Gastric metastasis in patients with leiomyosarcoma: A case report

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Abstract. Soft tissue sarcomas (STS) are very rare tumors, accounting for <1% of all malignancies. Leiomyosarcoma (LMS), accounts for 10-20% of STS. Gastric metastasis of LMS is extremely rare, and only a few cases have been reported. In the present report, two clinical cases of LMS with gastric metastasis. In the present cases, the metastases presented as a solitary lesion and was located in the upper body anterior wall in case 1, and body-greater curvature in case 2. It is debatable whether to perform any local treatment for gastric metastasis due to its poor prognosis. However, the progression of metastatic cancer in the stomach can lead to gastric bleeding, abdominal pain, and dysphagia, which may further shorten survival and decrease a patient's quality of life. Therefore, metastasectomy was performed in the present cases. This should be considered if digestive tract symptoms occur during the treatment of LMS.

Introduction

Soft tissue sarcomas (STS) are very rare tumors, accounting for <1% of all malignancies. Leiomyosarcoma (LMS), which accounts for 10-20% of STS cases, has a poor prognosis, with a tendency for distant recurrence and a decreased disease-free survival (1,2). The 5-year survival rate for patients with LMS is reported to be 72% (3), and common metastatic sites include the lung, liver, and bone. Gastric metastasis in patients with STS including LMS is rare (4). Only a few cases of gastric metastasis in patients with LMS from the viscera such as the atrium, kidney, and uterus have been reported and there are no studies concerning gastric metastasis from soft tissue LMS (5-8). In the present study, two cases of soft tissue LMS that developed gastric metastasis are described. Surgical treatment was performed in the current cases to improve or maintain a patient's quality of life. It was suggested that surgical treatment may be considered in select patients with symptomatic metastasis.

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Case reports

Case 1. A 59-year-old woman visited Mie University hospital on January, 2013 due to a painless mass on her right thigh. After a needle biopsy was performed and she was diagnosed with LMS, she was subsequently referred to Mie University hospital. A physical examination and computed tomography (CT) confirmed a mass with a diameter of 5 cm on the postero-lateral side of the right thigh (Fig. 1). CT of the chest, abdomen and pelvis did not demonstrate any distant metastases. Wide resection of the tumor was performed. Tissue was fixed in 10% neutral-buffered formalin, embedded in paraffin. Tissue sections were sliced at 4 μm thickness, and stained with hematoxylin and eosin. Histological analysis using light microscope showed the proliferation of spindle cells with pleomorphic nuclei. The cells were set in long intersecting fascicles parallel and perpendicular to the plane of the section. Immunohistochemically, the tumor was positive for α-smooth muscle actin, desmin, and HHF35, but negative for S100 (Table I), which was consistent with the findings of LMS (Figs. 2A and B, and 3). After 1 year, she developed lung and bone metastases. Therefore, systemic chemotherapy using doxorubicin and ifosfamide was administered. Radiofrequency ablation (RFA) was performed for multiple bilateral pulmonary metastases. The bone metastasis was located in the mid-shaft of the femur. Cryoablation, curettage, and fixation with plate and cementation were performed to prevent fracturing. A total of 3 years after the initial surgery, she developed a bone metastasis in the right sixth rib. A resection of the sixth rib combined with resection of the fifth and seventh rib, to acquire a wide surgical margin was performed. A total of 5 years after the surgery, the patient developed sacral and skull bone metastases; thus, 11 cycles of trabectedin plus radiotherapy was prescribed. RFA was performed for residual multiple bilateral pulmonary metastases. After 6 years, abdominal CT revealed pancreatic metastasis. Therefore, eribulin treatment was administered. After 9 years, the patient was admitted to the general hospital for melaena. A submucosal tumor with central erosion was identified in the stomach by endoscopy, and a biopsy was performed (Fig. 4). The histological findings were consistent with a diagnosis of LMS. On CT, the gastric metastatic tumor was not detected, and the size of the metastatic mass in the pancreas was found to be gradually increasing (Fig. 5). The

resection ability of both pancreatic and gastric metastatic tumors was discussed with a multidisciplinary team, and laparoscopic distal pancreatectomy and splenectomy, with partial gastrectomy, were performed. Subsequent histopathological examination confirmed metastasis of the LMS (Fig. 2C). At the final follow-up, 6 months after the gastrectomy (10 years from initial treatment), systemic chemotherapy was administered for residual pulmonary nodules.

