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ABOUT COVER

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AIMS AND SCOPE

World Journal of Gastroenterology (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. *WJG* was established on October 1, 1995. It is published weekly on the 7th, 14th, 21st, and 28th each month. The *WJG* Editorial Board consists of 642 experts in gastroenterology and hepatology from 59 countries.

The primary task of *WJG* is to rapidly publish high-quality original articles, reviews, and commentaries in the fields of gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, hepatobiliary surgery, gastrointestinal oncology, gastrointestinal radiation oncology, gastrointestinal imaging, gastrointestinal interventional therapy, gastrointestinal infectious diseases, gastrointestinal pharmacology, gastrointestinal pathophysiology, gastrointestinal pathology, evidence-based medicine in gastroenterology, pancreatology, gastrointestinal laboratory medicine, gastrointestinal molecular biology, gastrointestinal immunology, gastrointestinal microbiology, gastrointestinal genetics, gastrointestinal translational medicine, gastrointestinal diagnostics, and gastrointestinal therapeutics. *WJG* is dedicated to become an influential and prestigious journal in gastroenterology and hepatology, to promote the development of above disciplines, and to improve the diagnostic and therapeutic skill and expertise of clinicians.

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CASE REPORT

Liposarcoma of the stomach: Report of two cases and review of the literature

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Author contributions: Tian YT, Xue LY, and Wang GQ designed the report; Ma FH, Guo L, Li Y, and Li WK collected the patient's clinical data; and Kang WZ and Feng XL analyzed the data and wrote the paper.

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Abstract

Liposarcoma of the stomach is extremely rare, and only 37 cases have been reported worldwide. We herein report two cases of liposarcoma of the stomach. The first patient was referred to our hospital with upper abdominal discomfort. The endoscopic examination revealed a tumor mass about 3 cm in diameter. The patient underwent a partial gastrectomy and had an uneventful recovery. The histopathological examination revealed a well-differentiated liposarcoma. The second patient had symptoms of upper abdominal discomfort combined with nausea and anorexia. Several palpable masses were found with endoscopy. Endoscopic submucosal dissection

was the treatment used, and the postoperative course was uneventful. The histopathological diagnosis was a well-differentiated liposarcoma. The two patients did not undergo any adjuvant therapy. They are both currently in good condition without recurrence. Therefore, we believe that the outcome of liposarcoma of the stomach is positive, and surgical resection may be the first choice for treatment at present.

Key words: Pathology; Signs and symptoms; Diagnosis; Liposarcoma; Therapeutics

Core tip: Liposarcoma of the stomach is extremely rare, and only 37 cases have been reported in the literature. We herein report two cases and review the literature. These cases might contribute to improving our understanding of the etiology, diagnosis, treatment strategies, and outcome of liposarcoma of the stomach. This report can also serve as a reminder to gastroenterologists, surgeons, and pathologists who encounter liposarcoma of the stomach in their clinical practice.

Kang WZ, Xue LY, Wang GQ, Ma FH, Feng XL, Guo L, Li Y, Li WK, Tian YT. Liposarcoma of the stomach: Report of two cases and review of the literature. *World J Gastroenterol* 2018; 24(25): 2776-2784 Available from: URL: http://www.wjgnet.com/1007-9327/full/v24/i25/2776.htm DOI: http://dx.doi.org/10.3748/wjg.v24.i25.2776

INTRODUCTION

Liposarcoma is one of the most common mesenchymal neoplasms[1], and liposarcomas are classified histologically into five subtypes[2]. However liposarcoma of the stomach is rare, and only 37 cases have been reported in the literature. Liposarcoma of the stomach is mainly located in the antrum, and it is usually of submucosal origin. Definitive diagnosis is reached only by histopathological examination. Because of the low incidence of this tumor, treatment of gastric liposarcoma is still not well-standardized. However, the prognosis may remain satisfactory if the condition is diagnosed early and treated appropriately. Herein, two cases of liposarcoma of the stomach are described, and we also discuss the histopathological types, etiology, diagnosis, and treatment strategies in this report.

CASE REPORT

In the Chinese Academy of Medical Sciences Cancer Hospital we encountered two cases, one in 2009 and one in 2016.

Case 1

The first patient was a 45-year-old woman who presented with the symptom of upper abdominal discomfort, which she had experienced for 6 mo. She complained of abdominal pain without any fever or gastrointestinal bleeding. During the physical examination, no special physical signs were found.

