The Korean Journal of Pathology 2010; 44: 87-91
DOI: 10.4132/KoreanJPathol.2010.44.1.87

A Case of Gastric Carcinosarcoma with Neuroendocrine and Smooth Muscle Differentiation

Se Min Jang · Si-Hyong Jang Kyueng-Whan Min · Woong Na Young Jin Jun · Seung Sam Paik

Department of Pathology, Hanyang University College of Medicine, Seoul, Korea

Received : February 17, 2009
Accepted : May 12, 2009

Corresponding Author
Seung Sam Paik, M.D.
Department of Pathology, Hanyang University College of Medicine, 17 Haengdang-dong, Seongdong-gu, Seoul 133-792, Korea
Tel: 02-2290-8252
Fax: 02-2296-7502
E-mail: sspaik@hanyang.ac.kr

Carcinosarcoma of the stomach is a rarely occurring malignant biphasic tumor that consists of both carcinomatous and sarcomatous components simultaneously in a single tumor. The common carcinoma component is tubular or papillary adenocarcinoma and the mesenchymal sarcomatous components are variable and these include leiomyosarcoma, rhabdomyosarcoma, osteosarcoma and chondrosarcoma. However, neuroendocrine carcinomatous differentiation in the carcinomatous component is extremely rare. We present here a rare gastric carcinosarcoma that demonstrated neuroendocrine carcinomatous and leiomyosarcomatous differentiation in a 47-year-old man.

Key Words : Stomach; Carcinosarcoma; Neurosecretory systems; Leiomyosarcoma

Gastric carcinosarcoma is a rare malignant tumor that is composed of both epithelial and mesenchymal elements.[1,2] The esophagus is the most common site of origin for this tumor in the gastrointestinal tract.[3] The stomach has been less frequently reported as a site of origin with only about 52 such cases having been reported in the English literature.[2-4] The most common epithelial malignancy is tubular or papillary adenocarcinoma, and the mesenchymal malignancies include leiomyosarcoma, rhabdomyosarcoma, osteosarcoma and chondrosarcoma.[1,5-7] Neuroendocrine carcinomatous differentiation is quite unusual in the areas of the carcinoma component. To the best of our knowledge, only five cases of gastric carcinosarcoma with a neuroendocrine carcinomatous component have been reported.[1,4,6,8,9] We report herein on a rare case of gastric carcinosarcoma that had neuroendocrine carcinomatous and leiomyosarcomatous components.

CASE REPORT

A 47-year-old man was admitted to our hospital due to dyspepsia that had been aggravated for the previous week. The patient had a history of melena for the past two months. The rest of the medical history and family history were unremarkable. The physical examination revealed no specific findings. An abdominal computed tomography scan revealed a polypoid mass with underlying wall thickening of the gastric antrum, and enlargement of the lymph nodes in the adjacent perigastric, gastrohepatic and peripancreatic areas (Fig. 1A). A huge polypoid mass with surface ulceration was found on the endoscopic examination (Fig. 1B). The histopathologic diagnosis of the biopsy was a poorly differentiated adenocarcinoma. The patient underwent a subtotal gastrectomy and lymph node dissection. He has been disease-free for 6-months since the operation.

The gastrectomy specimen showed a huge polypoid tumor (Borrmann type I), which measured 9 × 6 cm, in the lesser curvature side of the gastric antrum. The tumor surface was ulcerated and covered with yellowish purulent exudative material. The cut surface of the tumor was grayish white and solid, and it had a nodular, lobulated appearance. The tumor had infiltrated throughout the gastric wall and it extended to the subserosal layer with a pushing margin (Fig. 1C). Regional lymph node