Case 2. A 64-year-old man was referred to Mie University hospital on October, 2011 due to a mass on the posterior aspect of the left proximal leg. The patient had a history of a Billroth I gastroduodenostomy for a peptic ulcer. A radiograph showed an osteolytic lesion in the left proximal fibula. MRI of the left knee revealed a 6 cm mass around the proximal left fibula (Fig. 6). CT of the head, chest, abdomen, and pelvis did not demonstrate any distant metastases. An incisional biopsy was performed. Histological analysis revealed remarkably polymorphous spindle cell proliferation. Immunohistochemically, the tumor was positive for α-smooth muscle actin, desmin, and caldesmon, but negative for S100, C56, and pan CK (Table I). The aforementioned morphological and immunohistochemical findings were consistent with LMS (Figs. 7A and B, and 8). Neoadjuvant chemotherapy using doxorubicin and ifosfamide was administered. However, the lower leg could not be salvaged due to the diffuse spread to the tibia and popliteal artery. Thus, an above-knee amputation was performed. A total of 2 months after surgery, he developed multiple lung metastases. RFA was performed regularly for the lung metastases. After 1 year, the patient developed a bone metastasis of the left femur, and cryoablation and internal fixation, using a compression hip screw were performed. After 2 years, the patient presented with severe anemia without any gastrointestinal manifestations. CT revealed a protruding mass in the upper part of the stomach (Fig. 9A), and a large pericardial mass with a diameter of 56 mm. Intense FDG uptake in the stomach, left diaphragm, pericardial mass, and paraspinal muscles at the L1 and L4 levels were observed on FDG-Positron emission tomography (Fig. 9B). Cryoablation was performed for the diaphragm metastasis and paraspinal muscle metastasis. Endoscopy revealed a protruding lesion in the anastomotic site of the Billroth I, which was spreading to the jejunum (Fig. 10). The patient underwent combined resection of the stomach and transverse colon. Subsequent histochemical staining confirmed the diagnosis of gastric metastasis from LMS (Fig. 7C).

Systemic chemotherapy using gemcitabine and docetaxel was performed for the multiple metastases. However, it was discontinued due to a decrease in appetite and fatigue. Finally, the patient received the best supportive care available. He died from the sarcoma 6 months after gastrectomy (33 months after initial treatment).

Discussion

The lung and liver are the most common sites of metastasis for LMS. Metastasectomy may contribute to prolonging survival, although survival after metastasis is generally poor (9). Previously, the feasibility and effectiveness of local interventional treatments, such as RFA, cryoablation, and stereotactic body radiation therapy for lung and liver metastasis were

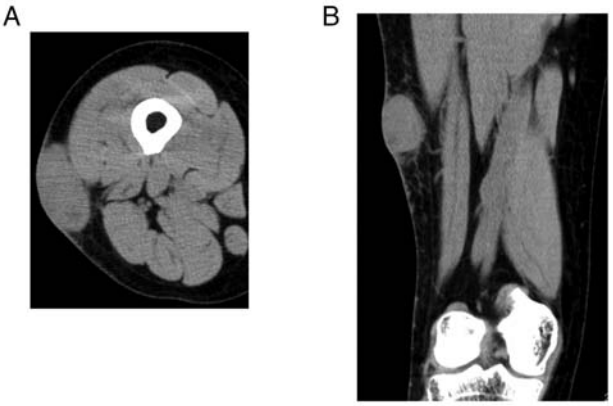

Figure 1. Computed tomography showing a 5 cm mass in the thigh (A) Axial view and (B) coronal view (Case 1).

reported (10-13). Gastric metastasis is rare, with an estimated incidence at autopsy in patients with cancer varying from 1.7 to 5.4% (14). Breast cancer is the most common type of tumor that metastasizes to the stomach (27.9%), followed by lung cancer (23.8%), esophageal cancer (19.1%), renal cell carcinoma (RCC; 7.6%), and malignant melanoma (7.0%) (15).