The gastroscopy revealed a large tumor mass about 5 cm in diameter located in the junction of the body and fundus of the stomach; it had been considered a benign tumor. Computed tomography confirmed a spherical tumor in the stomach, which was approximately 5.6 cm × 4.2 cm × 3.5 cm in size. The border of the tumor was clear and presented a significantly strengthened edge, and the center of the tumor was inhomogeneous. There were no visible signs of metastatic disease. Upper gastrointestinal imaging also found a circular tumor with smooth edges. The patient had no distinctive past medical history and denied any relevant family history. On March 30, 2009, the patient underwent a resection of the stomach tumor, and surgeons resected part of the omentum. An intraoperative pathology freezing study revealed mesenchymal neoplasms.

She had an uneventful recovery and was discharged after 9 d. The patient did not undergo any adjuvant treatment. She has remained under close follow-up supervision and is currently disease free.

The histopathological examination revealed a well-differentiated liposarcoma measuring 6 cm × 5 cm × 4 cm, which had infiltrated the muscle and serosal layers of the gastric wall (Figure 1). The immunohistochemistry finds were S-100+, CD34++, SMA+, Desmin++, CD117-, HMB45-, and Ki-67 < 1%. Fluorescent *in situ* hybridization (FISH) detection showed amplification of the MDM2 gene (Figure 2).

Case 2

A 69-year-old man was admitted to our department because of upper abdominal discomfort combined with nausea and anorexia that he had been experiencing for about 6 mo. During this period he lost 10 kg in weight. At first he pursued treatment with traditional Chinese medicine, and his symptoms were relieved. He underwent pituitary surgery in 2014 because of a pituitary tumor, and he had suffered from hypertension for 30 years. As a result of regular medication, his blood pressure was well controlled. His family history was unremarkable.

Our hospital's endoscopic examination showed that a limited knurl was distributed from the lower part of the gastric body to the corner of the stomach (Figure 3A), and a knurl was also found in the gastric fundus (figure 3B). Multiple biopsies were obtained, but they were all superficial and showed only unspecific inflammation of the gastric mucosa. Gastric endoscopic ultrasound (EUS) examination revealed that the tumor was mainly located in the submucosa of the gastric wall and was potentially a liposarcoma (Figure 4). Computed tomography confirmed a fat density tumor about 5.1 cm × 2.8 cm in size. No hepatic metastasis or nodal involvements were detected.

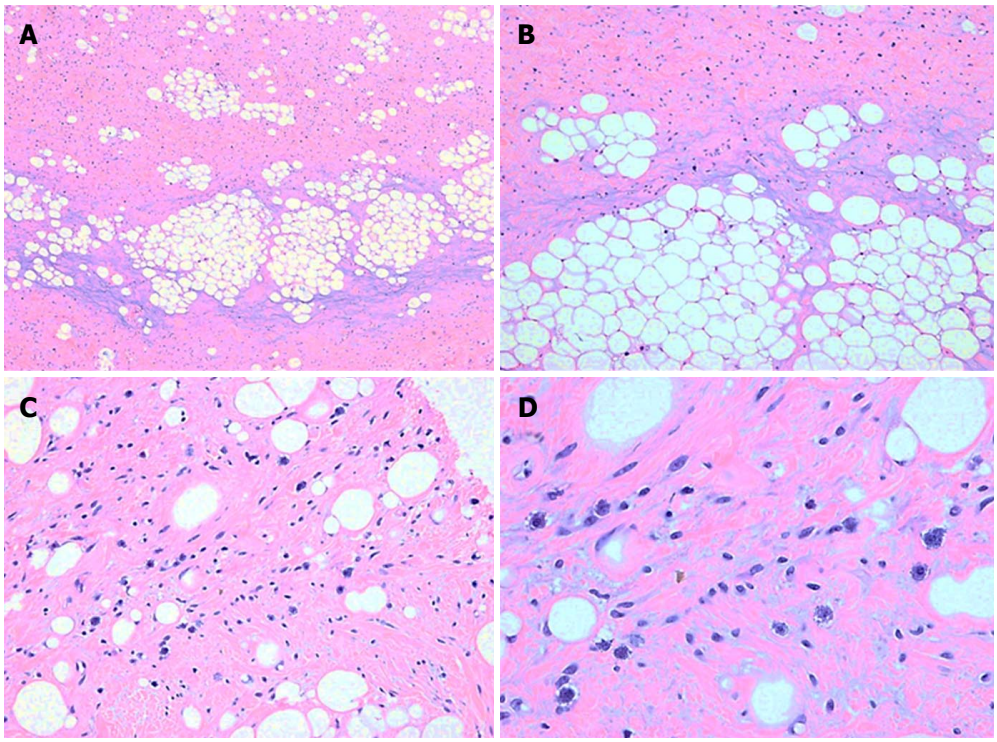

Figure 1 Histological finding. Low magnification shows that the immature fat cells are interspersed among smooth muscle tissues (A: HE, × 40 and B: HE; × 100). The large nuclear dark-stained lipoblast, which appears as a mononuclear or multinucleated cell with one or more cytoplasmic vacuoles, are seen under high magnification (C; HE; × 200 and D: HE; × 400).

