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【 CASE REPORT 】

A Rare Duodenal Carcinosarcoma: A Case Report and Literature Review

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Abstract:
Carcinosarcoma is a biphasic malignant tumor comprising both carcinomatous and sarcomatous components; its occurrence in the duodenum is very rare. We herein report the case of a 96-year-old woman with duodenal carcinosarcoma showing rapid growth within the past year. The tumor was found to be bulging into the lumen and predominantly comprised sarcomatoid components with focal positive staining for cytokeratin. Therefore, the tumor was diagnosed as duodenal carcinosarcoma. The clinical information of the present case and our literature review of the 12 cases reported to date will help physicians diagnose and treat this rare tumor.

Key words: carcinosarcoma, duodenum, vimentin, AE1/AE3, CAM 5.2, rapid growth

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Introduction

Carcinosarcomas are rare malignant tumors comprising both carcinomatous and sarcomatous components that show intermingled growth (1, 2). In 1864, Virchow reported the first case of sarcoma carcinomatoides (3), and Meyer later defined it as carcinosarcoma (4). Although this tumor can occur in various organs, such as the uterus, lung, and hepatobiliary tract, duodenal carcinosarcoma is extremely rare, and only a few cases have been reported (2, 5, 6).

We herein report a patient with duodenal carcinosarcoma that showed rapid growth within one year and describe its subsequent clinical characteristics and histological findings following an autopsy. In addition, the information available from all 12 cases of duodenal carcinosarcoma that have been reported to date is summarized, which will help physicians appropriately diagnose and treat this rare tumor.

Case Report

A 96-year-old Japanese woman presented to our hospital with vomiting and loss of appetite. She had been previously treated for hypertension, and an annual checkup had been conducted every year. No abdominal tumor had been observed on computed tomography (CT) performed one year prior to admission.

A physical examination on admission revealed right hypochondrial pain with no fever or jaundice. Laboratory results on the day of admission showed an increase in the white blood cell count (WBC, 10,540/μL) and aspartate aminotransferase (AST, 50 IU/L), alanine aminotransferase (ALT, 56 IU/L), alkaline phosphatase (ALP, 1,133 IU/L), gamma-glutamyl transpeptidase (γ-GTP, 285 IU/L), and C-reactive protein (CRP, 8.8 mg/dL) levels and a mild decrease in hemoglobin (9.5 g/dL) and albumin (3.0 g/dL) levels (Table 1). Contrast-enhanced CT revealed a 10-cm, low-density

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Table 1. Results of Laboratory Investigation on the Day of Admission.

Hematology		Biochemistry			
WBC	10,540 /mm^3	TP	6.2 g/dL	ALP	1,133 IU/L
RBC	296×10^4 μL	Alb	3.0 g/dL	LDH	188 IU/L
Hb	9.5 g/dL	BUN	26.4 mg/dL	γGTP	285 IU/L
Ht	26.1 %	Cre	0.94 mg/dL	CRP	8.8 mg/dL
PLT	18.8×10^4 μL	T-Bil	1.1 mg/dL		
		D-Bil	0.3 mg/dL		
		AST	50 IU/L		
		ALT	56 IU/L		

WBC: white blood cell, RBC: red blood cell, Hb: hemoglobin, Ht: hematocrit, PLT: platelet, TP: total protein, Alb: albumin, BUN: blood urea nitrogen, Cre: creatinine, T-Bil: total bilirubin, D-Bil: direct bilirubin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, LDH: lactate dehydrogenase, γGTP: gamma-glutamyl transpeptidase, CRP: C-reactive protein

