CASE REPORT
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A Rare Case of Gastric Carcinosarcoma with Neuroendocrine Differentiation

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Carcinosarcoma of the stomach is a rare biphasic tumor that consists of both carcinomatous and sarcomatous components. In the gastrointestinal tract, carcinosarcoma is most frequently seen in the esophagus and rarely in the stomach. Tubular or papillary adenocarcinomas are common carcinomatous components, whereas mesenchymal sarcomatous components may vary. Neuroendocrine carcinomatous differentiation in carcinomatous components is extremely rare. We report a 62-year-old female patient with a history of dyspepsia for one-month-history. Endoscopic findings showed a ulcerofungating lesion, which infiltrated from the posterior wall of the antrum to the posterior wall of the gastric angle. Radical subtotal gastrectomy was performed. In the resected specimen, immunohistochemical studies showed two positive reactions for epithelial and mesenchymal markers. Based on the above findings, the patient was diagnosed with a gastric carcinosarcoma with neuroendocrine differentiation. **(Korean J *Helicobacter* Up Gastrointest Res 2014;14:121-125)**

Key Words: Carcinosarcoma; Stomach; Neuroendocrine differentiation factor, human; Immunohistochemistry

INTRODUCTION

A gastric carcinosarcoma is an uncommon malignant tumor that is composed of both epithelial and mesenchymal elements.[1] It is usually found in the uterus, breast, thyroid, lung, and upper gastrointestinal system.[2] The esophagus is the most common site of origin for this tumor in the upper gastrointestinal tract, and the stomach has been less frequently reported as a site of origin.[3-5] Although epithelial malignancies are usually tubular or papillary adenocarcinomas, neuroendocrine carcinomatous differentiation is not often seen in carcinomatous components. Mesenchymal malignancies may be leiomyosarcomas, rhabdomyosarcomas, osteosarcomas, and chondrosarcomas.[1,6-8] Carcinosarcomas can easily be mistaken for advanced gastric cancer, and therefore immunohistochemical analysis plays an important role in making a diagnosis.[7] In this study, we report a case of a 62-year-old woman with a gastric carcinosarcoma, together with its clinical, macroscopic, and histopathological characteristics.

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CASE REPORT

The patient was a 62-year-old woman with a one-month-history of dyspepsia. A health screening endoscopy was performed, and an endoscopic biopsy revealed a well-differentiated adenocarcinoma. She was referred to our hospital for further evaluation and treatment.

Most routine laboratory parameters were found to be in the normal range except for the presence of microcytic anemia (hemoglobin 9.1 g/dL, hematocrit 28.1%, mean corpuscular volume 77.4 fL). The level of CEA was 1.72 ng/mL.

Abdomino-pelvic CT scans showed a fungating mass arising from the posterior wall of the gastric antrum. Additionally, there were variable-sized multiple perigastric and left gastric lymph node enlargements (Fig. 1).

Endoscopic findings showed an ulcerofungating lesion (Borrmann type II) that originated from the posterior wall of the antrum. It proceeded to the posterior wall of the gastric angle, and its surface was covered with exudates and spontaneous bleeding (Fig. 2A). An endoscopic biopsy was not performed. The patient subsequently underwent radical subtotal gastrectomy with gastroduodenostomy

(Billroth I). Macroscopically, a 4.5×3.0 cm sized ulcerofungating mass was found that involved the antrum and gastric angle (Fig. 2B).

The tumor showed a mixed undifferentiated carcinoma and a sarcoma in H&E staining (Fig. 3). Immunohistochemical analysis showed positive readings for vimentin (mesenchymal marker), CK (epithelial marker), chromogranin (neuroendocrine marker), and synaptophysin (neuroendocrine marker) (Fig. 4). According to pathology reports, the final diagnosis was a poorly differentiated carcinosarcoma, with neuroendocrine differentiation. Five metastatic lymph nodes were identified among 19 regional perigastric lymph nodes (tumor-node-metastasis staging system: pT4aN2M0). Invasions of the serosa, lymphovascular, and perineural were present.