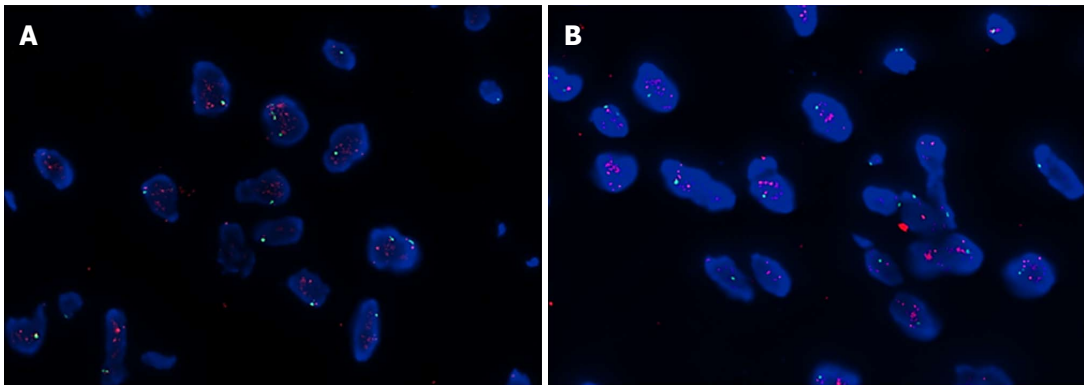

Figure 2 Fluorescence *in situ* hybridization detection shows amplification of *MDM2* gene (A and B), case 1.

On August 1, 2016, an endoscopic submucosal dissection (ESD) was performed (Figure 5). During the operation, we found that the surface of the tumor was complete and smooth, and the substrate was sturdy. The operation was successful without any complications. The postoperative course was uneventful, and the patient was discharged on postoperative day 7. He did not undergo any adjuvant treatment and remained free of metastasis 20 mo after surgery.

The histopathological diagnosis was a well-differentiated liposarcoma (Figures 6 and 7). FISH testing demonstrated amplification of the MDM2 gene (Figure 8).

DISCUSSION

Liposarcoma, a kind of malignant tumor of mesenchymal origin, is one of the most common soft tissue sarcomas[1]. However, liposarcoma of the stomach is extremely rare. The first case was reported by Abrama and Tuberville in 1941, and until now only 37 cases (with a mean age of 57.0 years) have been reported worldwide (Table 1).

According to the 2013 WHO classification of soft tissue tumors, liposarcoma is a malignant fat cell tumor that can be histologically subdivided into the following five types: atypical lipomatous tumor/well differentiated liposarcoma, dedifferentiated liposarcoma, myxoid liposarcoma, pleomorphic liposarcoma, and liposarcoma, not otherwise specified[2].

Both of our cases had well-differentiated liposarcomas. Well-differentiated liposarcoma (including atypical lipomas) is the most common subtype, accounting for about 40%-45% of all liposarcomas[3]. Under the

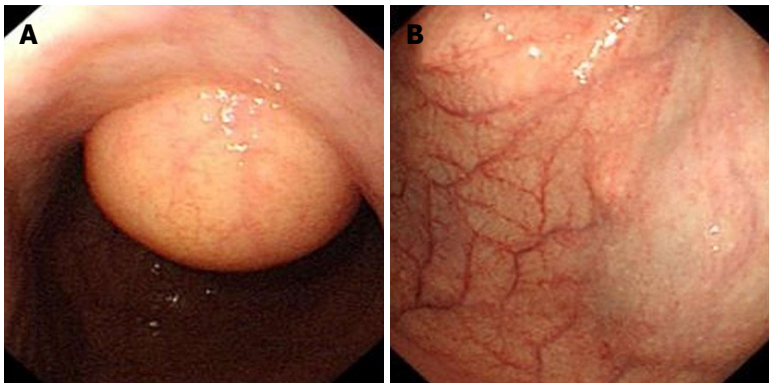

Figure 3 A limited knurl was distributed from lower part of the gastric body to the corner of the stomach (A), and a knurl was also found in the gastric fundus (B).

