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Gastric Carcinosarcoma with CD10-Positive Sarcoma Component: A Case Report

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1. Abstract

Carcinosarcoma of the stomach is rare and shows intimately mixed epithelial and mesenchymal elements, which has been described as carcinosarcoma and sarcomatoid carcinoma. The most common site of origin is the uterus and only few cases of gastric carcinosarcoma have been reported in the literature. We report a case of gastric carcinosarcoma with CD10 expression in sarcomatous component.

2. Introduction

Carcinosarcoma is a malignant neoplasm characterized histologically by admixture of distinct carcinomatous and sarcomatous component without a transition zone that rarely occur in the stomach. Nie et al. estimated that carcinosarcoma accounts for only 0.05% of all radically resected gastric cancers.[1] Histologically, the two components of malignancy varied widely. In the carcinomatous component, the histologic type was commonly the Lauren intestinal-type adenocarcinoma, and rarely squamous cell carcinoma and neuroendocrine carcinoma.[1] The sarcomatous component was usually unclassified pleomorphic sarcoma, while heterogeneous chondroid, osteoid, leiomyomatous, fibrous, and rhabdoid differentiations were also observed [1]. CD10 is a 90- to 110-kDa cell surface zinc-dependent metalloprotease that was initially described as a tumor-specific antigen for acute lymphoblastic leukemia [2]. CD10 has been found to be positive in in renal cell carcinoma, hepatocellular carcinoma, non-small cell lung cancer, pancreatic solid pseudopaillary tumor, urinary bladder and prostate carcinoma, gestational trophoblastic diseases(GTDs), breast, colon carcinoma and endometrial stromal sarcoma [3-5]. Recent reports indicate that CD10-positive stromal cells belong to the myofibroblast group, are correlated with poor prognosis in breast carcinoma, and are also involved in colorectal carcinogenesis [6,7]. In gastric cancer, stromal CD10 expression had a significant correlation with differentiaation, invasion, metastasis and vessel invasion [8]. However, no reports of CD10 expression in sarcomatous component of gastric carcinosarcoma have been found so far. We discuss a case of a patient with gastric carcinosarcoma with CD10 positive stromal component.

3. Clinical Summary

70-year-old man with dyspnea and anemia was found to have a gastric tumor on endoscopic examination (Figure 1). A 6cm sized fungating mass was detected in the gastric antrum of anterior wall and lymph nodes in the perigastric area, common hepatic artery, portocaval area and retrocarval area were enlarged in computed tomography (CT) scan. In the laboratory data, severe anemia (Hb, 6.2 g/dl) was detected and serum levels of tumor markers were normal: CEA 3.78 ng/ml, CA19-9 32.4 U/ml. He was submitted to radical subtotal gastrectomy and Billroth I reconstruction surgery. The tumor was 9.0x5.5cm in size and infiltrated into the perigastric adipose tissue. The patient was discharged from the hospital and hospitalized again for chemotherapy after 2 month later of surgery. However, he was unable to receive chemotherapy due to pneumonia. He refused all treatment, was discharged from the hospital, and did not visit again.