The mechanisms underlying gastric metastasis have not been clearly elucidated; four pathways may be involved in the metastatic spread of an original primary cancer to the stomach: Peritoneal dissemination, hematogenous dissemination, lymphatic spread, and direct tumor invasion (15). Chest radiography and CT scans during follow-up are recommended as the lung is the most common site of metastasis from STS (16). A chest CT scan typically includes the upper abdomen, leading to an evaluation of the upper part of the stomach. However, it is difficult to identify gastric metastasis on CT images. The rate of detection of early gastric cancer, which is confined to the mucosa or submucosa, on CT is low, at 14.3% (17). In case 1, the gastric metastasis was confined to the submucosa, therefore the metastatic lesion was not detected on CT. Conversely, endoscopic screening reduced the incidence of advanced gastric cancer and mortality from gastric cancer in the Japanese population. In the endoscopic screening group, the mortality from gastric cancer and incidence of advanced gastric cancer were reduced by 61 and 22%, respectively (18). However, endoscopy is not usually performed except for cases with gastrointestinal manifestations. Therefore, gastric metastasis is difficult to detect in the early stages.

Palma *et al* (19) reviewed 64 patients with gastric metastasis from solid malignant tumors, which included one case of STS. It was found that the mean time between the diagnosis of primary tumors and the development of metastatic lesions was 25.7 months (1-40 months).

In >50% of patients with gastric metastases, they are symptomatic, most commonly with bleeding, epigastric pain, vomiting, and anorexia (19). In the present cases, melena was observed in case 1 and severe anemia in case 2. The possibility of gastric metastasis should be considered in patients who present with gastrointestinal manifestations. In the endoscopic findings, the metastases presented as solitary (65%) or multiple lesions (35%), and were more frequently located in the middle or upper third of the stomach (14). In the present study, the

Table I. Antibodies used for immunohistochemical staining.

Antibody name	Source	Type	cat. no./clone	Dilution	Pretreatment	Manufacturer
CD56	Mouse	Monoclonal	NCL-CD56/1B6	1:400	Heat (95˚C, 36 min)	Novocastra; Leica Biosystems
S100	Rabbit	polyclonal	760-2523	1:100	Heat (95˚C, 36 min)	Roche Diagnostics
Desmin	Mouse	Monoclonal	M0760/D33	1:400	Heat (95˚C, 8 min)	DAKO; Agilent Technologies, Inc.
Smooth Muscle Action	Mouse	Monoclonal	M0851/1A4	1:400	None	DAKO; Agilent Technologies, Inc.
Caldesmon	Mouse	Monoclonal	M3557/h-CD	1:200	Heat (95˚C, 36 min)	DAKO; Agilent Technologies, Inc.
Pan-CK	Mouse	Monoclonal	NCL-PAN-CK/ 5D3+LP34	1:400	Heat (95˚C, 64 min)	Novocastra; Leica Biosystems
HHF35	Mouse	Monoclonal	M0635/HHF35	1:200	None	DAKO; Agilent Technologies, Inc.

