

# Gastric carcinosarcoma: A case report and review of the literature

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**Abstract.** Carcinosarcoma of the stomach is a rare biphasic tumor that consists of both carcinomatous and sarcomatous components. The common carcinoma component is tubular or papillary adenocarcinoma and the mesenchymal sarcomatous components are variable but may include leiomyosarcoma, rhabdomyosarcoma and osteosarcoma. The aim of this study was to describe the characteristics of gastric carcinosarcoma and to present a review of the available literature. We report a case of carcinosarcoma in a 62-year-old female including the clinical and histopathological features of this tumor. Following ultrasound and computed tomography scans, laparotomy was performed, revealing a large mass, followed by radical surgery. Macroscopically, a polypoid tumor was observed. Microscopically, the tumor was composed of moderately differentiated adenocarcinoma and poorly differentiated sarcoma with a high mitotic index and necrotic areas. At present, the achievement of a definitive diagnosis is dependent on immunohistochemical staining and radical surgery. Thus, more effective diagnostic methods are required to improve patient survival.

## Introduction

Carcinosarcoma of the stomach is an extremely rare mixed tumor comprising carcinoma and sarcoma components (1). The most common carcinoma component is tubular or papillary adenocarcinoma, while neuroendocrine carcinomatous differentiation is less common. The mesenchymal sarcoma-

tous component is variable and may include leiomyosarcoma, rhabdomyosarcoma, osteosarcoma or chondrosarcoma (2).

Tumor in the upper gastrointestinal tract tends to be localized in the esophagus where it represents approximately 3% of all esophageal tumors. By contrast, only 52 cases of gastric carcinosarcoma have been reported in the literature thus far, most of which are described in the Japanese literature (3). Other terms for this tumor are sarcomatoid carcinoma of the stomach and spindle cell carcinoma of the stomach. The average survival of these patients is 2-6 months. In the present study, we report a case of gastric carcinosarcoma and review some of the literature. Consent was obtained from the patient.

## Case report

A 62 year-old woman was admitted to our division reporting a history of epigastric pain with asthenia and weight loss (8 kilos over 3 months). The physical examination revealed no specific findings. The patient underwent the following laboratory tests and endoscopic examinations: esophagogastroduodenoscopy (EGD), ultrasound (US) and computed tomography (CT) scanning. The EGD revealed an ulcerated mass in the gastric body-fundus.

On abdominal US, three hepatic mass lesions were revealed, the largest one being 5x3 cm in size. Abdominal CT revealed that the tumor had metastasized through the gastric wall up to the serosa and confirmed the hepatic US report. The patient subsequently underwent an exploratory laparotomy that revealed a large mass (20x15 cm in size). The tumor had infiltrated the pancreatic body-tail, gastric body fundus, splenic hilum and left adrenal gland. A total gastrectomy with Roux-en-Y esophagojejunostomy with body-tail pancreatic resection and left surrenalectomy was performed.

Despite the poor prognosis, radical surgery was performed since the tumor had invaded most of the organ and perivisceral structures. Radiofrequency ablation (RFA) was used for the treatment of the hepatic lesions.

Macroscopically, an ulcerative polypoid tumor (13x10 cm) arising from the gastric body fundus was observed. The mass had infiltrated through all layers of the gastric wall and extended to the pancreatic tail. The spleen was not infiltrated

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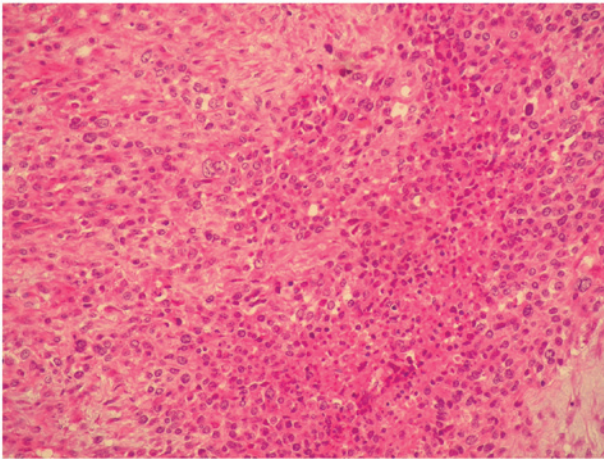


Figure 1. The sarcomatoid component of carcinosarcoma.