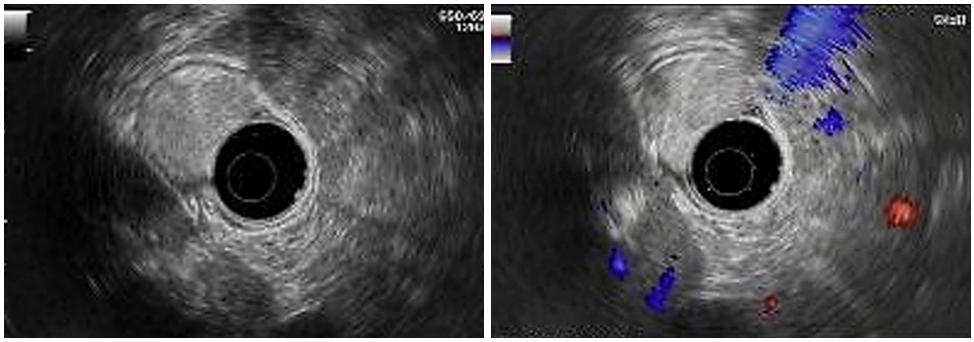

Figure 4 Endoscopic ultrasound examination located the tumor mainly in the submucosa of the gastric wall.

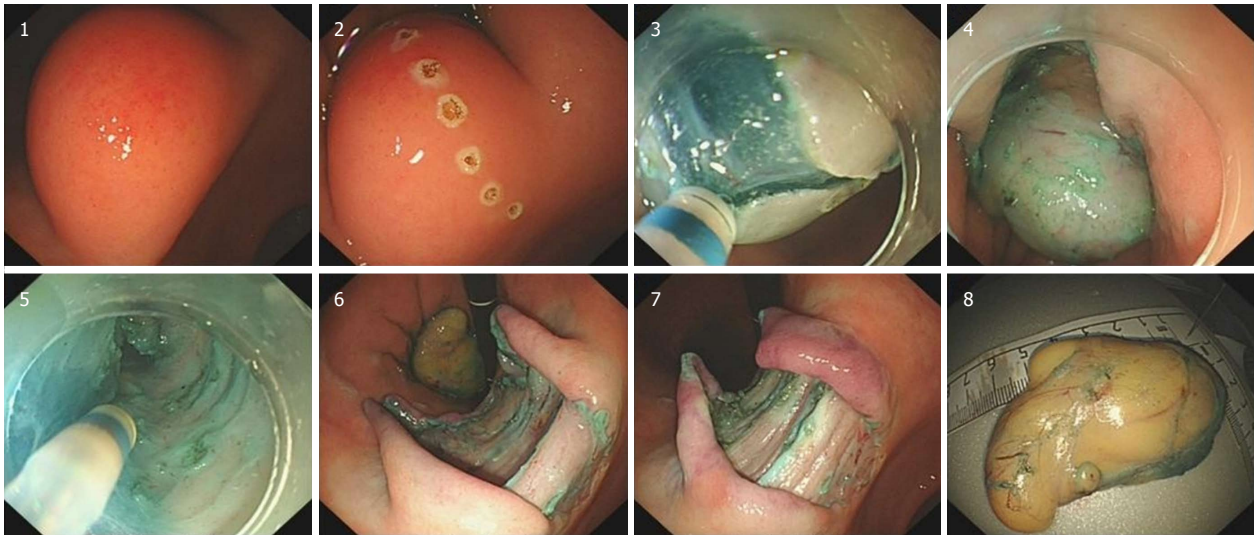

Figure 5 Process of the endoscopic submucosal dissection.

microscope, the tumor cells look like normal fat cells. This kind of liposarcoma is usually a low-grade tumor in the early stages and grows slowly[4]. There is a risk of local recurrence but a low potential for metastasis[5]. Dedifferentiated liposarcomas and well-differentiated liposarcomas are related[1]. Approximately 10% of dedifferentiated liposarcomas are recurrences of well-differentiated liposarcomas[3]. The second most common subtype is myxoid liposarcoma, which represents about a third of all liposarcomas[3]. Myxoid liposarcoma is characterized by a myxoid matrix[6]. Under the microscope, its cells look less normal and may have a high grade component. Tumor cells infiltrate blood vessels in the fibromyxoid stroma that form characteristic clusters or branches. Therefore, we usually categorize myxoid liposarcomas as intermediate to high