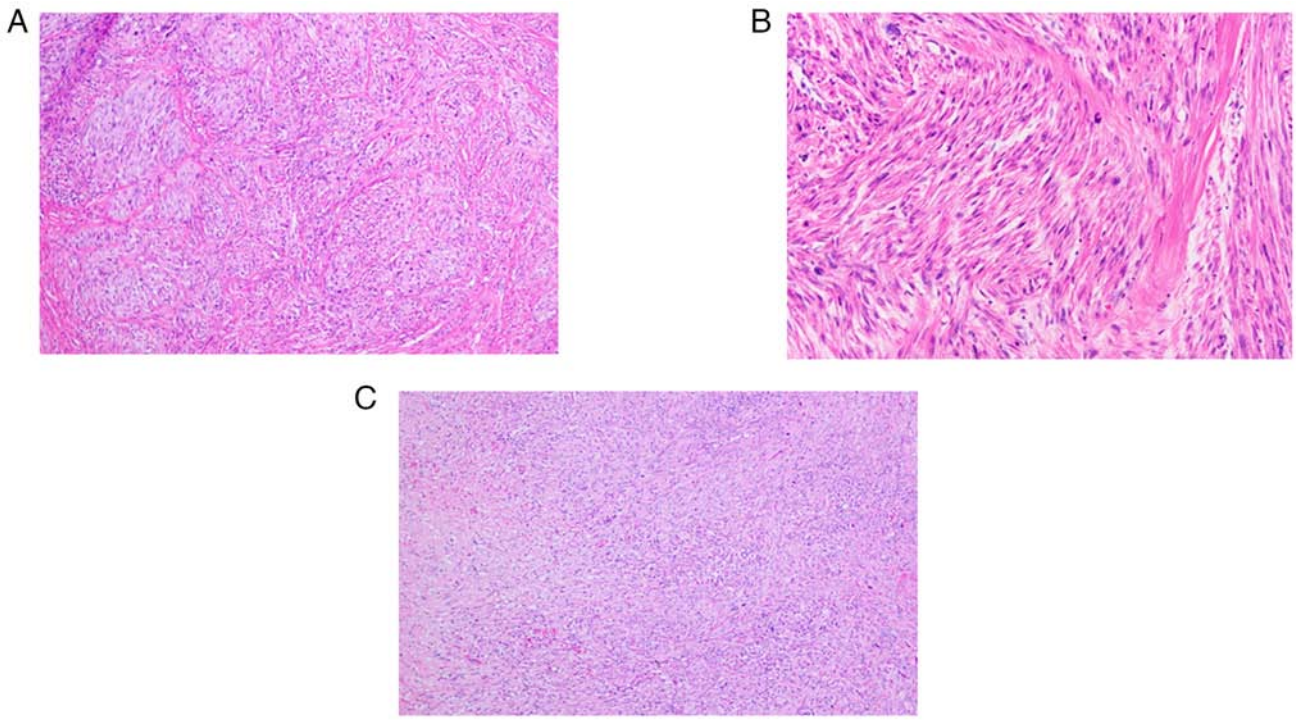

Figure 2. Microscopic findings showing the proliferation of spindle cells with pleomorphic nuclei (Case 1). H&E staining (A) magnification, x10; and (B) magnification, x20 of the primary site. (C) H&E staining of the stomach leiomyosarcoma; magnification, x10.

metastasis presented as a solitary lesion, and was located in the anterior wall of the upper body in case 1, and the greater curvature of the body in case 2.

Generally, the patient's prognosis after gastric metastasis was poor as the presence of gastric metastasis is indicative of advanced-stage disease (19). Although there have been no reports concerning gastric metastasis from soft tissue LMS, to the best of our knowledge, gastric metastasis from other subtypes of STS have been reported (20,21). Akatsu *et al* (22) reported a case and reviewed 10 cases of malignant fibrous histiocytoma with gastric metastases. The patients they reported on underwent surgery as they suffered from uncontrollable tumor bleeding, which led to severe anemia; 60% (6/10) of the reported cases of gastric metastases were treated with distal gastrectomy and only 2 of these patients survived >16 months. The average survival time for the other 4 patients who underwent resection was 7 months. Therefore, the prognosis of patients with gastric metastasis is poor. Samuel *et al* (20) reported a case of synovial sarcoma with gastric metastasis. The patient developed gastric and lung metastases. Complete resection of the primary lesion with postoperative chemotherapy was performed. However, the CT