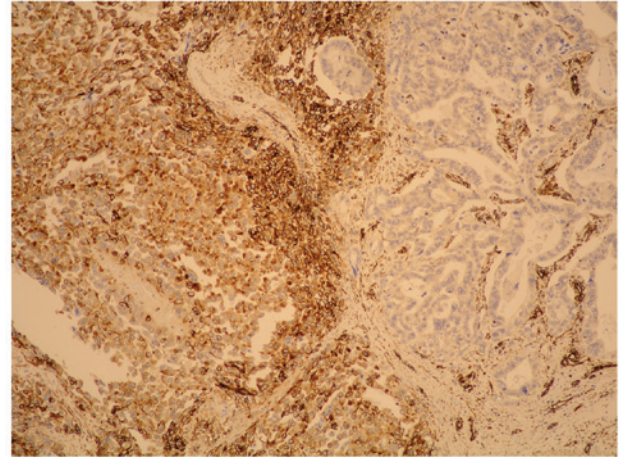


Figure 4. Immunohistochemistry shows intense positivity for vimentin in the sarcomatoid component.

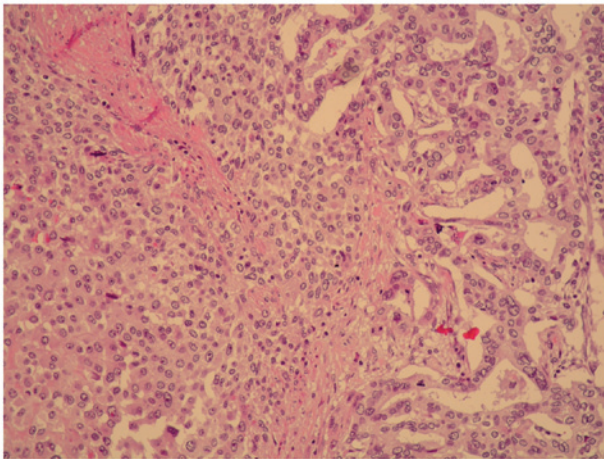


Figure 2. The sarcomatoid component is on the left section of the image and the adenocarcinoma is on the right section of the image.

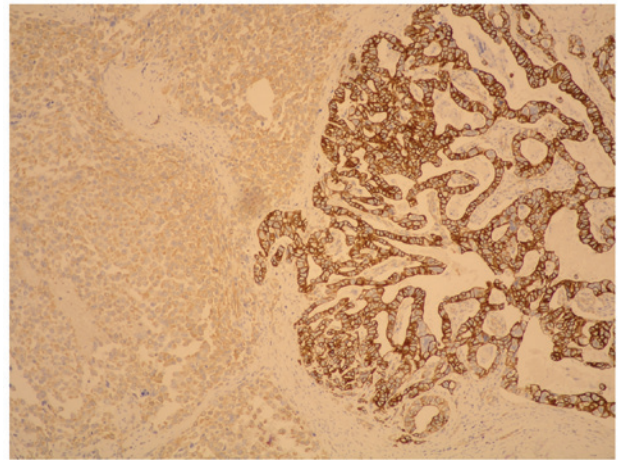


Figure 5. Positivity for CD-57 in the carcinomatous component.

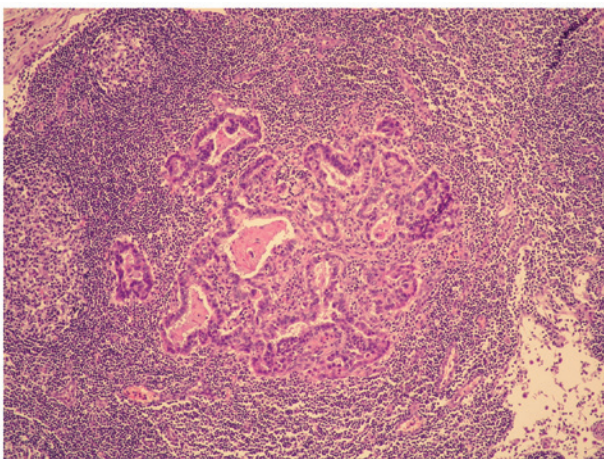


Figure 3. A lymph node with metastases of the carcinomatous component.

by the tumor. Microscopically, the tumor was composed of moderately differentiated adenocarcinoma and poorly differentiated sarcoma with a high mitotic index and necrotic areas (Figs. 1 and 2).

The carcinoma component exhibited a positive reaction to pan-cytokeratin whereas fusiform cells showed positive reactions to vimentin: HHF35; CD56; EMA (weak); desmin (singular component) and negative reactions to cytokeratin, actine, caldesmon, CD-34, S-100 and cromogranin; synaptophysin, CD-57 and c-kit. These immunohistochemical findings led to a diagnosis of gastric carcinosarcoma (Figs. 4 and 5).