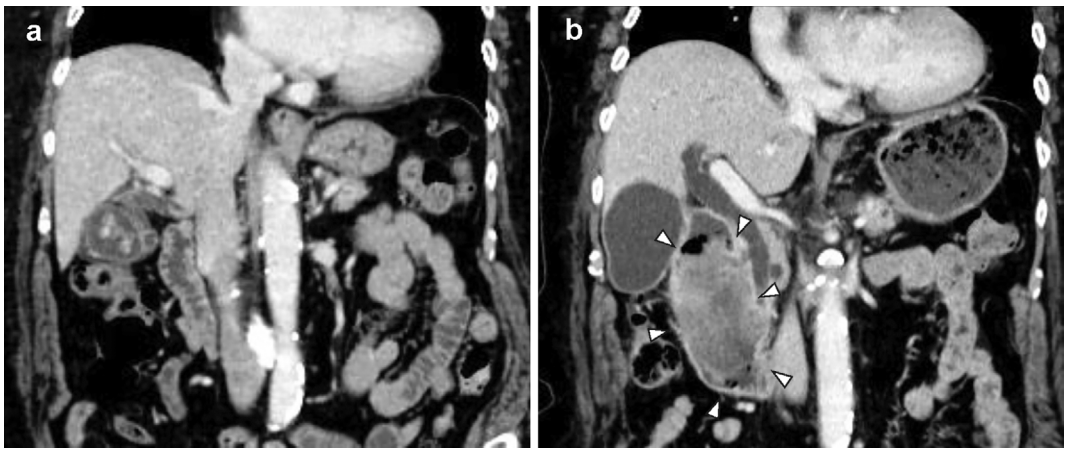

Figure 1. Contrast-enhanced abdominal CT. (a) No mass was observed one year prior to the diagnosis. (b) A 10-cm tumor in the duodenum with dilatation of the common bile duct (white arrowheads).

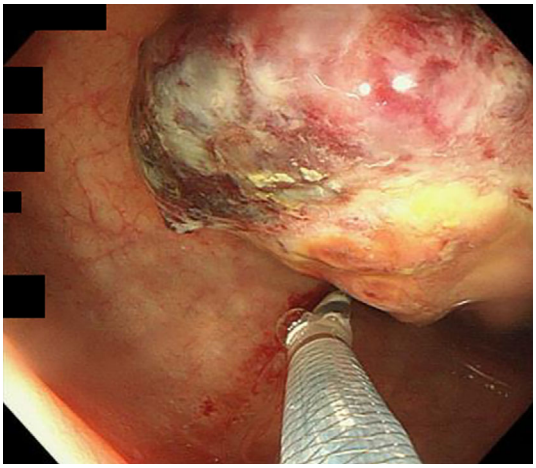

Figure 2. Esophagogastroduodenoscopy (EGD). Significant stenosis of the duodenum occurred due to the mass being located in the descending portion. Necrotic tissue and mild hemorrhaging were observed on the surface.

mass in the descending portion of the duodenum with mild contrast effects in the delayed phase of the dynamic study (Fig. 1). An upper endoscopic examination revealed an extremely large, whitish, hard mass in the descending portion to the bulbus, with the tumor surface showing necrotic tissue and mild hemorrhaging. Due to this tumor, the duodenal tract showed severe stenosis, resulting in difficulty passing food and thereby leading to vomiting and loss of appetite (Fig. 2). A biopsy of the tumor showed necrotic tissue, but no histological diagnosis was made at that point.

Following the tissue collection, a gastrointestinal stent (Niti-S 22 mm, 10 cm) was successfully placed for stenosis. However, because of tumor progression, her general condition gradually worsened, and she died at 39 days after admission. With consent from the family, an autopsy was performed for the diagnosis of the tumor. Macroscopically, a 60 ×100-mm, whitish, solid tumor with necrotic tissue was observed. The major part of the tumor showed growth into the lumen of the duodenum. Due to the tumor progression, the ampulla of Vater could not be recognized (Fig. 3). A histological analysis (Fig. 4) revealed that the major part of the

