Carcinosarcoma of Stomach Confined to the Mucosa

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ABSTRACT

Carcinosarcoma is a malignant tumor composed of both epithelial and mesenchymal malignant tumor components. A 78-year-old man was transferred to our hospital because of hematemesis and tarry stool. An emergency gastrointestinal endoscopic examination revealed active bleeding from an ulcerative lesion on the posterior wall of the gastric body; endoscopic hemostasis was successfully performed. A gastrointestinal endoscopy performed two months later showed a polypoid lesion at the same place where the ulcer had been. The biopsy specimen was histologically diagnosed as well to moderately differentiated tubular adenocarcinoma. The patient underwent a laparoscopic distal gastrectomy with D2 lymph node dissection under a diagnosis of gastric adenocarcinoma. A 28 × 15 mm polypoid tumor was resected from the gastric body, and was found on microscopic examination to consist of both carcinoma and sarcoma components, showing atypical spindle cells, which were positive for α-smooth muscular actin, calponin, and h-caldesmon, but negative for CD34, CD117 (c-kit), desmin, and dog 1. These findings led to a diagnosis of gastric carcinosarcoma. The tumor was confined to the mucous membrane. Lymph node metastasis was found in one node and contained only the carcinoma component. The postoperative course was uneventful. The patient lived without recurrence for 2 years. Carcinosarcoma of the stomach is a rare tumor with high malignant potential and poor prognosis. Careful follow up is required for early detection of any recurrence.

Key words carcinosarcoma; gastric cancer; stomach

Carcinosarcoma is a malignant tumor composed of both epithelial and mesenchymal malignant tumor components.[1] It typically occurs in the uterus, esophagus, and breasts, but only about 70 cases have been reported in the stomach to date.[2–8] Most cases are diagnosed at advanced stages, which indicates that this is a rapidly progressing tumor.[9, 10] Here, we report a case of gastric carcinosarcoma confined to the mucosa of the gastric wall. To our knowledge, this is the first case in which gastric carcinosarcoma was confined to the gastric mucosa.

PATIENT REPORT

A 78-year-old man was transferred to our hospital because of hematemesis and tarry stool. Laboratory examinations revealed moderate anemia (hemoglobin: 9.2 g/dL). An emergent gastrointestinal endoscopic examination revealed active bleeding from an ulcerative lesion on the posterior wall of the gastric body; endoscopic hemostasis was successfully performed. A proton pump inhibitor (esomeprazole magnesium hydrate) was given to treat the gastric ulcer. A follow-up gastrointestinal endoscopy performed two months later showed a polypoid lesion at the same place where the ulcer was previously (Fig. 1). The biopsied specimen was histologically diagnosed as well to moderately differentiated tubular adenocarcinoma. Preoperative laboratory examination again revealed moderate anemia (hemoglobin: 9.3 g/dL). He was positive for the serum anti-*Helicobacter pylori* IgG antibody (17 U/mL). Serum levels of tumor markers, including carcinoembryonic antigen (CEA), carbohydrate antigen (CA) 19-9, and CA 125, were in normal range. Computed tomography (CT) of the abdomen revealed a protruding, 2.1 × 1.5-cm lesion inside the gastric body (Fig. 2). The patient underwent a laparoscopic distal gastrectomy with D2 lymph node dissection under the diagnosis of gastric adenocarcinoma.

A polypoid tumor measuring 28 × 15 mm was found at the gastric body (Fig. 3). Microscopic examination of the resected specimens (hematoxylin–eosin stain) showed the tumor to include both carcinoma and sarcoma components (Fig. 4a). There was fibrosis indicating the ulcer scar in the submucosal layer. The carcinoma component predominated and was composed of well to moderately differentiated adenocarcinoma. The sarcoma component mainly consisted of atypical spindle cells

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Abbreviations: CA, carbohydrate antigen; CD, cluster of differentiation; CEA, carcinoembryonic antigen; CT, computed tomography; IHC, immunohistochemical; SMA, smooth muscular actin