The tumor was found to have infiltrated the perivisceral fat and peripancreatic areas. There was neoplastic vein thrombosis of the splenic hilum and, for 2 of 13 regional nodes, metastases were present (Fig. 3). These metastases belonged only to the carcinoma component (pTNM classification was: T4 N1 G3 R0). The post-operative course was unremarkable. Due to poor general health conditions, the patient did not undergo administration of chemotherapy. The patient succumbed to the disease approximately 4 months later.

## Discussion

Carcinosarcoma is defined by the WHO as 'a malignant tumor composed of intimately mixed epithelial and mesenchymal elements of a type ordinarily found in malignancies



Table I. Reported cases of gastric carcinosarcoma.

Author (Ref.)	Age	Gender	Medical history	Endoscopy	CT	Laboratory	Treatment	Histology	IHC (positivity)	Follow-up
Randjelovic <i>et al</i> (9) 2007	62	M	Epigastric pain, nausea, weight loss and intermittent bleeding from the upper gastrointestinal tract. In the epigastric region, an elastic, resistant, fixed mass.	Exophytic, lobulated mass that infiltrates the entire posterior wall of the stomach, obturating the lumen throughout.	Irregular, inhomogeneous, prominent formation (120x80x50 mm) in the stomach.	Hb: 10 g/dl; Hct: 26%; MCV 78 fL; CA 72.4: 110 U/ml.	Total gastrectomy with Roux-en-Y esophagojejunostomy and resection of the affected lymph nodes.	Moderately to well-differentiated adenocarcinoma with traces of neuroendocrine elements.	Cytokeratin 18, EMA, CEA, vimentin.	Eight months following surgery, liver metastases were observed on CT scanning. His general condition did not allow the administration of chemotherapy. He died approximately 4 months later.
Ikeda <i>et al</i> (7) 2007	70	F	Epigastric discomfort that had lasted >1 year prior to admission, elastic mass in the epigastric region, fever, extremely marked emaciation.	Submucosal tumor with an open ulcer in the anterior wall of the cardia.	Upper abdominal mass (21x14x8 cm) adjacent to the lesser curvature of the stomach.	Hb: 7.3 g/dl; CA 19-9: 71 U/ml; CA125: 47 U/ml	Palliative surgery.		CAM, vimentin, muscular markers, HHF35.	The patient's condition rapidly deteriorated and he died 16 days postoperatively.
Teramachi <i>et al</i> (1) 2003	62	M	Epigastric pain and anorexia.	Large ulcerative lesion in the stomach.		No abnormalities.	Total gastrectomy.	The carcinoma component was predominantly (95%) composed of undifferentiated carcinoma cells. The sarcoma component consisted of atypical spindle cells showing rhabdomyo-, chondro- or osteosarcomatous differentiation.	CAM5.2, EMA, αSMA, desmin.	Disease-free for 20 months following surgery.
Nakayama <i>et al</i> (5) 1997	69	M	Partial gastrectomy (Billroth II) for a duodenal ulcer 30 years earlier, epigastric pain, emaciation, anemia, elastic soft mass in the left upper quadrant of the abdomen.	A large polypoid tumor located on the greater curvature of the remnant stomach.	Huge tumor in the dilated stomach. There was no metastasis in the liver, the intra-abdominal lymph node or other organs.	Hb: 6.4 g/dl; Hct: 21.6%; normal CEA level.	Palliative therapy.	Diffuse sarcomatous and carcinomatous elements with large areas of necrosis.	Vimentin, desmin, HHF35, αSMA, EMA, cytokeratins (35pH11 and 34pE12).	
Kayaselcuk <i>et al</i> (12) 2002	53	M	Weight loss, asthenia, and gastric hemorrhage.	Tumoral mass in the antrum.	Liver showed many areas consistent in appearance with metastasis.		Subtotal gastrectomy and liver wedge resection.		Pancytokeratin, EMA, CEA, vimentin, desmin, αSMA.	The patient underwent adjuvant chemotherapy. Metastatic focus was determined in the first 8 months.

Table I. Continued.