Table 1 Review of literature

	Year	Author	Age	Sex	Treatment	Size (cm)	Histologic subtype	Outcome
1	1941	Abrams *et al*[23]	52	M	Exploratory laparotomy	Entire length of the stomach minor curvature	Unknown	DOD in 4 mo
2	1955	Hohf *et al*[20]	77	M	S + radiation	15 × 8 × 6 antrum	Unknown	WR in 8 mo
3	1965	Hawkins *et al*[21]	86	M	S	10 × 10 fundus	MY	WR in 24 mo
4	1968	Orita *et al*[22]	42	M	S	1.2 × 1.0 × 1.0 body	Unknown	WR 60 mo
5	1969	Souhei Suzuki *et al*[23]	42	F	S	13 × 11 × 9.5	Mixed	WR
6	1983	Hiroaki *et al*[24]	41	M	S	4.0 × 3.5 × 1.5	MY	DOD in 18 mo
7	1984	Lopez *et al*[28]	24	M	S	10 in diameter	MY	WR
8	1986	Kiyoshi Kagawa *et al*[23]	64	F	Tumor resection	About hen-egg	WD	WR
9	1986	Shokouh-Amiri *et al*[29]	15	M	S	30 × 20 Greater curvature	MY	WR 8 mo
10	1986	Laky *et al*[9]	67	F	P	5 × 2 × 1.5 antrum	Mixed	WR 12 mo
11	1988	Toshiki Hirose *et al*[23]	66	M	T	10 × 8 × 3	My	Dissemination
12	1990	Sacchiko Matsusaki[23]	42	F	S	about 600 g	MY	WR
13	1992	Costa *et al*[30]	70	F	S	9 in diameter	WD	WR
14	1993	Ryou Mochituki *et al*[23]	56	F	P	Child's head 1300 g	WD	Unknown
15	1993	Yoshiaki Suzuki *et al*[23]	59	M	T	/	Dedifferentiated	Unknown
16	1993	Ferrozzi *et al*[25]	58	M	Tumor resection	25 × 20 × 8 antrum	Pleomorphic	Unknown
17	1995	Shigeharu Suziki *et al*[23]	57	M	S + chemotherapy	4.8 in diameter	WD	WR
18	1995	Yamamoto *et al*[26]	58	M	P + endoscopic resection	1.3 × 0.5 Greater curvature	Mixed	WR 12 mo
19	1996	Mitsuyoshi Sakayani[23]	72	F	T	17.5 × 7.5 × 1.3; 1700 g	Pleomorphic	Unknown
20	1997	Tsutomu Andou *et al*[23]	68	F	T	10.6 × 4	WD	Unknown
21	1997	Masahiro Matsuzawa[23]	34	F	Distal gastrectomy	3.5 × 3 × 3	MY	Unknown
22	1997	Lopez-Negrete[15]	74	F	T	15 in diameter minor curvature	Mixed	Sudden death
23	1998	Seki *et al*[11]	68	F	T	10.5 × 5.5 × 4 body	WD	WR 13 mo
24	2000	Philipps *et al*[27]	74	F	S	3.4 × 1.3 × 0.5 antrum	MY	WR 15 d
25	2002	Hisanobu Saegusa *et al*[23]	34	F	S	4 × 2.8 minor curvature	WD	WR in 36 mo
26	2005	Noushin *et al*[15]	62	M	S	7 × 6 minor curvature	WD	Unknown
27	2007	Konstantinos *et al*[6]	68	M	T	9 × 4 fundus	WD	WR in 24 mo
28	2007	Michiels *et al*[7]	27	F	Subtotal gastrectomy, liver, diaphragm, pancreas, spleen, pericardium; adjuvant chemotherapy	30 × 20 (5 kg) minor curvature	Pleomorphic	DOD in 16 mo
29	2012	Mohamed *et al*[11]	51	M	T	9 × 7.5 × 5 antrum	WD	WR in 12 mo
30	2013	Akin *et al*[1]	59	F	Distal gastrectomy	4 × 3 × 2.5 antrum	WD	WR in 12 mo
31	2014	Kim *et al*[18]	46	F	Laparoscopic, distal gastrectomy; adjuvant treatment	7 in diameter body	WD	Unknown
32	2015	Abderrahman *et al*[3]	70	M	Antrectomy + adjuvant therapy	36 in diameter antrum	MY	DOD in 11 mo
33	2016	Matone *et al*[4]	76	M	Laparoscopic +P	7.5-7.0 in diameter antrum	WD	WR in 6 mo
34	2017	Jiang *et al*[14]	55	F	P + tail of pancreas and spleen was resected	1.5 in diameter fundus	WD	WR in 48 mo
35	2017	Hisata *et al*[13]	79	F	Surgery for the cardiac tumor	0.5-1.0 in diameter greater curvature	Dedifferentiated	DOD in 55 d
36	2017	Tomofuji *et al*[31]	61	F	Laparoscopic total gastrectomy	5 in diameter fundus	WD	WR in 14 mo
37	2018	Girardot-Miglierina *et al*[32]	/	/	/	Gastro-esophageal junction	Unknown	Unknown
38	2016	Our case	70	M	Endoscopic resection	6 × 3.5 × 2 minor curvature	WD	WR in 20 mo
39	2009	Our case	45	F	Tumor resection	6 × 5 × 4 body	WD	WR in 9 yr