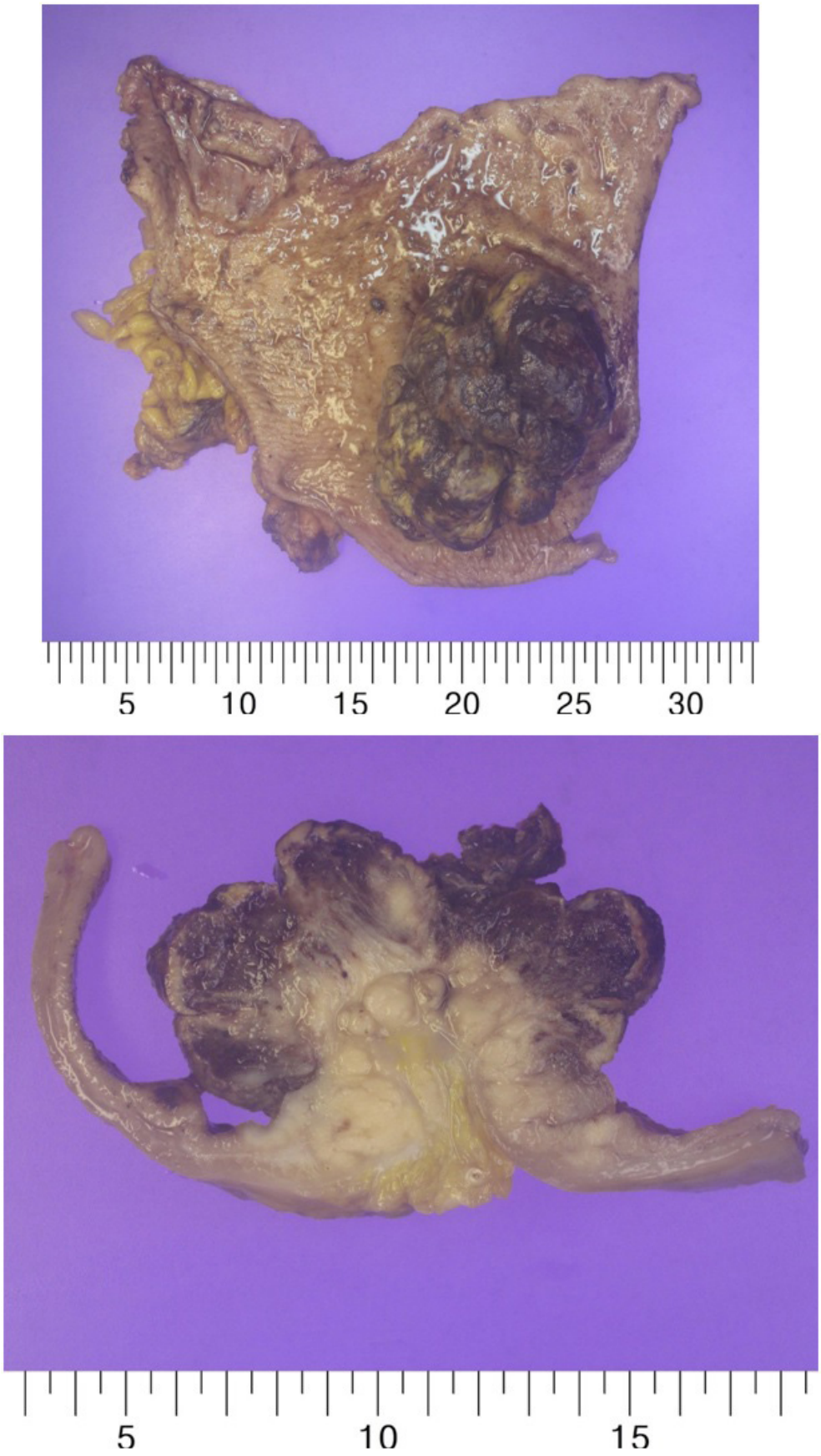

Figure 1: Macroscopic findings of the resected specimen. A: An 9.0x5.5cm sized exophytic tumor located in the gastric antrum. B: Cut surface of tumor showed pale yellow solid lesion with hemorrhage.

4. Pathological Findings

The cut section of tumor showed solid, grayish-pink lesion mixed with hemorrhage and necrosis. Microscopic findings of resected tumor showed the mixture of well differentiated tubular adenocarcinoma and sarcomatous spindle cells (Figure 2). Spindle cells show mild to moderate nuclear pleomorphism and frequent mitosis with atypical form. Proliferation of arteriole-sized vessels and spindle cells encircled the small vessels. However, definitive heterogeneous sarcomatous elements, such as cartilaginous, osteoblastic, fat, nerve, or rhabdomyoid features were not be seen in the present tumor. Tumor was infiltrated in perigastric adipose tissue and metastasis in 28 out of 38 perigastric lymph nodes (pT3N3b). Metastatic lesions showed only carcinomatous components (Figure 3). Immunohistochemistry showed carcinomatous cells were positive for cytokeratin and sarcomatous cells were strongly positive for vimentin. CD10 was expressed in brush border of cancer glands and cytoplasm of sarcomatous spindle cells (Figure 2). Smooth muscle actin, s-100 protein, desmin, myoD1, HMB45 were negative. Mutations of APC, TP53, CDKN2A and TERT gene were detected in next generation sequencing with tumor tissue.