Author (Ref.)	Age	Gender	Medical history	Endoscopy	CT	Laboratory	Treatment	Histology	IHC (positivity)	Follow-up
Yamazaki (17) 2003	56	M	Anorexia, rapid weight loss.	Infiltrating ulcerated gastric tumor in the posterior wall of the gastric body.	Swellings of para-abdominal aortic lymph nodes were revealed. The left subclavicular lymph node was also swollen.	Hb: 10.9 g/dl; CEA: 87.9 ng/ml; AFP 16 ng/ml; CA19-9: 1093 U/ml	Total gastrectomy	Three distinct, components: well to moderately differentiated tubular carcinoma (70%) neuroendocrine carcinoma (15%) and sarcoma (15%).	CAM5.2, αSMA, desmin.	The patient died of esophageal obstruction due to local recurrence of the tumor and liver metastasis approximately 2 months following surgery.
Kuroda <i>et al</i> (12) 2006	59	M	Epigastric pain and anorexia.			CEA elevated.	Total gastrectomy	The gastric tumor consisted of both epithelial and spindle cells.	Chromogranin A, synaptophysin, αSMA, h-caldesmon, S-100, CAM5.2.	
Matsukuma <i>et al</i> (18) 1997	74	M	Weight loss, asthenia.				Total gastrectomy	Adenocarcinomatous and sarcomatous component.	EMA, CEA, S-100 protein, desmin, vimentin.	Liver metastasis 4 months after surgery.
Pase <i>et al</i> (22) 2005	53	M	Epigastric pain and anorexia.	A gastric polypoid tumor.	Round nodular lesion (2 cm) on the lesser curvature.	No abnormalities.	Subtotal gastrectomy	Well-differentiated adenocarcinoma and carcinoïd.	Chromogranin, Synaptophysin, NSE, CD56.	6 months survival.
Melato <i>et al</i> (23) 1993	55	M	Epigastric pain, weight loss.				Total gastrectomy	Adenocarcinoma and fibro-mio-chondro-osteosarcoma highly indifferntiated with mixoid areas.	NSE, chromogranin, CEA, desmin calcitonin, synaptophysin.	
Tsuneyama <i>et al</i> (24) 1999	63	M	Epigastric pain and anorexia.	Large polypoid lesion on pylorus.	Partial gastrectomy.			Adenocarcinoma with rhabdomyosarcomatous and neuroendocrine tissue.	EMA, CEA, desmin, vimentin, chromogranin.	4 months survival.
Cruz <i>et al</i> (25) 1991	67	M	Asthenia, anorexia, fever.	Large polypoid mass of the lesser curvature of the stomach.		Anemia	Total gastrectomy		Vimentin, CEA, EMA, chromogranin	
Cirocchi <i>et al</i> (Present study)	62	F	Epigastric pain with marked asthenia and weight loss (8 kg over 3 months).	Ulcerated mass in the body-fundus gastric.	Abdominal CT revealed the tumor has spread through the gastric wall until the serose and three hepatic mass lesions.	Anemia	Total gastrectomy with Roux-en-Y esophagojejunostomy with body-tail, pancreatic resection and left surrenalectomy.	Moderately differentiated adenocarcinoma and poorly differentiated sarcoma.	HHF35, CD56, EMA, desmin.	4 months survival.

CT, computed tomography; IHC, immunohistochemistry.

of adults'. This definition is based on traditional histological findings (4). The localizations of this tumor are widespread.

The most common site of origin for these tumors is the uterus. Several other organs such as the salivary gland, thyroid gland, breast, gallbladder, esophagus, stomach, small and large intestine, pancreas, urinary system and the prostate gland may also be affected by this type of tumor.

Localization in the stomach has been less frequently reported (5); male (M) gender is more affected than female (F) (M:F=2.8:1). These data are considerably different from that of other locations where localization to other sites occurs more frequently in women (i.e., gallbladder M:F=1:3.25).

The median age of patients affected by gastric carcinosarcoma was 62 years (range, 29-80), slightly lower than other localizations in which the most frequent onset age is the geriatric age (6). The youngest patient was 29 years old and this case was originally reported by Saito in 1916 [described by Ashida *et al* (7)], while the oldest patient was 80 years old, as reported by Ooi in 1982 (8). The median age of male and female patients was 60.9 and 61.3 years, respectively.

The dimensions of this type of tumor calculated on data from 33 reviewed cases and our case report range in size from 4 cm [Cho *et al* (9)] to 15 cm [Saito, described in (7)]. The median dimension of the tumors was 9 cm. According to the macroscopic pattern of growth and particularly in relation to the gastric wall, carcinosarcoma has been classified into three types (10): i) a predominantly intramural infiltration; ii) a predominantly extramural mass; iii) a predominantly intramural mass with exophytic or crater-shaped growth.