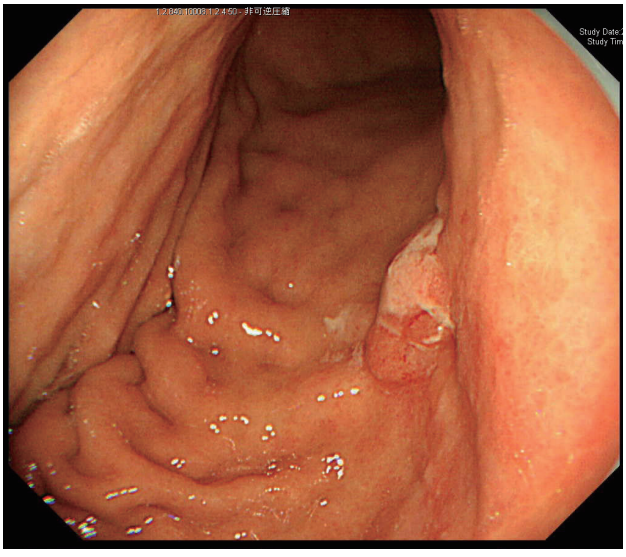

Fig. 1. A gastrointestinal endoscopy showing a polypoid lesion at the posterior wall of gastric body.

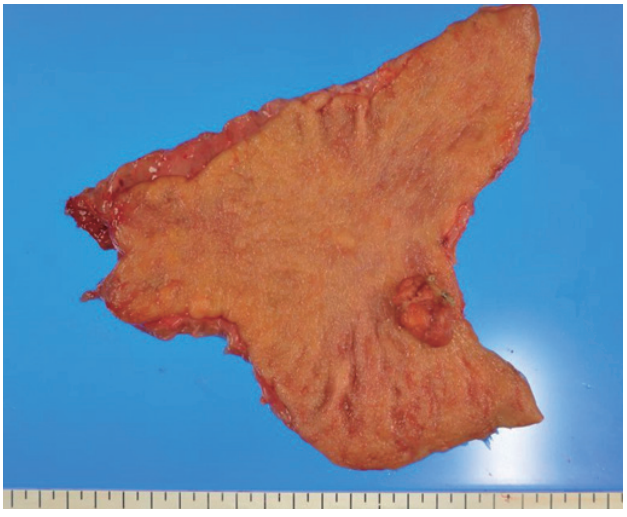

Fig. 3. Resected specimen. There was a polypoid tumor measuring 28 × 15 mm at the gastric body.

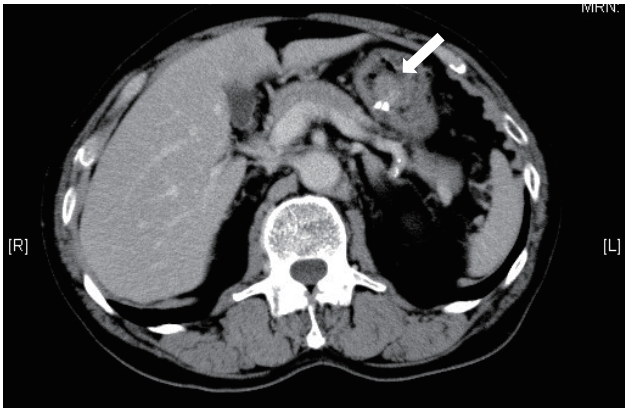

Fig. 2. A computed tomography of the abdomen revealed a protruded lesion (White arrow) measuring 2.1 × 1.5 cm at the gastric body.

with frequent mitotic activity. It also contained a few carcinoma components. Transition between malignant epithelial and spindle cells was evident (Fig 4b). No chondrosarcoma, osteosarcoma or rhabdomyosarcoma components were observed anywhere. Immunohistochemical (IHC) staining revealed that spindle cells were positive for α-smooth muscular actin (SMA; Fig. 5a), calponin (Fig. 5b), and h-caldesmon, but negative for cluster of differentiation (CD) 34, CD117 (c-kit), desmin, and dog 1. Furthermore, the carcinoma components were positive for cytokeratin AE1/3 (Fig. 6a), whereas the sarcoma components contained only a few cells positive for cytokeratin AE1/3 (Fig. 6b). These IHC findings led to a diagnosis of gastric carcinosarcoma (adenocarcinoma and leiomyosarcoma). The tumor was confined to the gastric mucous. Lymph node metastasis was found in one of the 70 dissected nodes and contained only the carcinoma component. According to the Japanese Classification of Gastric Cancer,[11] the pTNM classification was T1a N1 M0 Stage 1b R0. His postoperative course was uneventful; he did not undergo postoperative adjuvant chemotherapy. He survived without recurrence for 2 years.