DOD: Death of disease; WR: Without recurrence; MY: Myxoid liposarcoma; Mixed: Mixed type liposarcoma; WD: Well-differentiated liposarcoma; S: Subtotal gastrectomy; P: Partial gastrectomy; T: Total gastrectomy.

grade tumors. Pleomorphic liposarcoma is considered the least common subtype and has been properly characterized only recently. It accounts for approximately 5% of liposarcomas and is a highly malignant lesion[7]. Pleomorphic liposarcoma is characterized by increased mitotic activity and hemorrhage as well as necrosis[8].

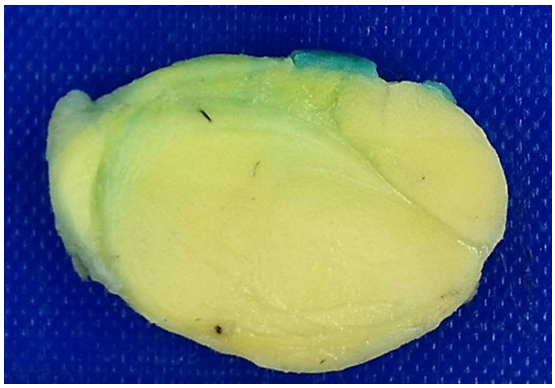

Figure 6 Gross specimen of the tumor.

Microscopically, the tumor cells consist of varying amounts of pleomorphic lipoblasts. Pleomorphic sarcoma consists of highly shaped spindle cells, round cells, polygonal cells, or giant tumor cells. Several grading systems have been developed to classify the tumors and to differentiate between low-grade and high-grade tumors.

These tumors can appear anywhere in the body but often occur in the limbs and retroperitoneal space, and the rest occur in the head and neck, abdominal wall, chest wall, and other areas. Liposarcomas hardly ever occurs in organs[6] and are mainly found in adults, with a peak incidence between the age of 50 and 65 years[4]. The origin of gastric liposarcomas is likely the proliferation of undifferentiated mesenchymal cells within the submucosa and the tunica muscularis layer of the stomach[9]. Gastric liposarcomas are characterized by an exophytic growth that adheres to the gastric wall, and the typical location of gastric liposarcomas is the antrum. According our statistics, approximately 30.8% (8/26) of gastric liposarcomas are located in the antrum, and they are usually of submucosal origin. In addition, 23.1% (6/26) of gastric liposarcomas are located in the minor curvature, 15.4% (4/26) in the fundus, 15.4% (4/26) in the body, 11.5% (3/26) in the greater curvature, and 3.8% (1/26) in the gastro-esophageal junction. The diameter of the tumors described in the literature varies from 0.5 to 36 cm.

The etiology of liposarcoma is not yet clear; environmental factors, radiation, genetic variation, and immune defects are potential risk factors[10]. Some patients have a familial history of soft tissue tumors[4], which suggests genetic factors may play an important role in the occurrence of gastric liposarcoma.

Because the tumor develops within the gastric wall, it presents an extra-luminal growth, and the patient can remain asymptomatic for a long time. The symptoms of gastric liposarcoma range from dyspepsia, nausea, vomiting, anorexia, abnormal bowel movements, asthenia, and epigastric abdominal pain to upper gastrointestinal tract bleeding. The type of symptom that appears depends on the location and size of the tumor and the presence of ulcerations[3]. Space-occupying lesions of the stomach or abdominal cavity contribute to the appearance of clinical symptoms[1]. When the submucosal mass extrudes into the lumen, it can cause traumatic and inflammatory changes and result in necrosis, ulceration, and hemorrhage[11]. For patients with giant tumors, the main clinical sign may be the presence of a large abdominal mass of unknown origin[3]. In our cases, the main clinical sign in both patients was epigastric abdominal pain that continued for longer than 6 mo. In both cases, the typical exophytic growth explains the lack of specific gastrointestinal symptoms and the delayed diagnosis[12]. Some cases of gastric liposarcoma can involve other organs synchronously, and unique symptoms may be present[13,14].