Microscopically, carcinosarcoma is classified into two types: true carcinosarcoma and false carcinosarcoma or so-called sarcomatoid carcinoma. Most of the reviewed cases were polypoid (20 cases) or ulcerated (19 cases) in appearance. This type of tumor, as with all visceral carcinomas, tends to develop rapidly, appearing similar to an endophytic polypoid mass. It can arise from all areas of the stomach. Cancer does not occur more frequently in any one area. The exact histogenesis remains controversial and remains unknown. However, some authors have proposed two hypotheses (11). The first is the biclonal origin hypothesis that 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 may originate from a stem cell that is capable of undergoing both epithelial and mesenchymal differentiation.

In most cases, no specific symptoms of carcinosarcoma were reported and it was the epiphenomenon of locally advanced gastric cancer: asthenia, epigastric pain, dysphagia and vomiting. However, the occurrence of hematemesis and melena were infrequent (12). A mass in the epigastric region is frequently revealed on physical examination. Endoscopic examination is the gold standard in diagnosis as is contrast-enhanced CT in the staging of the disease. However, clinical symptoms of carcinosarcomas do not differ from gastric adenocarcinomas, and a discriminating diagnosis is endoscopically or radiologically impossible. Furthermore, only an epithelial or sarcomatous component of the tumor may be observed in small endoscopic biopsies (13).

In 89% of patients a surgical procedure was performed. In most cases curative surgery was performed. In some rare cases

palliative surgery was carried out to restore intestinal continuity or cytoreductive surgery to remove a mass necrosis (14).

The most frequent surgical procedure performed was total gastrectomy, which was often carried out on principle and not of necessity (the tumor had invaded the majority of the organ and/or perivisceral structures, or prior gastrectomy for peptic ulcer disease).

Splenectomy and partial pancreatectomy were not performed on principle but only as a necessity to intervene in patients with tumors that had invaded the surrounding structures. When feasible, resection of liver metastasis was performed at the same time as gastrectomy (15).

In the past, the diagnosis of carcinosarcoma was obtained by conventional histology. The first association between traditional histology and immunohistochemistry in the diagnosis of carcinosarcoma was in a case report in 1988 (16). A third neuroendocrin component has been identified in certain cases in addition to the carcinoma and sarcoma components

CEA, EMA, pancreatin, chromogranin A, CD56 and synaptophysin staining are highly specific markers used to identify carcinomatous components, whereas desmin, vimentin and  $\alpha$ -smooth muscle/sarcomeric actin show affinity for the sarcomatous elements (17).

A differential diagnosis between GIST and mesotelioma is crucial. GIST often occurs as a large intra-abdominal tumor and sometimes consists of spindle-shaped or epithelioid cells. However, carcinosarcoma shows no immunoreactivity for CD117 or CD34 and it does not demonstrate papillary or glandular structures on H&E sections, such as those usually observed in malignant mesotheliomas. It also tests negative for mesothelial cell markers, such as calretinin.

In all reviewed cases the mean survival period was extremely poor, approximately 6.5 months excluding the four major (up to 2 years) and minor survivals (less than 30 days). There was no difference in the survival of patients with gastric cancer where the neuroendocrin component was present. Overall tumor recurrence in the first postoperative year was greater than 50%.

From the review of the literature it was not possible to identify any prognostic factor because only a few cases had a survival of longer than 12 months: i) in the case report described by Ashida *et al* (7), the patient survived 7 years; ii) in that by Tominaga [described in (7)], the patient survived 5 years; iii) in that by Kyogoku *et al* (18), the patient survived 3 years; iv) in that by Kumagai *et al* (19), the patient survived 2 years; v) in the one by Teramachi *et al* (1) the patient survived 20 months; and vi) in the case report described by Kitamura (20), the patient survived for 1 year (Table I).

The most common site of recurrence is the liver where metastases occur immediately after surgery (17,21). In the present case report, liver metastases originate from the adenocarcinoma component.

In conclusion, we reported a case of carcinosarcoma and the procedure for achieving a definitive diagnosis. The simultaneous presence of epithelial and mesenchymal elements in a gastric tumor is a rare event, found almost exclusively in areas with high incidence of gastric cancer and with only few cases reported in literature. Carcinosarcoma of the stomach is a rare malignant tumor of often unclear etiology and pathogenesis. At present, the gold standard for definitive diagnosis is based on immunohistochemical staining of endoscopic biopsy or

surgical findings. Radical gastrectomy is the treatment of choice when feasible even if the tumor has rapid growth and malignant potential. However, the recurrence of this type of tumor may be expected within the first postoperative year. Therefore, more effective diagnostic techniques should be identified to improve patient survival.

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