The patient underwent chemotherapy treatment (cisplatin with etoposide, administered at three-week intervals). Due to delirium and extra-pyramidal symptoms, further chemotherapy was stopped after the first-cycle of chemotherapy. After a few outpatient visits, the patient failed to show up for further follow up.

DISCUSSION

Carcinosarcoma is defined by the World Health Organization (WHO) as "a malignant tumor composed of intimately mixed epithelial and mesenchymal elements of a type ordinarily found in malignancies of adults". This def-

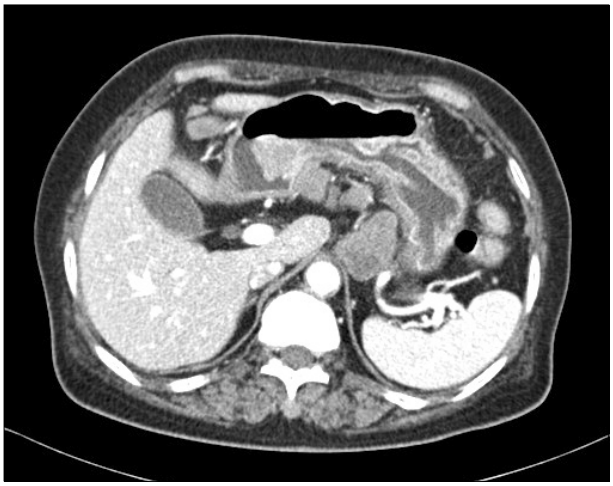

Fig. 1. CT scan showed a fungating mass arising from the posterior wall of the gastric antrum, with variable sized multiple perigastric and left gastric lymph node enlargement.

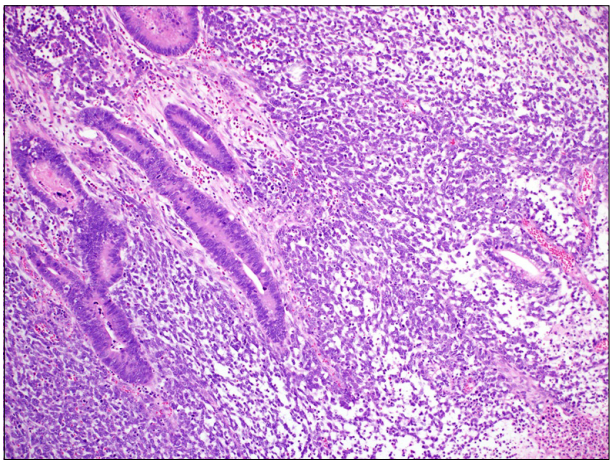

Fig. 3. H&E staining showed a mixed undifferentiated carcinoma and a sarcoma (×200).

