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Case report

Carcinosarcoma of the gallbladder with chondroid differentiation

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Carcinosarcoma of the gallbladder is an uncommon neoplasm. We herein report the case of a patient with carcinosarcoma of the gallbladder with chondroid differentiation, treated by cholecystectomy with liver segmentectomy and lymph node dissection for a tumor which occupied the entire gallbladder and spread to the liver. Histologically, the tumor contained two distinct components: a mixture of both well and poorly differentiated tubular adenocarcinoma and sarcomatoid tissue with chondroid differentiation. From a review of the literature, it was seen that carcinosarcomas of the gallbladder could be divided into two groups: one group with apparent sarcomatous differentiation, such as chondroid, osteoid, and rhabdomyosarcomatous differentiation, and the other group, of carcinosarcomas with a sarcomatous portion composed of anaplastic spindle cells. Each group had a poor prognosis in spite of surgical resection of tumors. Our patient died of peritoneal dissemination 7 months after surgery.

Key words: carcinosarcoma, gallbladder, chondroid differentiation

Introduction

Carcinosarcomas are rare tumors that are characterized by malignant epithelial and mesenchymal elements. These tumors have been reported in many different organs, including the uterus, lung, esophagus, kidney, and pancreas.[1–5] Carcinosarcomas of the gallbladder are rare, and only 40 reports were published in the world literature prior to this report.[6–45] Here, we present a case of carcinosarcoma of the gallbladder with a chondrosarcomatous component. In addition, we review carcinosarcomas of the gallbladder from the viewpoint of mesenchymal differentiation and prognosis.

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Case report

A 69-year-old woman visited our hospital complaining of epigastralgia. The patient had no history of either abdominal surgery or serious illness. Ultrasonography revealed gallstones. In addition, abdominal computed tomography (CT) revealed a left renal tumor, and she was admitted to the Department of Urology at our hospital. Laboratory data revealed that liver and renal function were normal, but the level of carbohydrate antigen 19-9 (CA 19-9) was elevated (74 IU/ml). Endoscopic retrograde cholangiography resulted in nonvisualization of the gallbladder. Magnetic resonance imaging (MRI) revealed a tumor in the gallbladder (Fig. 1), and re-examination of the enhanced CT revealed an irregular shadow in the liver adjacent to the gallbladder wall. The test results led to a diagnosis of double cancers, of the left kidney and gallbladder. A left renal excision, cholecystectomy with liver segmentectomy (S4a, S5), and lymph node dissection were performed. The gallbladder was filled with a necrotic polypoid mass, and the tumor in the gallbladder had spread to the liver, with several metastases within the resected liver (Fig. 2). Histologically, the tumor contained two distinct components: a mixture of both well and poorly differentiated tubular adenocarcinoma and sarcomatoid tissue with chondroid differentiation (Fig. 3a,b). The sarcomatous component was almost completely located in the part of the tumor that had spread to the liver. Anaplastic spindle cells or other differentiated elements were not observed. The sarcomatous tumor cells blended continuously with the poorly differentiated adenocarcinomatous tumor cells. The results of histochemical and immunohistochemical studies of this tumor, per-