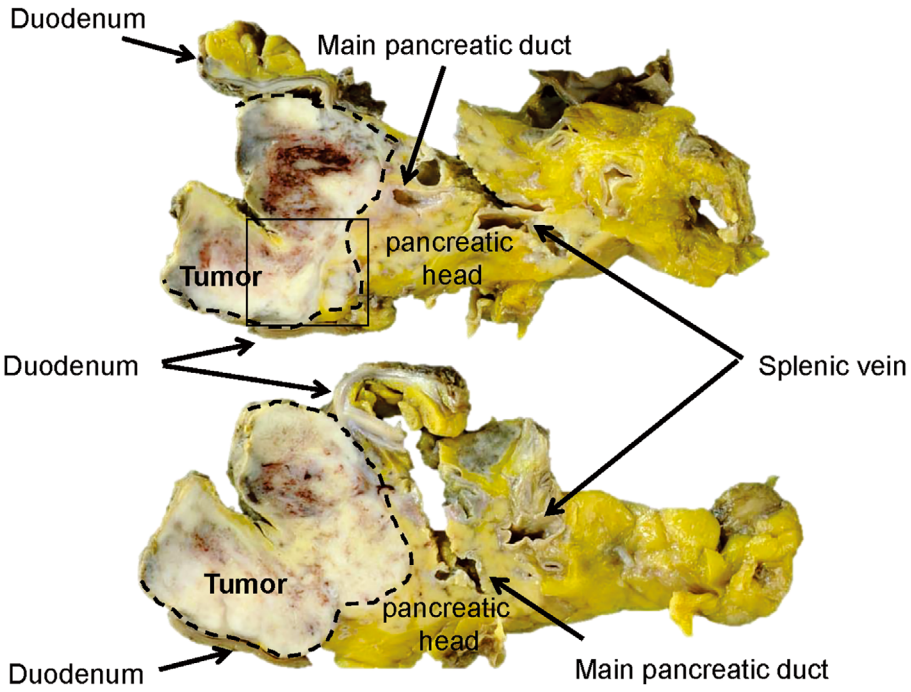

Figure 3. **Macroscopic findings of the tumor. An autopsy revealed a whitish solid tumor with necrotic tissue bulging into the lumen of the duodenum. The tumor was 60×100 mm in diameter.**

tumor showed growth in the duodenal submucosal layer with infiltration from the duodenal serosal layer to the pancreatic head (Fig. 4a). The tumor predominantly comprised a sarcomatous component of pleomorphic cells that was strongly positive for vimentin, (Fig. 4c) with a mixture of a carcinomatous component (Fig. 4a). The carcinomatous component comprised a moderate-to-poorly differentiated tubular adenocarcinoma, as evidenced by immunohistochemical staining of epithelial markers, including AE1/AE3 and CAM5.2 (Fig. 4d and e). Part of the sarcomatous component was positively stained for AE1/AE3 and CAM5.2. (insets in Fig. 4d and e). No transition was observed between the adenocarcinoma and sarcomatous atypical cells (Fig. 4b). No specific tissue differentiation in the tumor, such as osseous, muscular, or cartilaginous tissue, was observed. Based on the above findings, the tumor was diagnosed as a carcinosarcoma of the duodenum.

At the autopsy, a small metastatic tumor was found in the liver that had not been detected on imaging. No other tumors were observed. The liver metastasis comprised a sarcomatous component with positivity for vimentin and focally positivity for CAM5.2 but without such findings for the carcinomatous component.

Discussion

Carcinosarcoma is a biphasic malignant tumor comprising both carcinomatous and sarcomatous components (5) and has been reported in the uterus, ovary, gastrointestinal tract, pancreas, bile duct, liver, lung, and breast (6). Duodenal carcinosarcoma is quite rare, with only 12 cases reported to date (2, 5-15). The mechanism underlying the tumor development has not yet been clarified, but a few have been proposed, as follows: 1) two types of stem cells of the mesenchymal and epithelial origin independently become separate tumors (collision theory), 2) the sarcomatoid component develops in reaction to carcinoma invasion (composition tumor theory), 3) the sarcomatoid component develops as a consequence of sarcomatoid changes in carcinoma (metaplastic tumor theory), and 4) each component arises from a single common stem cell (combination tumor therapy) (7). Recently, analyses of the p53 mutation and loss of heterozygosity have supported the monoclonal hypothesis (16). Since our case showed a mixture of both sarcomatoid and carcinomatous components, and part of these sarcomatoid tissues were stained positively with cytokeratin, we considered that our patient's tumor might have developed based on the hypothesis of the sarcomatoid component developing as a consequence of sarcomatoid change in a carcinomatous tumor.

However, the possibility that the sarcomatoid component developed in reaction to the invasion of the carcinomatous tumor cannot be ruled out. Carcinosarcoma is classified into true and so-called carcinosarcomas (6). True carcinosarcoma has three features: 1) the presence of a genuine sarcomatous component, such as chondrosarcoma, osteosarcoma, rhabdomyosarcoma, and leiomyosarcoma; 2) no transitional zone between carcinomatous and sarcomatous components; and 3) the sarcomatous component is positive for mesenchymal markers and negative for epithelial markers (5). In contrast, so-called carcinosarcoma is histologically diagnosed carcinosarcoma that shows none of the abovementioned features. In our case, most of the tumor was located in the duodenal submucosal layer, with a few components located in the pancreas. Thus, based on the WHO Classification of Tumors