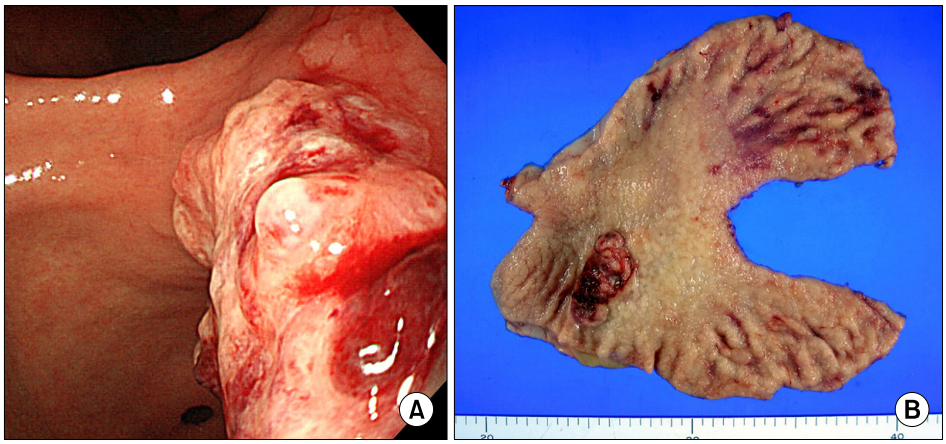

Fig. 2. Endoscopic finding and macroscopic finding. (A) Endoscopic finding of an ulcerofungating lesion (Borrmann type II) that infiltrated from the posterior wall of the antrum to the posterior wall of the gastric angle, with its surface covered with exudates and spontaneous bleeding. (B) Macroscopic finding of resected specimen showing an ulcerofungating mass, measuring 4.5×3.0 cm in size, with antrum and gastric angle involvement.