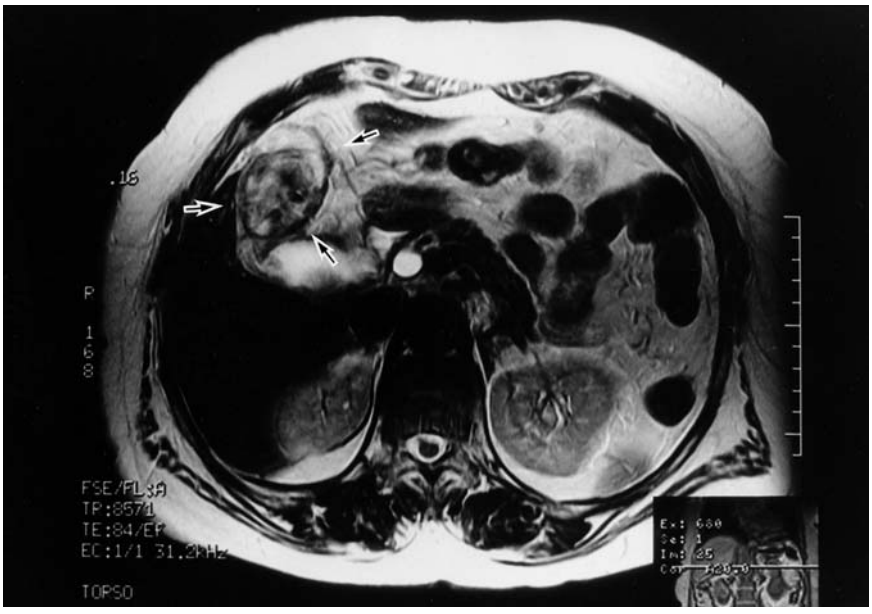

Fig. 1. Magnetic resonance imaging (MRI) revealing a tumor in the gallbladder (*arrows*). *Inset*, axial view, showing an irregular high-intensity mass in the gallbladder

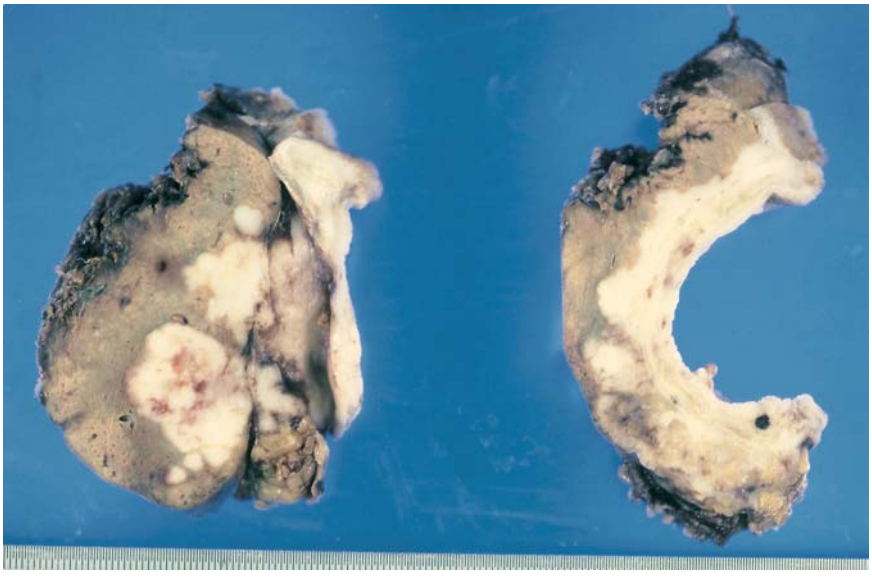

Fig. 2. The cut surface of the resected specimen. The tumor had spread to the liver

formed by a labeled streptavidin-biotin technique, are shown in Table 1. Keratin staining was seen in most of the adenocarcinomatous components. The chondromatous sarcomatoid portions were focally positive for vimentin and keratin (Fig. 4a) and strongly positive for S-100 protein (Fig. 4b) and periodic acid Schiff (PAS). From these results, the tumor was diagnosed as carcinosarcoma with chondroid differentiation. There was a solitary peritoneal dissemination to the lesser omentum, which was histologically diagnosed as metastatic sarcoma with chondroid differentiation. The left renal tumor was diagnosed as clear-cell carcinoma. The patient had an uneventful postoperative course and was treated as an outpatient with tegafur-uracil. However, she was readmitted due to a recurrence of the peritoneal dissemination. Sarcomatous cells were detected in the ascites, and she died 7 months after the surgery.

Discussion

Carcinosarcomas of the gallbladder, which are composed of carcinomatous and sarcomatous portions, are divided into two groups. One group shows apparent sarcomatous differentiation, such as chondroid, osteoid, and rhabdomyosarcomatous differentiation. The other group, which is referred to by various terms, including "sarcomatoid carcinoma", "spindle-cell carcinoma",