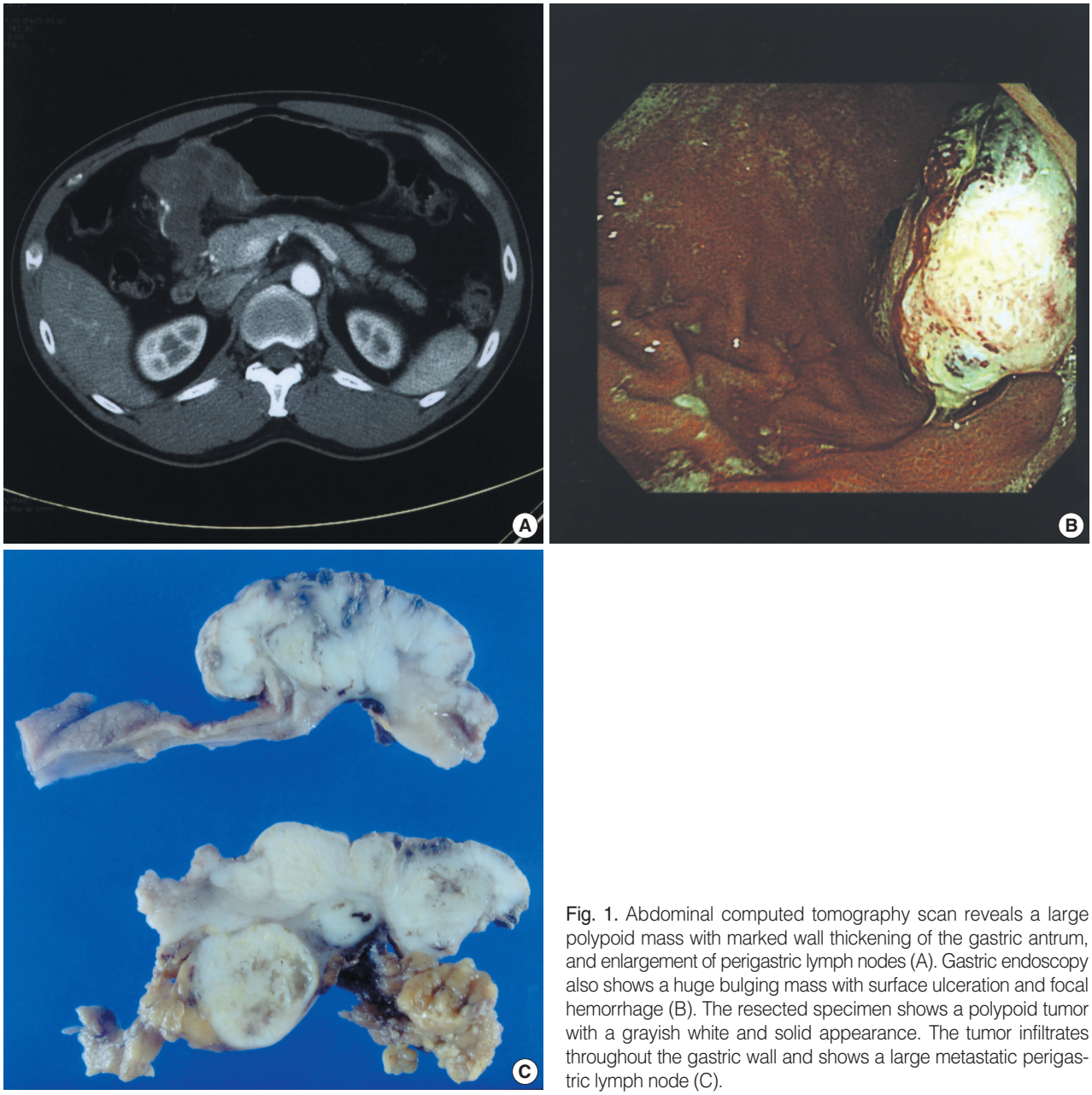

Fig. 1. Abdominal computed tomography scan reveals a large polypoid mass with marked wall thickening of the gastric antrum, and enlargement of perigastric lymph nodes (A). Gastric endoscopy also shows a huge bulging mass with surface ulceration and focal hemorrhage (B). The resected specimen shows a polypoid tumor with a grayish white and solid appearance. The tumor infiltrates throughout the gastric wall and shows a large metastatic perigastric lymph node (C).