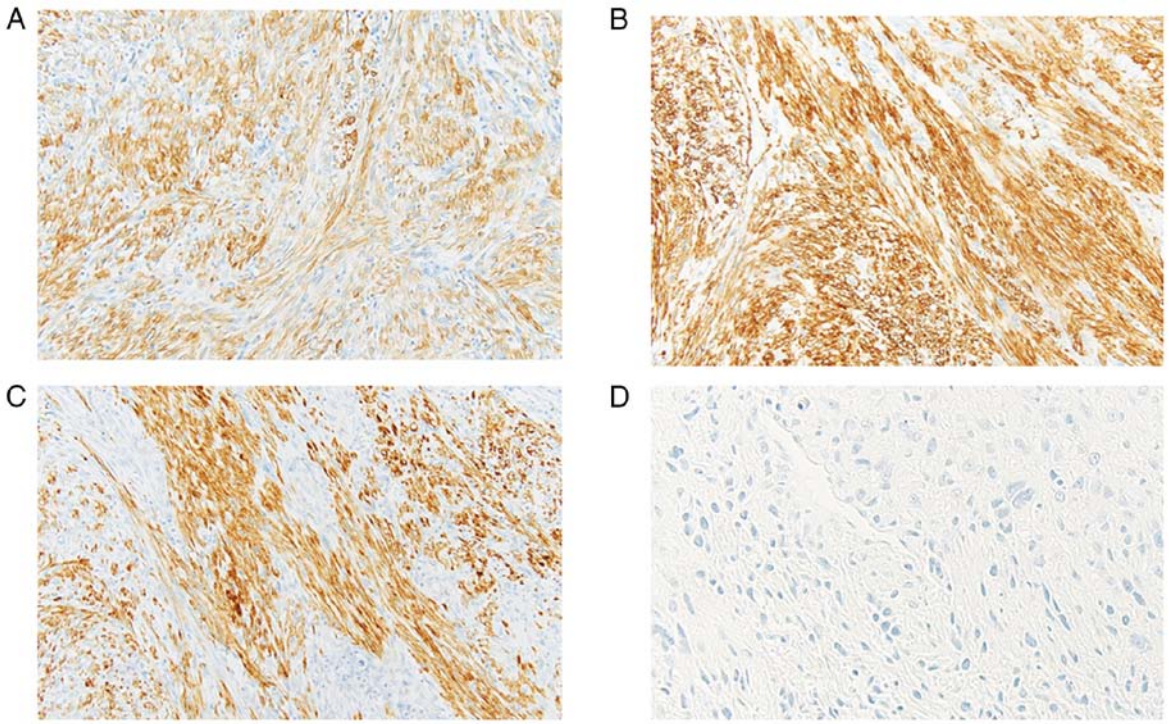

Figure 3. Immunohistochemical staining showing positive expression of (A) α-smooth muscle actin, (B) HHF35, (C) desmin and (D) S-100. Magnification, x20 (Case 1).

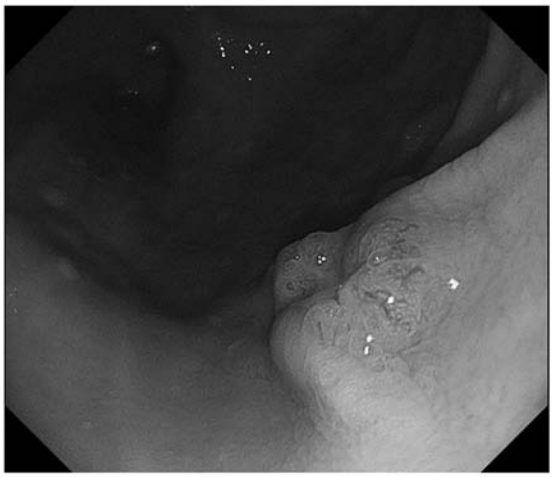

Figure 4. Gastroscopy showing a submucosal tumor with central erosion in the anterior upper body of the stomach (Case 2).

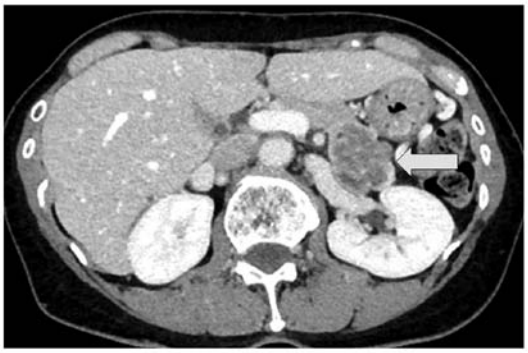

Figure 5. Computed tomography scan showing a pancreatic mass (arrow) (Case 2).

