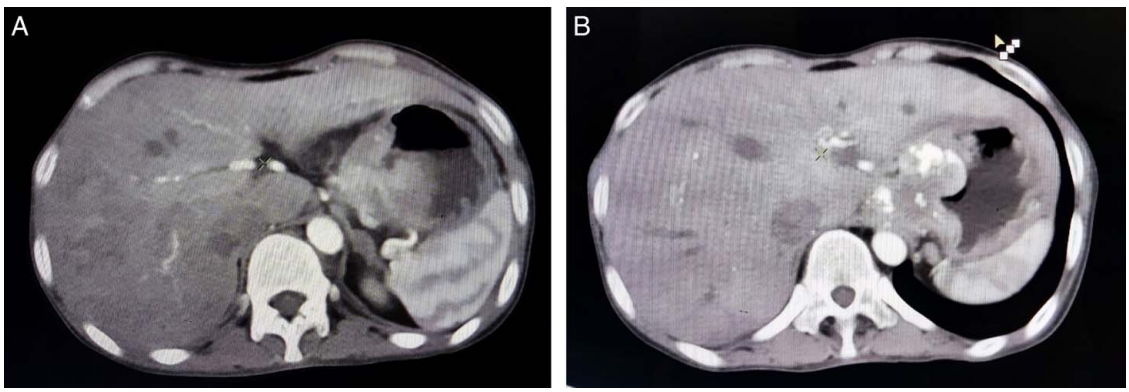

Figure 2. (A) and 2 (B): CECT abdomen and pelvis, axial section showing heterogeneous thickening of distal esophagus and cardia of stomach extending to lesser curvature with multiple nodular irregular calcifications and calcified lymph nodes.

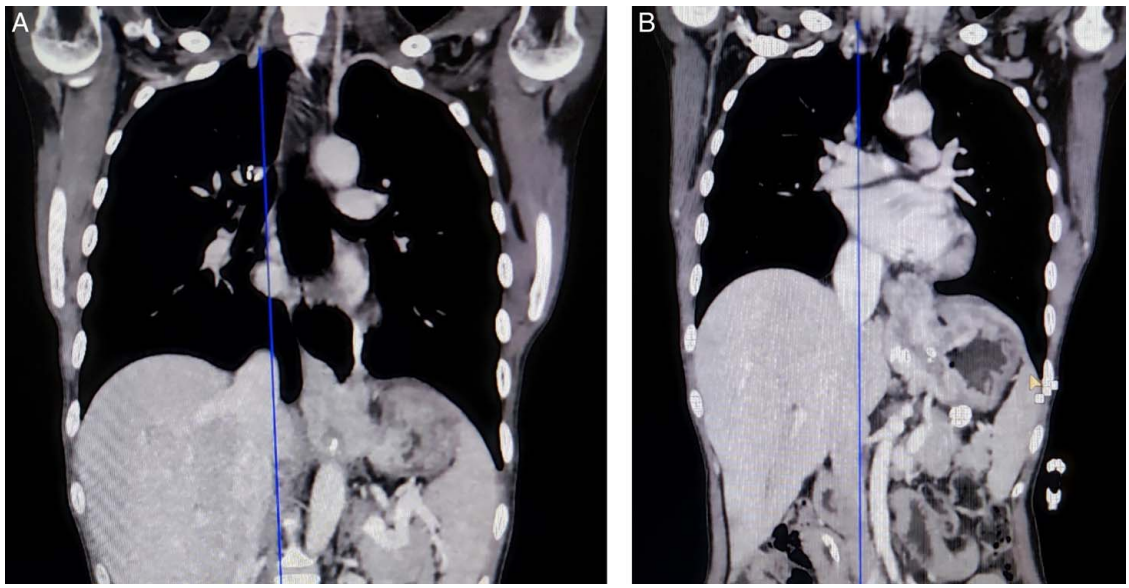

Figure 3. (A) and 3 (B): CECT abdomen and pelvis, coronal section, showing upstream dilatation of esophagus secondary to heterogeneous lesion involving distal esophagus, esophageal junction, and proximal stomach with nodular intramural calcification and calcified lymph nodes.

leiomyoma may show false positive results[13]. Therefore, the value of PET/CT in the differential diagnosis of leiomyosarcoma from leiomyoma deserves further exploration.

Immunohistochemical staining panel shows positive staining with smooth muscle actin, desmin, and vimentin, which are specific smooth muscle markers. Previously, mesenchymal tumors were misidentified but at present, differentiation of GIST based on the expression of KIT receptor (CD117) and DOG-1 has been established. Another marker CD34, despite of lower sensitivity and specificity is being used to distinguish GIST from other mesenchymal neoplasms. Leiomyosarcoma are generally positive for α-SMA, desmin, calponin, h-caldesmon or smoothelin, and negative for KIT or DOG-1. This differentiation between GIST and gastrointestinal leiomyosarcoma enables consideration of KIT-directed therapy with imatinib or sunitinib for GIST[14].