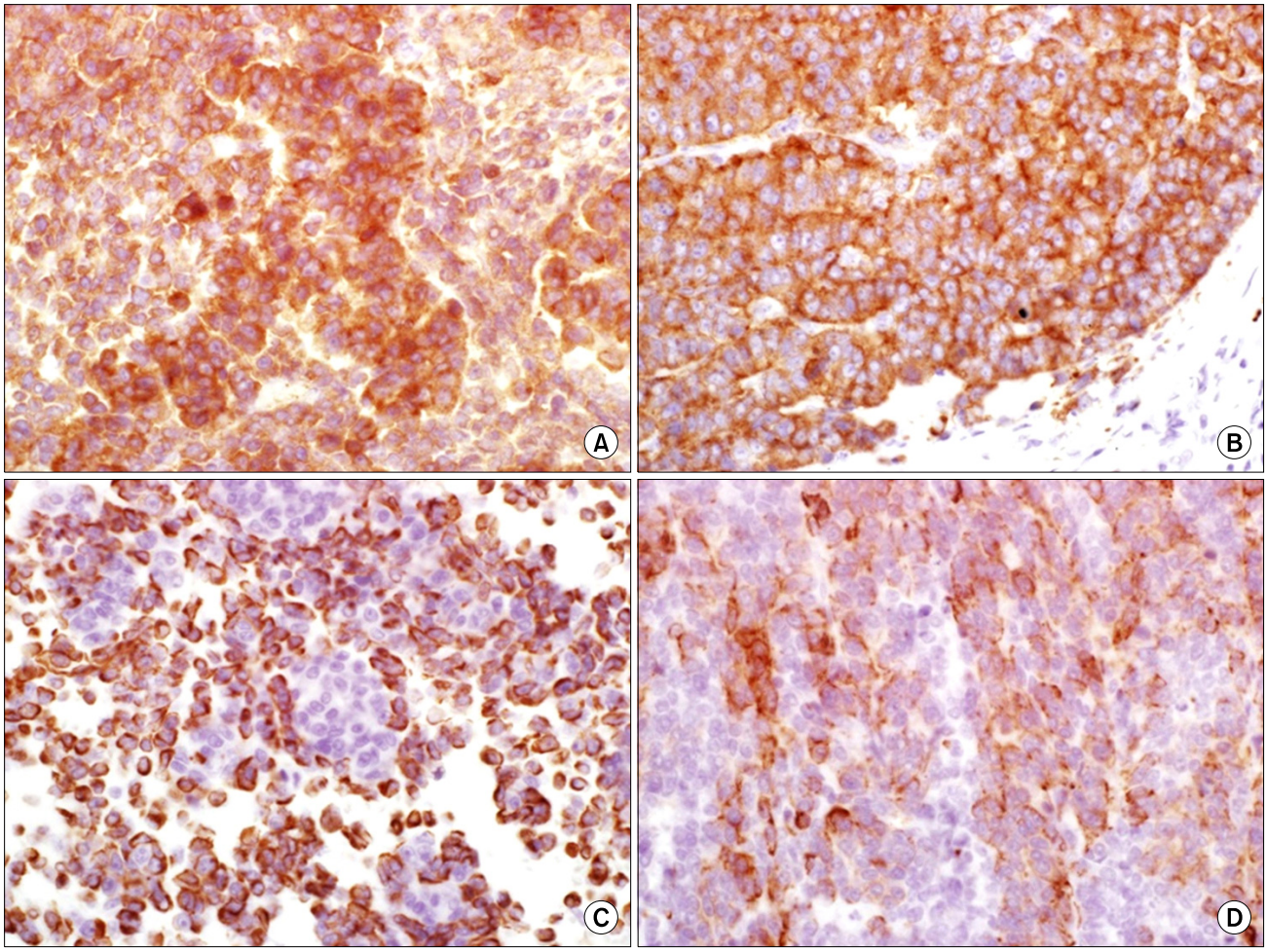

Fig. 4. Microscopic findings (×400). (A) Carcinosarcoma with chromogranin-positive cells (chromogranin immunohistochemical stain, ×400); (B) carcinosarcoma with synaptophysin-positive cells (synaptophysin immunohistochemical stain, ×400); (C) carcinosarcoma with vimentin-positive cells (vimentin immunohistochemical stain, ×400); (D) carcinosarcoma with CK-positive cells (CK immunohistochemical stain, ×400).

inition is based on traditional histological findings.[9]

In 1865, Virchow named the malignant neoplasm consisting of carcinomatous and sarcomatous components as a 'carcinosarcoma.'[1] Since then, it has also been referred to as a sarcomatoid carcinoma or a pseudosarcoma. As its name suggests, a carcinosarcoma is made up of two components: carcinoma components and sarcoma components. It is a very rare type of tumor. Although the carcinomatous component is most often an intestinal adenocarcinoma, endocrine and neuroendocrine components may also be present. In some cases, the sarcomatous component may contain leiomyosarcoma, rhabdomyosarcoma, osteosarcoma, and chondrosarcoma.[1,5,8,10] The first case of carcinosarcoma in Korea was reported by Kim et al.[11] in 1991.

In gastric carcinosarcoma, the most common carcinomatous component is tubular or papillary adenocarcinoma.[6-8] Neuroendocrine differentiation in the carcinomatous component is extremely rare. Seven cases of gastric carcinosarcoma have been published in the Korean medical journals (Table 1). Among them, only one case describes neuroendocrine differentiation of the carcinoma component.[12]

Depending on its place of origin, carcinosarcomas are classified into three types. Type 1 (collision tumors) have a clear boundary between the carcinomatous and sarcomatous components. Type 2 (combined tumors) contain two tumor components that overlap. Type 3 (composite

Table 1. Previous Seven Cases of Gastric Carcinosarcoma in Korea

Case	Age (yr)	Sex	Endoscopic finding (location)	Macroscopic finding (size)	Microscopic finding	Treatment	Prognosis
Kim et al.	63	Male	Fungating lesion (antrum)	Polypoid mass (5.5×3.5 cm)	CEA(+) Vimentin(+)	Subtotal gastrec, 5-fluorouracil	Death after 7 months
Kim et al.[11]	54	Male	Not described	Polypoid mass (17×14 cm)	Cytokeratin(+) Vimentin(+)	Total gastrec, chemotherapy	Not described
Lee et al.	56	Male	Ulcerofungating lesion (antrum)	Polypoid mass (5.5×5.5 cm)	Cytokeratin(+) CEA(+) Vimentin(+)	Subtotal gastretomy	Not described
Hwang et al.	61	Male	Ulcerofungating lesion (antrum, pylorus, duodenum)	Polypoid mass (13×15 cm)	Cytokeratin(+) CEA(+) Desmin(+) S-100 protein(+)	Subtotal gastretomy, ifosfamide, adriamycin	Liver metastasis after 2 months
Shin et al.	28	Female	Ulcerofungating lesion (body)	Polypoid mass (11.8×9 cm)	Cytokeratin(+) Vimentin(+)	Subtotal gastretomy	Death after 3 months
Jang et al.[12]	47	Male	Fungating lesion (antrum)	Polypoid mass (9×6 cm)	Cytokeratin(+) Vimentin(+) CD 56(+) h-caldesmon(+) α-smooth muscle actin(+)	Total gastretomy	Survival after 6 months
Choi et al.	51	Female	Ulcerofungating lesion (antrum, mid-body)	Polypoid mass (12×10.1 cm)	Cytokeratin(+) Vimentin(+)	Subtotal gastrectomy, cisplatin, 5-fluorouracil, docetaxel	Follow up loss after 7 months (received 9th chemotherapy)