DISCUSSION

Queckenstedt described the first case of carcinosarcoma of the stomach in 1904.[12] Since then, 72 cases of gastric carcinosarcoma have been reported to date in the Japanese and English scientific literature.[2–8] Table 1 shows the clinicopathologic characteristics of these 72 reported cases of gastric carcinosarcoma. Carcinosarcoma of the stomach is much more common in men (n = 50) than women (n = 22). The average age at diagnosis was 62.5 ± 3.0 years old. Macroscopic appearance is often as a huge polypoid mass; the average tumor size is 8.6 ± 1.0 cm.

As its clinical symptoms do not seem to differ from gastric adenocarcinomas, distinguishing carcinosarcoma of the stomach from gastric adenocarcinoma through endoscopy or radiology can be difficult.[1] Histologically, the most common carcinomatous component of this tumor is tubular or papillary adenocarcinoma, whereas leiomyosarcoma, osteosarcoma, chondrosarcoma or rhabdomyosarcoma have been reported as sarcoma components.[13–16]

Although the pathogenesis of gastric carcinosarcoma remains controversial, two hypotheses have been

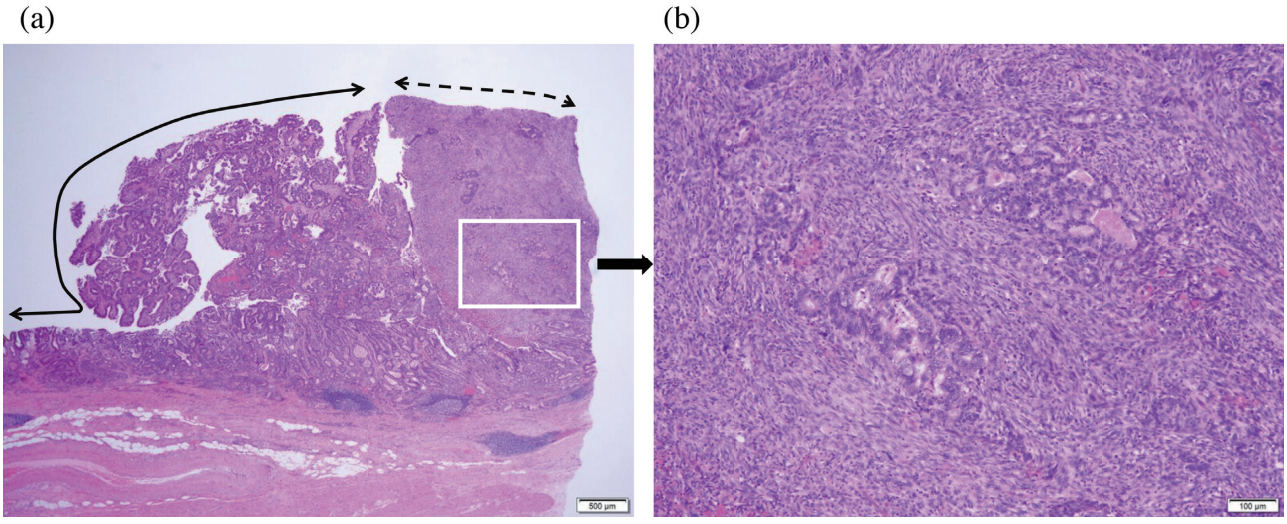

Fig. 4. Photomicrographs of hematoxylin–eosin-stained tissue sections of the tumor. (**a**) The tumor consisted of both carcinoma (solid line) and sarcoma components (dotted line) (Bar = 500 μm). (**b**) High-magnification image of the area surrounded by a white line. Transition between malignant epithelial and spindle cells was evident (Bar = 100 μm).