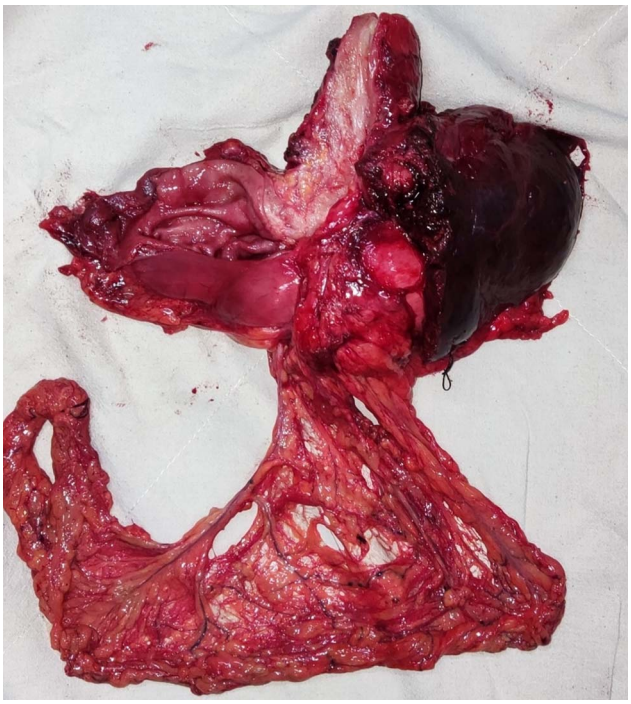

Figure 4. Operative specimen showing hard, irregular, and nodular thickening of distal esophagus, gastroesophageal junction, cardia and body along the lesser curvature, following total gastrectomy with distal esophagectomy with lateral segmentectomy of liver.

The standard treatment for leiomyosarcoma of stomach is complete surgical resection of the tumor because it has malignant potential and does not respond to targeted treatment with tyrosine kinase inhibitor. The type of surgery depends on the size and localization of the tumor[15]. It ranges from endoscopic submucosal dissection for small intraluminal growth or a wedge resection to a total gastrectomy with en-bloc resection if adjacent organs are involved[16]. Laparoscopic and Endoscopic Cooperative Surgery (LECS) is a useful approach that allows endoscopic evaluation of an intraluminal mass such as gastric submucosal tumors and is less invasive than laparotomy. Resection margins determines the prognosis[17]. Systematic lymphadenectomy is not recommended as the involvement of lymph node is rare[17]. However, tumors should be resected without the capsule damage because the tumor rupture is classified to high-risk group for the recurrence[17]. Radical resection for leiomyosarcoma esophagus has good prognosis and surgical resection is recommended in patients with resectable metastases as well[18]. Mortality associated with surgery for leiomyosarcoma of the esophagus may be due to pulmonary and anastomotic complications. Approaching esophageal leiomyosarcomas by minimally invasive techniques minimize the complications despite of larger tumor size[19].

Leiomyosarcoma have predilection for hematogenous spread. Liver and lungs are the most common sites of metastasis followed by pancreas, small bowel, cardiac chambers, skin, submandibular salivary gland, scalp, skeletal muscles, and subcutaneous

tissue[20]. Hepatic resection for liver metastases in combination with chemotherapy has been established as a standard treatment of leiomyosarcoma metastasizing to the liver even though disease recurrence rate is high up to 84%[20,21]. However, in our case, there was no metastatic lesion at the time of diagnosis resulting in better prognosis.

National Comprehensive Cancer Network (NCCN) treatment guidelines recommend anthracycline-based chemotherapy, primarily anthracyclines alone or in combination with ifosfamide for soft tissue sarcomas. Choi *et al*.[22] observed the response of gemcitabine and docetaxel in 26.3% of the leiomyosarcoma patients with median overall survival and progression-free survival of 10.3 months (95% CI: 8.4–12.2) and 3.3 months (95% CI: 2.8–4.7), respectively. Pazopanib, which inhibits multiple tyrosine kinases, including VEGFR-1, -2, and -3, PDGFR-α and -β, FGFR-1 and -3, c-kit, IL-2 receptor-inducible T-cell kinase, leukocyte-specific protein tyrosine kinase, and transmembrane glycoprotein receptor tyrosine kinase (c-fms) have shown promising results in treating leiomyosarcoma[20].

Conclusion

Gastric leiomyosarcoma is rare malignant tumor of stomach, which may present with rare complaints like dysphagia. Early diagnosis with proper imaging, immunohistochemistry, and biopsy plays important role in differentiating gastric leiomyosarcoma from GIST. Surgical resection is the mainstay of treatment for gastric leiomyosarcoma to avoid potential recurrence and metastasis.

Ethical approval statement

Not applicable.

Consent

Written informed consent taken for the publication of the case report and the images. A copy of it is available for review by Editor-in-Chief of this journal on request.

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Author contribution

L.R. and S.G.: contributed in the study concept, data collection, process of original draft preparation, and editing of final manuscript; S.B. and S.S.: contributed in data collection, review, and editing of final manuscript. All the authors approved of the final version of the manuscript and agreed to be accountable for all aspects of the work ensuring questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of interest disclosures

The authors declare that there are no conflicts of interest.

Research registration unique identifying number (UIN)

This manuscript is a case report and not a human study; therefore, does not need to be registered.

Guarantor

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Data availability statement

This submission is a case report and therefore does not include any results derived from research data.

Provenance and peer review

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