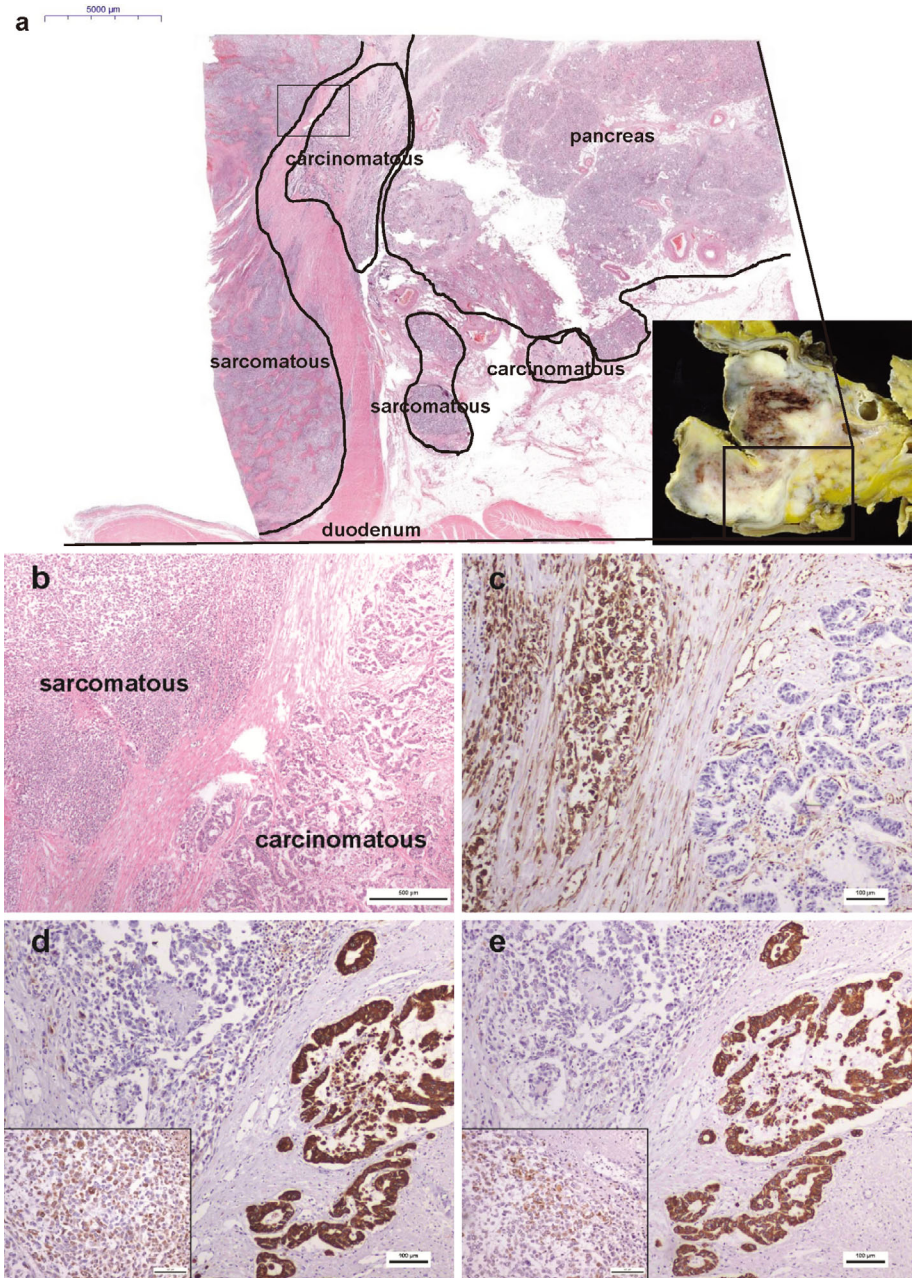

Figure 4. **A histological analysis of the tumor. (a) The tumor predominantly comprised sarcomatous and carcinomatous components. (b) Hematoxylin and Eosin staining of the tumor. No transition was observed between adenocarcinoma and sarcomatous atypical cells. (c) Vimentin. (d) AE1/AE3. (e) CAM5.2. Insets in (d) and (e) show the sarcomatous component positively stained for AE1/AE3 and CAM5.2.**

of the Digestive System (17), we concluded that the primary lesion was in the duodenum. In addition, in our case, there were no genuine sarcomatous components, no transitional zone between carcinomatous and sarcomatous components, and sarcomatous components positive for cytokeratin, which is an epithelial marker. Therefore, based on these findings, the tumor was diagnosed as a so-called carcinosarcoma.