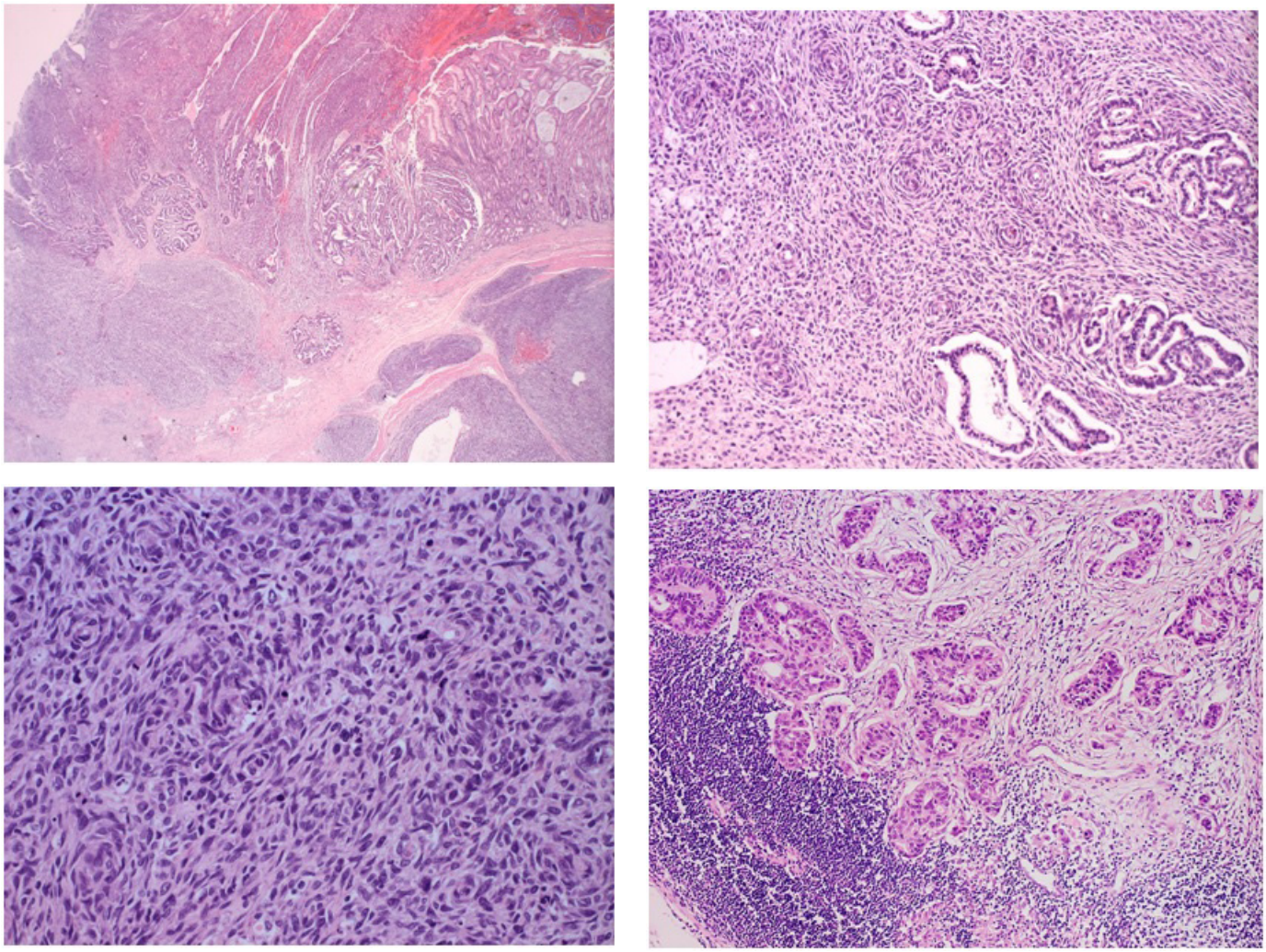

Figure 2: Microscopic findings. A, B: Hematoxylin and eosin stained slide showed gland forming carcinomatous component (arrow) and sarcomatous spindle cells (A: x10, B:x200). C: Spindle cells revealed mild to moderate nuclear pleomorphism and frequent mitosis (x400). D: Only adenocarcinoma component was detected in dissected lymph nodes. (x200).