metastases were also present. Microscopically, the gastric tumor consisted of intermixed epithelial and mesenchymal tumor components. The composition ratio of the carcinoma to sarcoma was 40% vs 60% for the total amount of the tumor. The epithelial tumor component predominantly showed a solid sheet or trabecular growth pattern. Glandular differentiation with mucin secretion, which suggested adenocarcinoma, was not observed on the periodic acid-Schiff stain, the periodic acid-Schiff stain with diastase digestion and the Alcian blue stain. The epithelial tumor cells exhibited markedly pleomorphic, oval to polygonal-shaped, vesicular nuclei with occasional conspicuous nucleoli. The sarcomatous component was mainly composed of spindle cells with marked cytologic atypia. These spindle cells formed closely packed, interlacing bundles or fascicles, and they occasionally showed bizarre, highly atypical large cells with multinucleated giant tumor cells. The spindle cells contained elongated, vesicular and blunt-ended nuclei with distinctly bordered weakly eosinophilic cytoplasm. Mitotic figures were frequently noted. The two tumor components were intermixed with each other and transitions between epithelial cells and spindle cells were evident (Fig. 2A). Lymphatic invasion, perineural invasion and vascular invasion were present. Twelve perigastric lymph

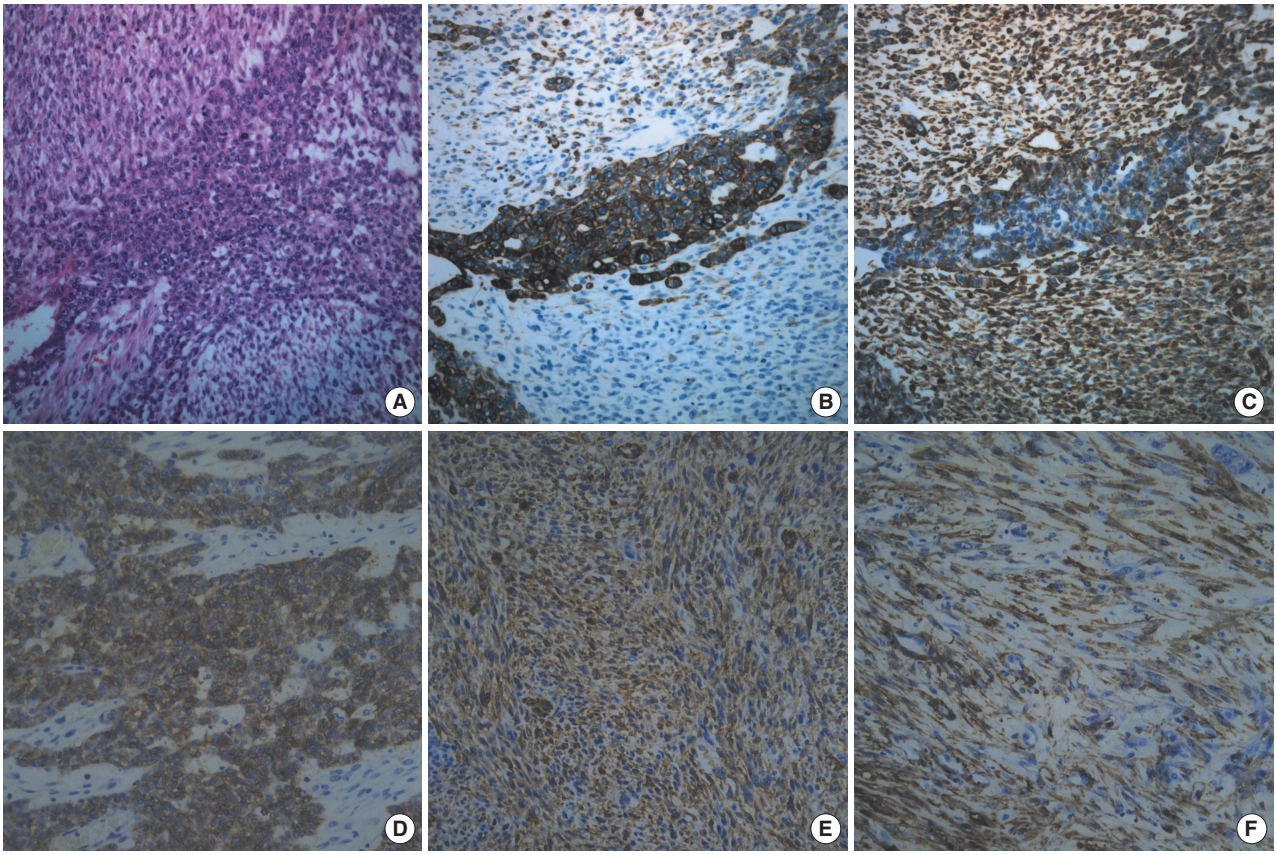

Fig. 2. The gastric tumor consists of poorly differentiated carcinoma component showing neuroendocrine differentiation and leiomyosarcomatous spindle cell component. The transition between two components is evident (A). The cytokeratin (B) and vimentin (C) immunostainings show positivity in both components. The epithelial component shows patchy strong positivity for CD56 (D). The spindle component shows diffuse strong positivity for h-caldesmon (E) and focal strong positivity for α-smooth muscle actin (F).

Table 1. Used antibodies and results of immunohistochemical stainings

Antibodies	Source	Dilution	Carcinoma area	Sarcoma area
Cytokeratin	Novocastra	1 : 100	+++, 100%	+, 10%
Vimentin	Novocastra	1 : 1	+, 50%	+++, 100%
CD56	Novocastra	1 : 1	+++, 60%	-
Chromogranin A	Dako	1 : 1	+, 5%	-