Unfortunately, because of the lack of specific symptoms, it is difficult to achieve an early diagnosis[7]. The diagnosis of gastric liposarcoma mainly relies on pathological examination. Cytogenetics and molecular biology provide effective tools for differentiating among types of lipomatous tumors[11]. Macroscopically, liposarcoma present intricate myxomatous zones, which include round cells, pleomorphous clearly differentiated lipoblastic aspects, and hemorrhagic areas[15]. Because endoscopic biopsies do not penetrate the submucosa, the diagnostic value of the endoscopy is unclear, and it is difficult to make a precise judgment on the basis of biopsy findings. Endoscopic biopsies may be useful when the tumor presents endoluminal development. With the guidance of EUS or abdominal ultrasound, biopsy may be possible, and a histological examination, immunohistochemistry, and a cytogenetic study can be performed[3]. Detection of MDM2 is probably important in diagnosis. In terms of imaging, computed tomography is considered the most informative examination. The presence of fat density areas is pathognomonic for fatty tumors, and an association with enhanced areas is highly suggestive of the diagnosis[16]. CT scans can also show secondary lesions in the liver, lung, peritoneum, or other places.

Currently, the main therapy for gastric liposarcoma is surgical removal. The type of gastrectomy chosen depends on the location of the tumor. According to the rules of sarcoma resection, surgeons should resect the tumor with a wide margin of healthy tissue around it and make sure there is no remaining tumor tissue[3]. Lymph node dissection may be unnecessary[17]. One of our patients underwent a ESD. Due to the lack of sufficient data, the advantages and disadvantages of this method are unknown. In consideration of the successful application of ESD in early gastric cancer, we believe this method is available for a low-grade tumor in the early stages. Chemotherapy and radiotherapy combined with surgery have been successful in most malignant tumors; however, we still cannot develop a guideline for chemotherapy and radiotherapy in patients with gastric liposarcoma. There is very little information in the literature about the use of chemotherapy for gastric liposarcoma. Because of a high local recurrence rate

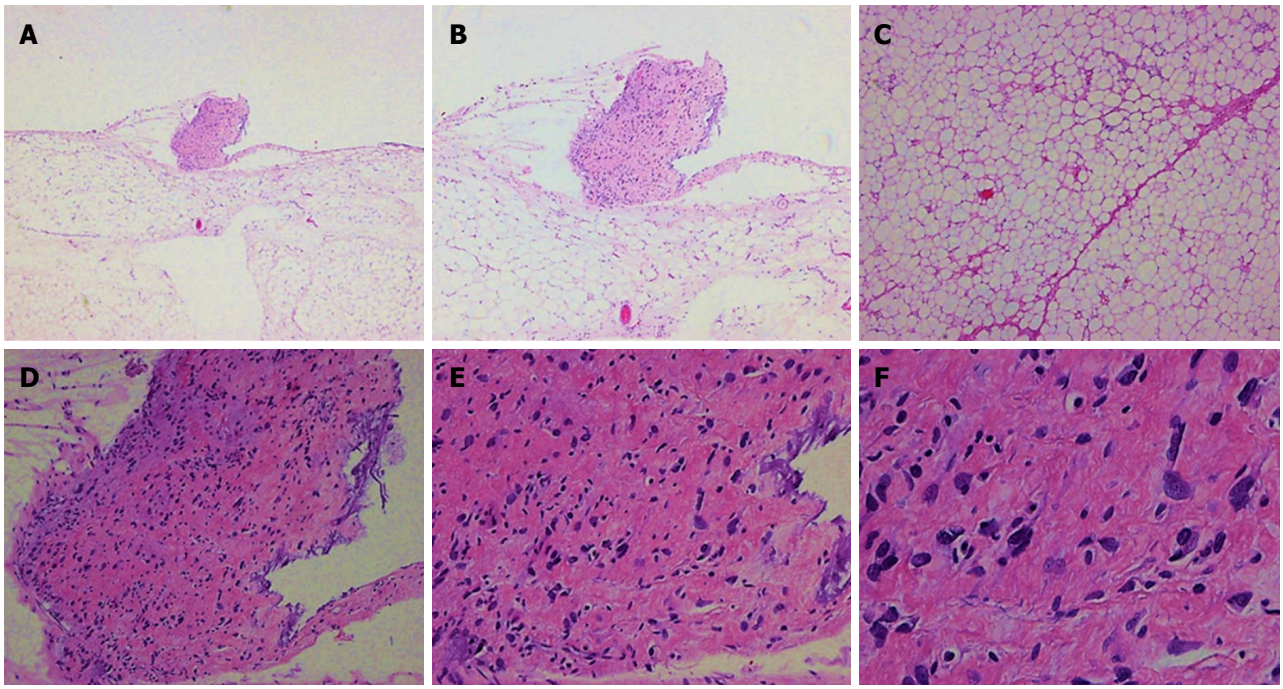

Figure 7 Histological findings. Under low magnification, irregular cell cluster nests were seen around the mature adipocytes (A: HE; × 20 and B: HE; × 40); intermediate magnification and high magnification showed that the heteromorphic cell nests consisted of large nuclear dark-stained tumor cells, with distinct cell shapes, irregular cell morphologies, and visible Mitosis icon (C: HE; × 100, D: HE; × 100, E: HE; × 200, and F: HE; × 400).