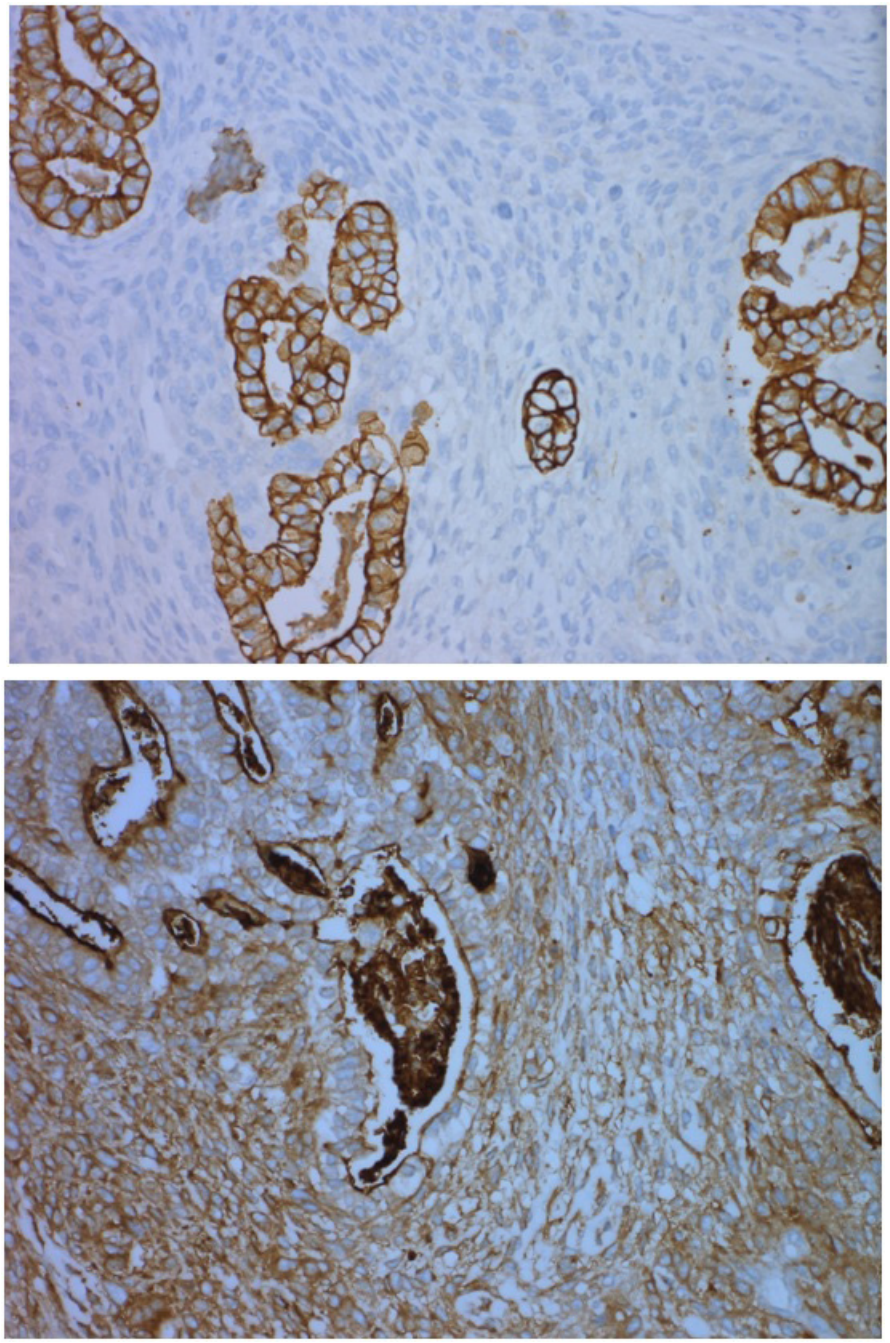

Figure 3: Immunohistochemical findings. A: Pancytokeratin was expressed in adenocarcinoma component but not in the sarcomatous component (x200). B: CD10 stain showed positive expression in both carcinomatous and sarcomatous compoments (x200).

5. Discussion

Gastric carcinosarcoma was first reported by Queckenstedt in 1904, and so far, less than 100 cases have been reported [1,9]. The clinical symptoms and laboratory, endoscopic, and radiological findings of carcinosarcoma of the stomach are generally indistinguishable from gastric adenocarcinomas. Therefore, its diagnosis largely relies on pathological analysis, such as cell morphology and immunohistochemical staining. The pathogenesis of gastric carcinosarcoma has not yet been precisely elucidated [10,11]. The "collision" theory indicates that synchronous but independent carcinoma and sarcoma coincidently arise and merge. Some researchers have argued that a primary carcinoma stimulates excessive stromal proliferation, resulting in carcinosarcoma [10]. The combination and conversion theories assume that the two components are derived from a common precursor with divergent and metaplastic differentiation, respectively [11]. Uterine carcinosarcoma is considered as sarcomatous transformation/transdifferentiation of endometrial carcinoma rather than a collision between two biologically distinct tumor types because cytokeratin is positive in both the carcinomatous and sarcomatous components. Also, Ki67 labeling studies on uterine carcinosarcoma show the carcinomatous component to have a higher Ki67 labeling than the sarcomatous component, suggesting that the sarcomatous component is derived from the carcinoma [12]. And in cases where the carcinomatous and sarcomatous components were separately an-