Synaptophysin	Novocastra	1 : 100	+, 10%	-
Neuron specific enolase	Signet	1 : 1	+, 5%	-
alpha-smooth muscle actin	Novocastra	1 : 1	-	++, 10%
h-caldesmon	Novocastra	1 : 200	-	+++, 90%
Desmin	Novocastra	1 : 1	-	+, 5%
c-kit	Dako	1 : 50	-	-
S-100 protein	Beckman Coulter	1 : 1	-	-

nodes showed metastatic tumor cell nests, which were mostly composed of a carcinomatous element. Immunohistochemical staining was performed on the formalin-fixed paraffin sections. The primary antibodies used for the immunohistochemical stainings and the staining results are shown in Table 1. Both the epithelial and mesenchymal tumor components showed positivity for cytokeratin (Fig. 2B) and vimentin (Fig. 2C). The epithelial tumor component showed patchy strong positivity for CD56 (Fig. 2D) and focal positivity for chromogranin A, synaptophysin and neuron specific enolase (NSE). The spindle tumor component showed diffuse strong positivity for h-caldesmon (Fig. 2E) and focal positivity for α-smooth muscle actin (Fig. 2F) and desmin. The immunohistochemical staining for c-kit and S-100 protein was negative. Other potential components such as chondrosarcoma, osteosarcoma or rhabdomyosarcoma were not observed.

DISCUSSION

In this report, we documented an exceedingly rare case of

Table 2. Clinicopathologic characteristics of reported gastric carcinosarcomas with neuroendocrine differentiation

Cases	Sex	Age (yr)	Symptoms	Appearance	Size (cm)	Location	Sarcoma component	Operation	Prognosis (mo)
Teramachi, *et al.*[1]	M	62	Epigastralgia, anorexia	Ulcerative	10 × 6	Lesser curvature	Leiomyosarcoma Rhabdomyosarcoma Osteosarcoma Chondrosarcoma	Total gastrectomy	NED (20)
Kuroda *et al.*[4]	M	59	Not described	Polypoid	9.2 × 8.4	Body	Leiomyosarcoma Myofibrosarcoma	Total gastrectomy	Not described
Tsuneyama, *et al.*[6]	M	63	Malaise	Polypoid	7 × 6.5	Pylorus	Rhabdomyosarcoma	Subtotal gastrectomy	NED (10)
Yamazaki[8]	M	59	Anorexia, weight loss	Ulcerative	9 × 9	Body	Undifferentiated spindle cell sarcoma	Total gastrectomy	DOD (2)
Cruz *et al.*[9]	M	67	Anorexia, weight loss	Polypoid	10 × 6	Subcardial	Spindle cell sarcoma	Total gastrectomy	DOD (4)
Our case	M	47	Dyspepsia, melena	Polypoid	9 × 6	Antrum	Leiomyosarcoma	Subtotal gastrectomy	NED (6)