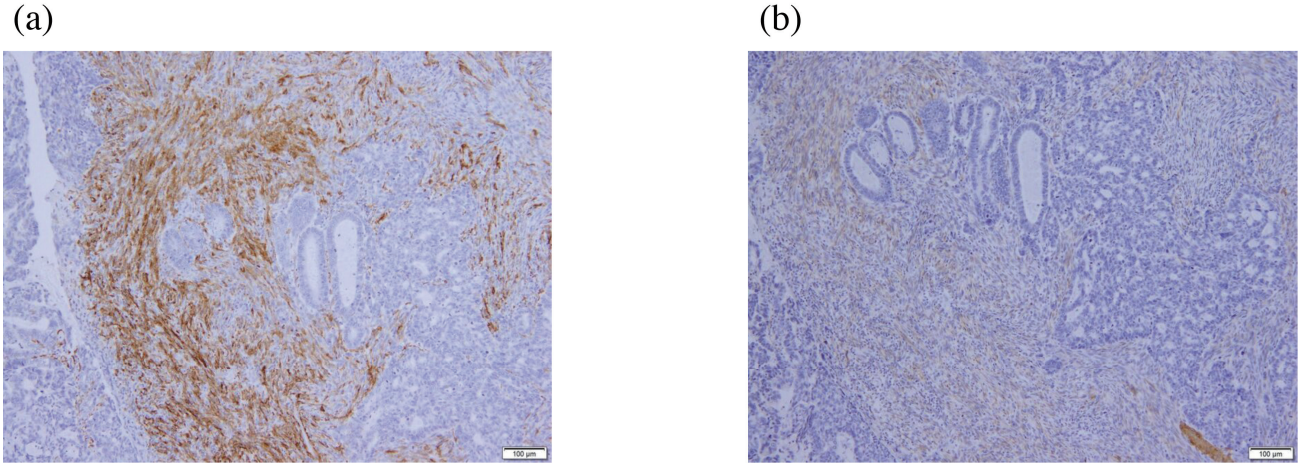

Fig. 5. Immunohistochemical staining revealed that tumor cells were positive for α-smooth muscular actin (**a**) and calponin (**b**) (Bar = 100 μm).

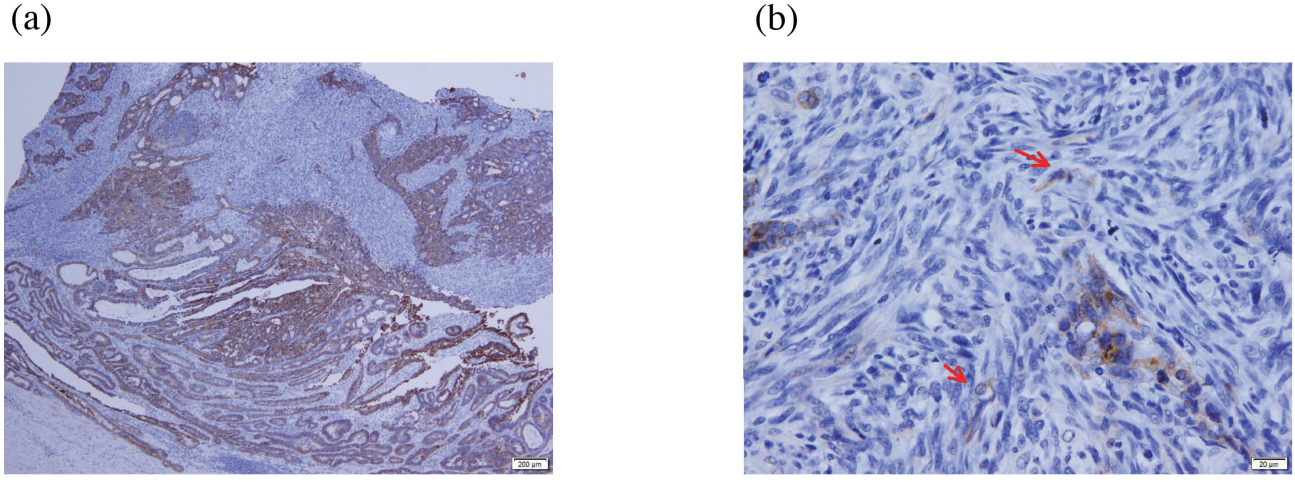

Fig. 6. Immunohistochemical staining of cytokeratin AE1/3. (**a**) The carcinoma components were positive for cytokeratin AE1/3 (Bar = 200 μm). (**b**) The sarcoma components contained only a few cells positive for cytokeratin AE1/3 (Red arrows; Bar = 20 μm).

proposed.[17] The first is the bi-clonal origin hypothesis, which supports the collision tumor theory, according to which the carcinosarcoma originates from two different tumor cell clones. The second is the monoclonal origin hypothesis, whereby the carcinosarcoma originates from a stem cell that can undergo both epithelial and mesenchymal differentiation. In our case, transition between malignant epithelial and spindle cells was evident, which supports the monoclonal origin hypothesis. IHC analysis was useful for a definitive diagnosis of carcinosarcoma. However, preoperative diagnosis of this tumor seems to be extremely difficult, possibly due to limited amount of biopsy specimen. In fact, the diagnosis of gastric carcinosarcoma tends to be established either postoperatively or at autopsy, whereas only 4 cases were reported in which diagnoses of gastric carcinosarcoma were made based on preoperative biopsy specimens.[14, 18–21]