An efficient therapeutic strategy for carcinosarcoma has not yet been developed. However, some cases of esophageal carcinosarcoma have shown a long-term survival after resection (18), and Tanaka et al. reported a 2-year survival following the resection of the duodenal carcinosarcoma (8). However, radiotherapy and chemotherapy have shown no beneficial effects on the survival in cases of bile duct carcinosarcoma (19), and although S-1 (2, 9) and gemcitabine (5) treatments have shown some promise, no standardized regimen has been developed.

The results of a literature search with the terms "duodenum" or "duodenal" and "carcinosarcoma" in Pubmed showed that only 12 cases of duodenal carcinosarcoma have been reported to date (2, 5-15), and the available clinical information is summarized in Table 2. There were 8 men and 5 women including our case, with ages ranging from 46 to 98 years (median age, 70 years). Our case was the second

Table 2. Summary of 12 Cases of Duodenal Carcinosarcoma Reported to Date.

Ref	Age	Sex	Symptom	Primary lesion	Size (mm)	Morphologic type	Initial Histological Diagnosis	True or so-called	Invasion/ metastasis	Recurrent	Prognosis
10	67	M	abdominal pain	papillary	20	1	carcinosarcoma	so-called	None/LN	None	5 months
6	73	M	jaundice	papillary	20×10	2	adenocarcinoma	so-called	None/None	None	5 months
5	79	M	jaundice	2nd portion (close to papilla)	61×43	1	anaplastic carcinoma of the pancreas	so-called	None/LN	liver	8 months
9	59	M	abdominal pain	2nd portion (close to papilla)	65×65	1	GIST	true	pancreas/ LN	lung, bone	702 days
11	61	M	abdominal pain	papillary	35×24	1	adenocarcinoma	so-called	None/LN	liver, pancreas, LN, peritoneal	63 days
7	79	F	jaundice	2nd portion (close to papilla)	120×100	1	adenocarcinoma	true	pancreas/ liver	None	90 days
12	98	F	jaundice	2nd portion (close to papilla)	110×60	1	None	so-called	pancreas/ LN	None	2 months
2	72	M	loss of appetite	2nd portion (far from papilla)	60×50	2	adenocarcinoma	true	None/LN	None	9 months
8	70	F	jaundice	papillary	24×15	1	None	so-called	None/LN	None	2 years
13	46	M	jaundice	papillary	30×25	2	None	so-called	None/None	N/A	N/A
14	46	F	melena	papillary	43×42	2	N/A	so-called	None/LN	liver	30 days
15	64	M	jaundice	papillary	35×30	1	N/A	so-called	None/None	liver	78 days
our case	96	F	loss of appetite	2nd portion (close to papilla)	100×60	1	N/A	so-called	None/liver	None	39 days

M: male, F: female, GIST: gastrointestinal stromal tumor, N/A: information not applicable, LN: lymph node, Morphologic type: Bormann's classification

oldest patient in the series. The major clinical symptom was jaundice in seven cases due to their primary lesion being located around the major papilla. Eleven cases underwent surgical resection, and only one was correctly diagnosed by a tissue biopsy. True carcinosarcoma was observed in 2 cases, and the remaining 10 did not meet the 3 features of true carcinosarcoma defined above. Metastatic lesions were observed in 10 cases, including 8 in the lymph node and 1 in the liver. The histology of these lesions included adenocarcinomas, sarcomatoid components, and small cell carcinoma-like lesions. Importantly, the prognosis of all patients was extremely poor, and seven patients died within one year after the diagnosis. Consistent with other reports (20, 21), our case report also showed the rapid growth of the tumor within one year. The aggressive growth pattern of the tumor might be due to the greater degree of malignancy in carcinosarcoma than in adenocarcinoma (22), with its rapid and infiltrative growth pattern and metastatic features. Further analyses with a greater number of cases are needed in order to understand the mechanism and how carcinomas progress into carcinosarcomas.

Conclusion

This case report described an extremely rare case of so-called duodenal carcinosarcoma exhibiting rapid growth. Although the prognosis is generally poor, our summary of the cases that have been reported to date will help physicians appropriately diagnose this tumor, and a careful review of similar cases will help clarify the mechanisms underlying the progression of this rare tumor.

The authors state that they have no Conflict of Interest (COI).

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