M, male; NED, alive with no evidence of disease; DOD, died of disease.

gastric carcinosarcoma that was composed of poorly differentiated carcinoma that exhibited neuroendocrine differentiation, and spindle cell sarcoma that showed leiomyosarcomatous differentiation. In gastric carcinosarcoma, the most common carcinoma component is tubular or papillary adenocarcinoma.[5,6] Finding neuroendocrine differentiation in the epithelial malignant component is quite uncommon. Four cases of gastric carcinosarcoma have been published in the Korean medical journals, but the authors didn't describe any neuroendocrine differentiation of the carcinoma component.[10-13] To date, we found only five such cases cited in the English medical literature.[1,4,6,8,9] The clinocopathologic characteristics of the reported cases are summarized in Table 2. All the patients were males. Their ages ranged was from 59 to 67 years (mean, 62 years). Their presenting symptoms were epigastralgia, anorexia, malaise, swallowing difficulty and weight loss. The macroscopic appearance was ulcerative or polypoid. Three cases had polypoid features (Borrmann type I) and two cases had ulcerative features (Borrmann type III). The tumor size ranged from 7 to 10 cm (mean, 9.04 cm). The presenting sarcomatous components were leiomyosarcoma, rhabdomyosarcoma, osteosarcoma, chondrosarcoma, myofibrosarcoma, and spindle cell sarcoma. All the patients underwent a total gastrectomy or subtotal gastrectomy with lymph node dissection. For our case, the patient was a 47-year-old man with the clinical symptoms of dyspepsia and melena. The computed tomography and endoscopic examination revealed a large polypoid tumor (Borrmann type I) that measured 9 × 6 cm, and it was located at the antrum. The tumor was composed of a carcinomatous component (40%) and a sarcomatous component (60%). The carcinoma component consisted entirely of poorly differentiated carcinoma that demonstrated neuroendocrine differentiation, and this component showed patchy immunoreactivity for CD56 and focal immunoreactivity for chromogranin A, synaptophysin, and NSE.

According to the macroscopic pattern of growth in relation to the gastric wall, gastric carcinosarcoma has been classified into three types: 1) predominantly intramural infiltration, 2) a predominantly extramural mass and 3) a predominantly intramural mass with exophytic or crater-shaped growth.[14] Microscopically, carcinosarcoma can be classified into two types: 1) true carcinosarcoma and 2) false carcinosarcoma or the so-called sarcomatoid carcinoma.[2,4] The former refers to a malignant tumor that consists of carcinoma and true sarcoma with a relatively sharp demarcation between its two components. The latter refers to a malignant tumor that consists of carcinoma and sarcomatous portions that originate from the carcinoma with evident transitional areas. In the present case, transitions from epithelial cells of the carcinoma component to the spindle cells of the sarcoma component were observed on the routine hematoxylin and eosin stained sections. Moreover, both the epithelial cells and spindle cells showed immunoreactivity for cytokeratin antibody. In conjunction with these histopathological and immunohistochemical findings, our case can be classified as false carcinosarcoma or the so-called sarcomatoid carcinoma.

Although the exact histogenesis remains controversial and is still unknown, some authors have proposed two hypotheses with respect to the histogenesis of gastric carcinosarcoma.[1,6] One is a biclonal origin hypothesis that supports the collision tumor theory. This hypothesis is that the carcinosarcoma originates from two different tumor cell clones. The other is a monoclonal ori-

gin hypothesis, that the carcinosarcoma originates from a common stem cell that has the ability to undergo both epithelial and mesenchymal differentiation. In our case, there were evident transitions between the carcinoma and sarcoma components. Both the carcinoma and sarcoma components showed immunoreactivity to both cytokeratin and vimentin antibodies. The histopathologic features and the results of the immunohistochemical stainings are more supportive of a monoclonal origin hypothesis.