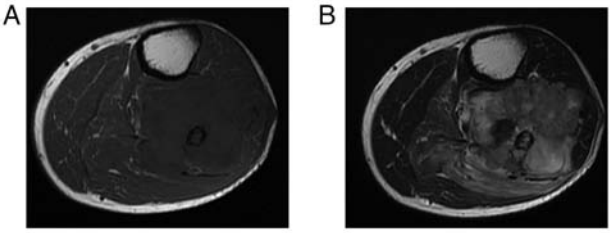

Figure 6. Magnetic resonance imaging showing a 6 cm mass around the proximal left fibula (A) T1 signal intensity; (B) T2 signal intensity (Case 2).

scan performed after chemotherapy revealed an increase in the size of the bilateral lung nodules and stomach mass, along with a new liver lesion, which was to be a liver metastasis. They did not administer local treatment for gastric metastasis as the patient was asymptomatic. It is debatable whether to perform local treatment for gastric metastasis due to its poor prognosis.

Appropriate systemic treatment for metastatic tumors in the stomach is the preferred mode of treatment. However, the progression of metastatic cancer in the stomach can lead to gastric bleeding, abdominal pain, and dysphagia, which may shorten survival and negatively impact a patient's quality of life. Surgical resection of metastatic gastric tumors may be recommended to control hemorrhaging, thus improving a patient's quality of life (15). Endoscopic resection, which is minimally invasive, is effective for submucosal metastasis, such as in Case 1.

In conclusion, our experience of gastric metastases from soft tissue LMS in 2 cases was reported. Gastric metastasis may be suspected in LMS patients with digestive tract symptoms. Surgical treatment may be considered in select patients with symptomatic metastasis. Minimally invasive treatment

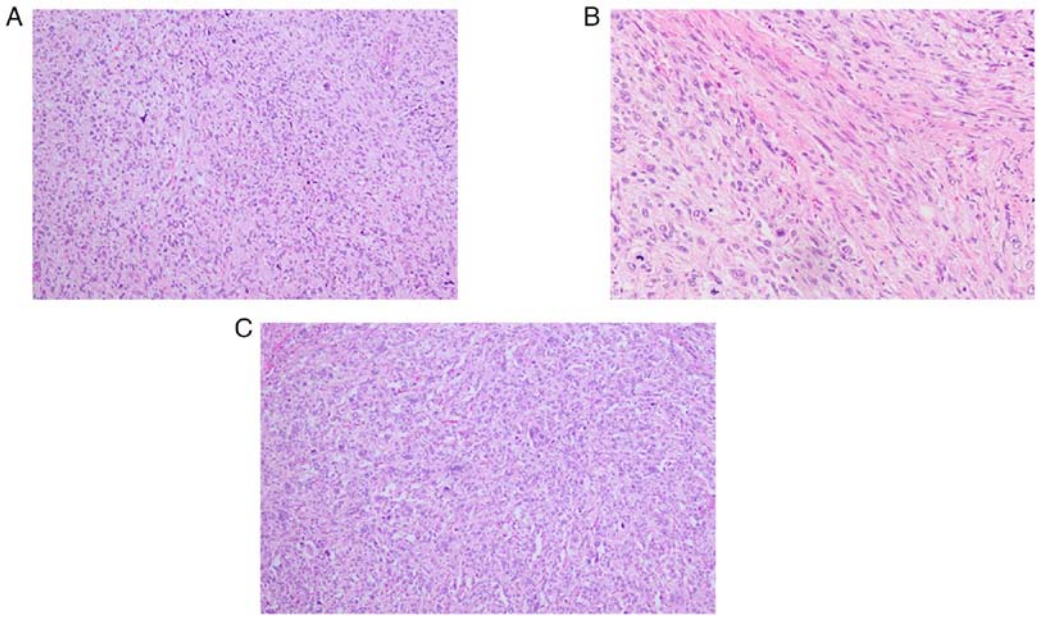

Figure 7. Microscopic findings showing polymorphous spindle cell proliferation at the primary site (Case 2). H&E staining (A) magnification, x10; and (B) magnification, x20 of the primary site. (C) H&E staining of the stomach leiomyosarcoma; magnification, x10.