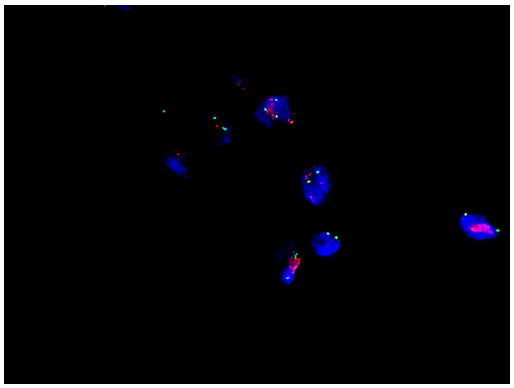

Figure 8 Fluorescence in situ hybridization detection shows *MDM2* gene amplification, case 2.

of 70%-90% for high-grade soft-tissue sarcomas[18], adjuvant therapy may be necessary. On the contrary, Matone *et al*[4] hold the opinion that there is currently no evidence that chemotherapy or radiotherapy improves survival rates. Three drugs, ifosfamide, doxo/epirubicin, and dacarbazine are active in the therapy of adult soft tissue sarcoma[7]; they provide a potential therapeutic pathway for gastric liposarcoma. Radiation therapy may be beneficial by killing tumor cells and reducing the chance of the tumor returning in the same location[3] and may be widely used in the treatment of sarcoma. Only six cases reported in the literature received adjuvant treatment. In our cases, patients did not undergo any adjuvant or neoadjuvant therapy. Both patients are free from recurrence after sarcoma resection.

The main prognostic factor for the primary tumor is histological type, and other factors include the scope and location of the tumor[7]. Kim *et al*[19] believe the main prognostic factor for the primary tumor is anatomical location. According to our statistics, mortality associated with gastric liposarcoma is usually found in cases of dedifferentiated liposarcoma, myxoid liposarcoma, pleomorphic liposarcoma, and mixed type liposarcoma. Of the 37 cases described, six patients died of the disease, while the outcome for nine patients is not known. Their survival time ranged from sudden death to 18 mo (specifically, the times were immediate, 55 d, 4 mo, 11 mo, 16 mo, and 18 mo). Some studies reported that 30% of well-differentiated liposarcomas present with local recurrence; however, metastasis is hardly ever seen[1,4]. Pleiomorphic liposarcoma is considered a highly malignant lesion and may indicate a poor outcome[7]. Due to the lack of sufficient data, we still cannot clearly determine the relationship between histological type and disease prognosis. The outcome of gastric liposarcoma is still unclear, and further study is needed.

From the reported cases and literature review[20-32], we conclude that liposarcoma is rarely seen in the viscera, especially the stomach. Diagnosis of this tumor mainly depends on histopathological examination. Gastric liposarcomas are extremely rare tumors for which there is no therapeutic consensus. Although medications and devices have improved in recent years, surgery may be the most reasonable treatment, and the role of adjuvant treatment is not clearly defined. The prognosis is still unclear, and more research is needed. However, we

believe that if the tumor is diagnosed early and treated effectively, the postoperative outcome may be positive.

ARTICLE HIGHLIGHTS

Case characteristics

Epigastric abdominal pain that continued for longer than 6 mo.

Clinical diagnosis

Gastrointestinal stromal tumor (GIST) and gastric lipoma.

Differential diagnosis

Differential diagnosis: GIST and gastric lipoma. Definitive diagnosis is reached only by histopathological examination.

Laboratory diagnosis

Gastric liposarcoma.

Imaging diagnosis

Computed tomography: Gastric lipoma.

Pathological diagnosis

Gastric liposarcoma.

Treatment

Partial gastrectomy and endoscopic submucosal dissection.

Related reports

The first case was reported by Abrama and Tuberville in 1941, and until now only 37 cases have been reported worldwide (Table 1).

Term explanation

Two cases of gastric liposarcoma are reported and a review of the literature.

Experiences and lessons

Diagnosis of gastric liposarcoma mainly depends on histopathological examination, and surgery may be the most reasonable treatment.

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