alysed, most of the mutations identified were present in both components, indicating a common origin for the two components [13]. In this case, epithelial markers were not expressed in sarcomatous component. We performed NGS (next generation sequencing) test with tumor tissue, but we did not perform test separately on carcinomatous and sarcomatous components. Truncating mutation of APC gene is known to be related with desmoid fibromatosis in subtypes of sarcoma. CD10 was expressed in carcinomatous and sarcomatous components of this case. Little is known about CD10 expression in soft tissue sarcoma. Deniz et al. reported that CD10 was expressed in 90 of 202 various kinds of sarcoma. 72% of malignant fibrous histiocytomas, 45% of fibrosarcomas, 34% of rhabdomyosarcomas, 50% of leiomyosarcomas, 22% of liposarcomas, 72% of malignant peripheral nerve sheath tumors were positive for CD10. But there was nothing histologically and immunohistochemically consistent with our case. They suggested that CD10 is not a lineage specific antigen and is probably related to an aggressive tumor phenotype [14]. Recently, research results on the expression of CD10 in stromal cells around carcinoma have been published [6-8]. Previous studies have indicated that this new reactive stroma environment enhances tumorigenesis by supporting cancer cell survival, proliferation and migration, and also by inducing angiogenesis. The most common marker of reactive stroma in cancer is the appearance of activated stromal cells with myofibroblastic characteristics [15]. In the study of Huang et al., the stromal cells expressing CD10 were also positive for α-smooth muscle actin [8]. But CD10 positive sarcomatous component of this case didn't express α-smooth muscle actin. Hypothesis that carcinosarcoma is caused by overgrowth of CD10-positive stromal cells in preexisting gastric carcinoma can be considered. Yosida et al. repoted a case in which the lesion initially diagnosed with ulcerative adenocarcinoma on endoscopy increased to an exophytic mass 2 month later, and the patient was diagnosed with carcinosarcoma consisting of more than 90% of sarcomatous component on histological examination [16]. They concluded that this finding supports the idea that gastric carcinosarcoma is epithelial in origin. However, like this case, epithelial cell marker was not expressed in sarcomatous components in the case reported by Yosida et al. [17]. Moreover, the liver metastasis that had been detected in the ante-mortem examination were composed of both spindle cells and adenocarcinoma componentsas, but metastasis of the lung first diagnosed showed only adenocarcinoma without sarcomatous components. Although these differences in tumor components at each metastatic site might have resulted from differences in affinities of each tumor component for lymphatics or veins, Yosida et al. claimed that the development of the adenocarcinoma component might have preceded. In this case, all the metastasized tumor cells in perigastric lymph nodes were adenocarcinoma. We believe that more extensive research is needed to further understand the pathogenesis of gastric carcinosarcoma. So far, there have been no reports of CD10 expression in gastric carcinosarcoma, Salibay et al. reported a case of primary pancreatic carcinosarcoma with CD10-positive sarcomatous component [17]. Pancreatic stellate cells that express CD10 are associated with more aggressive pancreatic carcinomas and increased metalloproteinease 3 enzyme production, which is involved in basement membrane degradation and, therefore, tumor invasiveness. (9 in pancreatic cs). It has been proposed that CD10 could be a target for treatment of pancreatic carcinomas using metalloproteinase inhibitors. As pancreatic carcinosarcomas are rare, no known reports have evaluated for CD10 positivity or mentioned use of any metalloproteinase inhibiting substances. Recently, Pan et al. demonstrated that CD10 is capable of cleaving CPI-0004Na and related peptide prodrugs such as N-succinyl-b-alanyl-L-isoleucyl-L-alanyl-L-leucyl-Dox (sAIAL-Dox), which have an improved antitumor efficacy profile with reduced toxicity compared with doxorubicin [18]. Therefore, a new cancer therapy that blocks the induction of CD10-positive stromal cells in gastric carcinosarcoma can be applied. This approach may reduce the activities of the CD10-positive stromal cells, which accelerate tumor aggressiveness. Further studies on the molecular basis of CD10 expression in stromal–cancer interaction will be required to pursue such new therapeutic strategies. This is the first report of CD10 expression in the sarcomatous component of gastric carcinosarcoma. In the future, it is necessary to investigate CD10 expression in gastric carcinosarcoma and further study its implication.

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