Radical gastrectomy is regarded as the only curative treatment for gastric carcinosarcoma. However, this tumor tends to develop rapidly and to be diagnosed at an advanced clinical stage (Table 1). It therefore has a worse prognosis than other types of gastric carcinoma, even after radical gastrectomy.[14] The mean survival period is estimated to be 7–10 months.[3, 17, 22] The most frequently observed distant metastasis site was the liver (Table 1). Reportedly, more than 50% of tumor recurrences occur in the first postoperative year.[17] Therefore, diagnosis and treatment as early as possible is crucial. To our knowledge, however, only four cases were diagnosed at early stage; in fact, our case was the first in which the tumor was confined to gastric mucosa. Table 2 shows the clinicopathologic characteristics of early carcinosarcoma of the stomach.[21, 23, 24] Notably, lymph node metastasis was observed in two of four cases, which indicates the aggressiveness of this type of tumor. Therefore, chemotherapy and radiation therapy as well as surgery may play important roles in its treatment. However, as gastric carcinosarcoma is very rare, the effects of chemotherapy and radiotherapy have not yet been reported.

Carcinosarcoma of the stomach is a rare tumor with high malignant potential and a tendency towards poor prognosis. Thus, gastric carcinosarcoma should be considered as a part of differential diagnosis. IHC staining is critical in making an accurate diagnosis of carcinosarcoma. Careful follow up is required for early detection of recurrence, especially in the first postoperative year.

Ethics approval and consent to participate: Consent for publication was obtained from the patient.

The authors declare no conflict of interest.

Table 1. Summary of 72 previously reported cases of gastric carcinosarcoma

Gender	Male	50
	Female	22
Age (average ± SD)	62.5 ± 3.0	
Symptom	Anemia	24
	Abdominal pain	20
	Hematemensis or melena	12
	Appetite loss	9
	Dysphagia	6
	None	3
	Other symptoms	14
	Not mentioned	1
Location	Upper third	21
	Middle third	17
	Lower third	24
	Whole	5
	Gastric stump	2
	Not mentioned	3
Tumor size (average ± SD)	8.6 ± 1.0 cm	
Preoperative diagnosis according to biopsy specimen	Adenocarcinoma	24
	Carcinosarcoma	4
	Sarcoma	4
	Other	6
	Not mentioned	34
Macroscopic appearance	Protruded	39
	Ulcerated	24
	SMT like	3
	Not mentioned	6
Depth of invasion [a]	M	1
	SM	3
	MP	4
	SS	19
	SE	12
	SI	8
	Not mentioned	25
Lymph node metastasis	Absent	17
	Present	28
	Not mentioned	27
Distant metastasis	Absent	18
	Present	29
	Liver metastasis	19
	Lung metastasis	3
	Distant Lymph node metastasis	2
	Peritoneal metastasis	2
	Other	2
	Unknown	4
	Not mentioned	25

[a]Depth of invasion: M, tumor invasion of the lamina propria; SM, tumor invasion of the submucosa; MP, tumor invasion of the muscularis propria; SS, tumor invasion of the subserosa; SE, tumor penetration of the serosa; SI, tumor invasion of adjacent organs.

Table 2. Summary of carcinosarcomas of the stomach confined to submucosa

Author	Gender	Age	Location	Depth of invasion [a]	Macroscopic appearance [b]	Tumor size (cm)	Lymph node metastasis	Distant metastasis
Fujii	M	72	Body	SM	Type 1	2.0 × 1.8	Absent	Absent
Yuasa	F	53	Antrum	SM	Type 1	5.0 × 4.5	Present	Absent
Uno	M	65	Pylorus	SM	Type 1	9.5 × 7.0	Absent	Absent
Our case	M	78	Body	M	Type 0-I	2.8 × 1.5	Present	Absent

[a]M: Tumor confined to the mucosa; SM: tumor confined to the submucosa
[b]Type 1: Polypoid tumors, sharply demarcated from the surrounding mucosa; Type 0-I: polypoid tumors

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