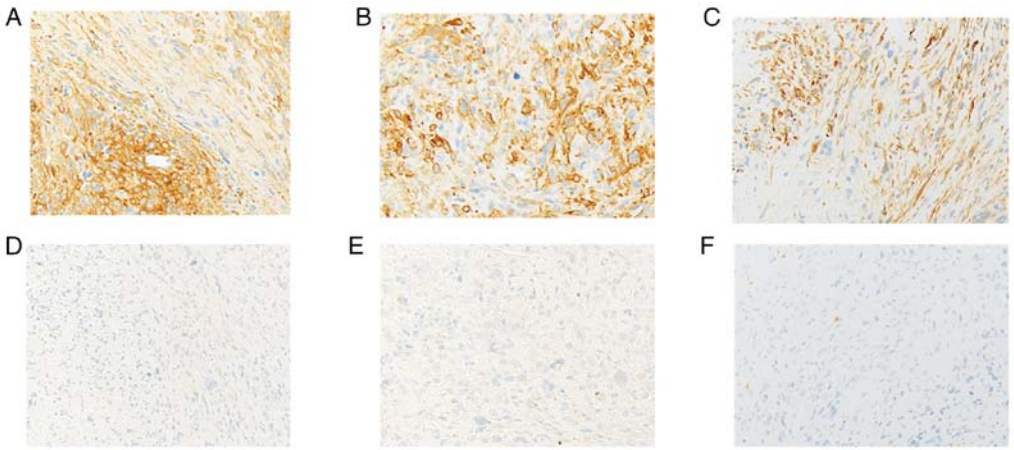

Figure 8. Immunohistochemical staining showing positive expression of (A) α-smooth muscle actin, (B) caldesmon and (C) desmin, and (D) negative expression of C 56, (E) pan CK and (F) S-100; magnification, x20 (Case 2).

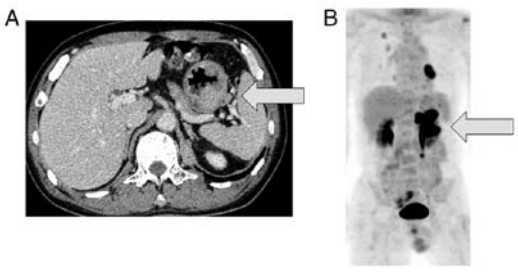

Figure 9. (A) Computed tomography scan showing a protruding mass in the upper part of the stomach (arrow). (B) FDG-positron emission tomography showing FDG uptake in the stomach (arrow), and pericardial metastasis (Case 2).

such as endoscopic resection is a potential treatment option to improve or maintain a patient's quality of life, even if their prognosis is poor.

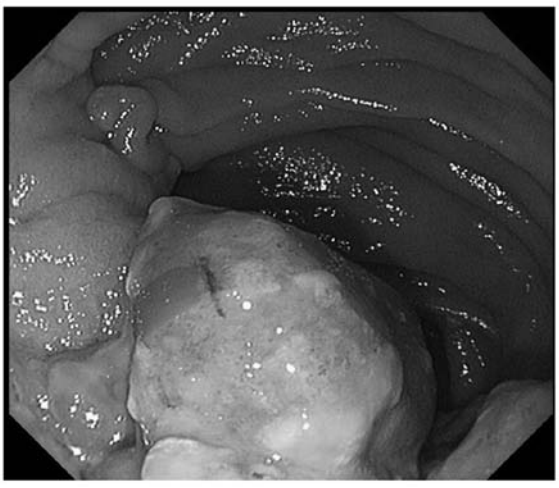

Figure 10. Gastroscopy showing a submucosal tumor in the anastomotic site of Billroth I, which was spreading to the jejunum (Case 2).

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

TN conceived the study, treated the patients, collected the data and wrote the manuscript. TU collected the data and wrote the manuscript. TH, KN and RA collected, analyzed, and interpreted the clinical data. KA performed the surgery, and analyzed and interpreted the clinical data. AS analyzed and interpreted the clinical data, and reviewed the manuscript. All authors have read and approved the final manuscript. KA and TH confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The requirement for institutional review board approval from our institute was waived owing to the anonymized and retrospective nature of this report; however, written informed consent was obtained from the patient to perform further studies when they received surgery.

Patient consent to publication

Written informed consent was obtained from the patients to perform further studies when they received surgery.

Competing interests

The authors declare that they have no competing interests.

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