tumors) comprise two tumor types with stromal components with various characteristics.[2,10] Recently, carcinosarcomas are classified into two types by the WHO according to microscopic findings. One is a true carcinosarcoma, another is a false carcinosarcoma (sarcomatoid carcinoma).

Although the exact histogenesis of gastric carcinosarcoma remains controversial and is still unclear, two hypotheses have been proposed.[1,7] The first hypothesis supports the collision tumor theory. It suggests a biclonal origin of the tumor, with the carcinosarcoma originating from two different tumor cell clones. The second hypothesis suggests that the tumor is derived from a monoclonal origin, with the carcinosarcoma derived from a common stem cell that has the ability to undergo both epithelial and mesenchymal differentiation.

As their surfaces are polypoid, exophytic, or endophytic, carcinosarcomas are often mistaken for advanced gastric cancer. Clinically, there is no difference between carcinosarcomas and gastric adenocarcinomas. A differential diagnosis cannot be made because it is impossible to distinguish the two endoscopically or radiologically. Conventional H&E staining has been used to histologically confirm that carcinomatous and sarcomatous components coexist, and additional immunohistochemical analyses have been used in some cases.[1,2] Tumor markers with high sensitivity for carcinomatous components in immunohistochemical staining are CEA, epithelial membrane antigen, pancreatin, chromogranin A, CD56, and synaptophysin. Desmin, vimentin, and α-smooth muscle/sarcomeric actin also show high sensitivity for sarcomatous components.[2,13] Immunohistochemical analysis of our patient showed positive readings for vimentin (mesenchymal marker), CK (epithelial marker), chromogranin (neuroendocrine marker), and synaptophysin (neuroendocrine marker).

Carcinosarcoma treatment consists of radical, subtotal, or total gastrectomy.[14,15] D2 gastrectomy is regarded as the standard treatment because it is associated with an outstanding cure rate and low loco-regional recurrence.[16] The roles of chemotherapy and radiotherapy in carcinosarcoma treatment have not been proven yet.

Prognosis of gastric carcinosarcoma is relatively poor, with gastric neuroendocrine carcinoma patients having a

poorer prognosis than those with other types of gastric carcinomas. The tendency of gastric carcinosarcoma to develop rapidly and for patients to be commonly diagnosed at an advanced clinical stage contribute to the poor prognosis.[1,3,4] The overall survival time of a patient with a gastric carcinosarcoma is 10～15 months and there is a possibility of relapse in over 50% of gastric carcinosarcoma cases within the first year following surgery.[1,10,17]

Gastric carcinosarcoma should be considered in the differential diagnosis of refractory gastric carcinoma cases that exhibit rapid progression.

In brief, we reported a case of carcinosarcoma with neuroendocrine differentiation and the process of making an accurate diagnosis. The co-occurrence of epithelial and mesenchymal elements in a gastric tumor is very rare, and only a handful of cases have been reported thus far in the literature. The etiology and the pathogenesis of carcinosarcoma of the stomach are often unclear. At present, the gold standard for an accurate diagnosis is based on immunohistochemical staining of an endoscopic biopsy or surgical specimens. When possible, radical gastrectomy is the treatment of choice, even if the tumor shows rapid growth and malignant potential. Within the first postoperative year, recurrence of carcinosarcoma may be expected. Therefore, it is necessary to identify more effective treatment modality to improve patient survival.

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