The prognosis of gastric carcinosarcoma is relatively poor. Patients with gastric neuroendocrine carcinoma have a poorer prognosis than those patients with other types of gastric carcinoma. Gastric carcinosarcoma tends to develop rapidly and to be diagnosed at an advanced clinical stage, and this all results in a poor prognosis.[1-3] The choice of treatment is partial or total gastrectomy with lymph node dissection. The effects of chemotherapy or radiotherapy have not yet been established.[2,3]

In brief, we report herein on an extremely rare case of gastric carcinosarcoma that demonstrated neuroendocrine differentiation as the carcinomatous component and leiomyosarcomatous differentiation as the sarcomatous component.

REFERENCES

1. Teramachi K, Kanomata N, Hasebe T, Ishii G, Sugito M, Ochiai A. Carcinosarcoma (pure endocrine cell carcinoma with sarcoma components) of the stomach. Pathol Int 2003; 53: 552-6.
2. Ikeda Y, Kosugi S, Nishikura K, *et al.* Gastric carcinosarcoma presenting as a huge epigastric mass. Gastric Cancer 2007; 10: 63-8.
3. Randjelovic T, Filipovic B, Babic D, Cemerikic V, Filipovic B. Carcinosarcoma of the stomach: a case report and review of the literature. World J Gastroenterol 2007; 13: 5533-6.
4. Kuroda N, Oonishi K, Iwamura S, *et al.* Gastric carcinosarcoma with neuroendocrine differentiation as the carcinoma component and leiomyosarcomatous and myofibroblastic differentiation as the sarcomatous component. APMIS 2006; 114: 234-8.
5. Matsukuma S, Wada R, Hase K, Sakai Y, Ogata S, Kawabara N. Gastric stump carcinosarcoma with rhabdomyosarcomatous differentiation. Pathol Int 1997; 47: 73-7.
6. Tsuneyama K, Sasaki M, Sabit A, *et al.* A case report of gastric carcinosarcoma with rhabdomyosarcomatous and neuroendocrinal differentiation. Pathol Res Pract 1999; 195: 93-7.
7. Nakayama Y, Murayama H, Iwasaki H, *et al.* Gastric carcinosarcoma (sarcomatoid carcinoma) with rhabdomyoblastic and osteoblastic differentiation. Pathol Int 1997; 47: 557-63.
8. Yamazaki K. A gastric carcinosarcoma with neuroendocrine cell differentiation and undifferentiated spindle-shaped sarcoma component possibly progressing from the conventional tubular adenocarcinoma: an immunohistochemical and ultrastructural study. Virchows Arch 2003; 442: 77-81.
9. Cruz JJ, Paz JI, Cordero M, Martín J, del Mar Abad M. Carcinosarcoma of the stomach with endocrine differentiation: a case report. Tumori 1991; 77: 355-7.
10. Chang YW, Kim BH, Kim HJ, *et al.* A case of gastric carcinosarcoma with pancreatic invasion. Korean J Gastrointest Endosc 1999; 19: 107-10.
11. Lee WM, Oh YH, Park MH, Lee KS, Lee JD. Carcinosarcoma and multiple early gastric carcinomas of the stomach. Korean J Pathol 1997; 31: 252-6.
12. Kim BB, Choi WJ, Park HR. Carcinosarcoma of the stomach. J Korean Surg Soc 1991; 40: 113-20.
13. Kim HR, Kim JW, Ryu SK, *et al.* A case of carcinosarcoma and adenocarcinoma of the stomach. Korean J Gastrointest Endosc 1989; 9: 183-6.
14. Iezzoni JC, Mills SE. Sarcomatoid carcinomas (carcinosarcomas) of the gastrointestinal tract: a review. Semin Diagn Pathol 1993; 10: 176-87.