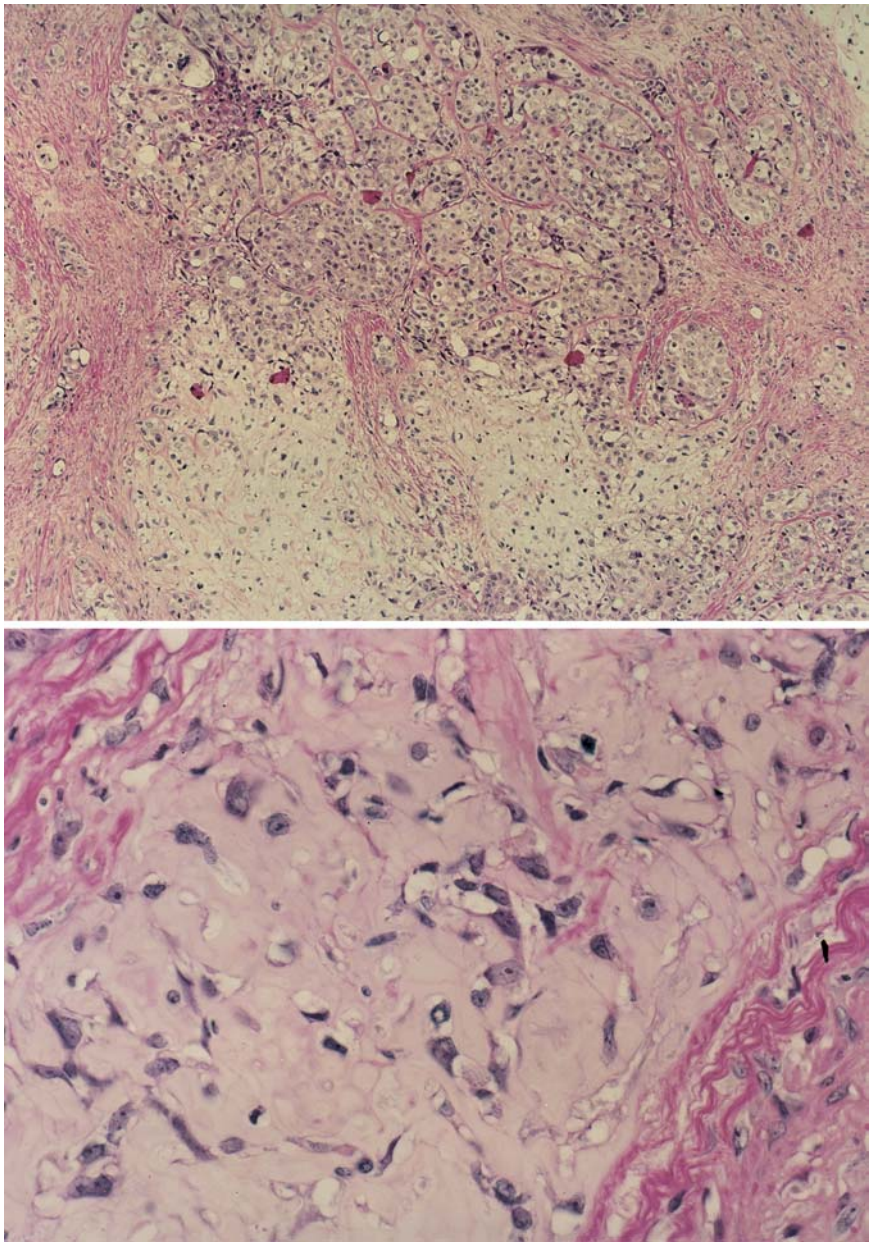

Fig. 3. a Microscopically, the tumor contained two divergent components, of tubular adenocarcinoma and sarcomatoid tissue with chondroid differentiation. Sarcomatous tumor cells blended continuously with the poorly differentiated adenocarcinoma. **b** High-power view of malignant cartilage. **a** H&E, ×50; **b** H&E, ×150

Table 1. Results of staining

Antibodies	Carcinoma cells	Sarcomatous cells
PAS	+	+
S-100 protein (Japan Tanner)	(+) Focally	+
Vimentin (Japan Tanner)	−	(+) Focally
Keratin (A575; Dako)	+	(+) Focally

PAS, Periodic acid Schiff

pseudosarcoma", or "malignant mixed tumors", has a sarcomatous portion composed of anaplastic spindle cells. This confusing terminology is based on the rarity and uncertainty of the histogenesis of the carcinosarcoma of the gallbladder. In order to clarify differences in the terminology and characteristics of cases with various sarcomatous lesions, we reviewed 40 articles mentioning carcinosarcomas of the gallbladder, including our patient's details.

A summary of the articles that classified gallbladder carcinosarcomas based on the dominant portions of mesenchymal differentiation is shown in Table 2. About half of the cases reported as gallbladder carcinosarcoma had apparent sarcomatous differentiation, and the remainder had portions composed of spindle cells. The largest group, with sarcomatous differentiation, revealed chondroid differentiation. In the group with

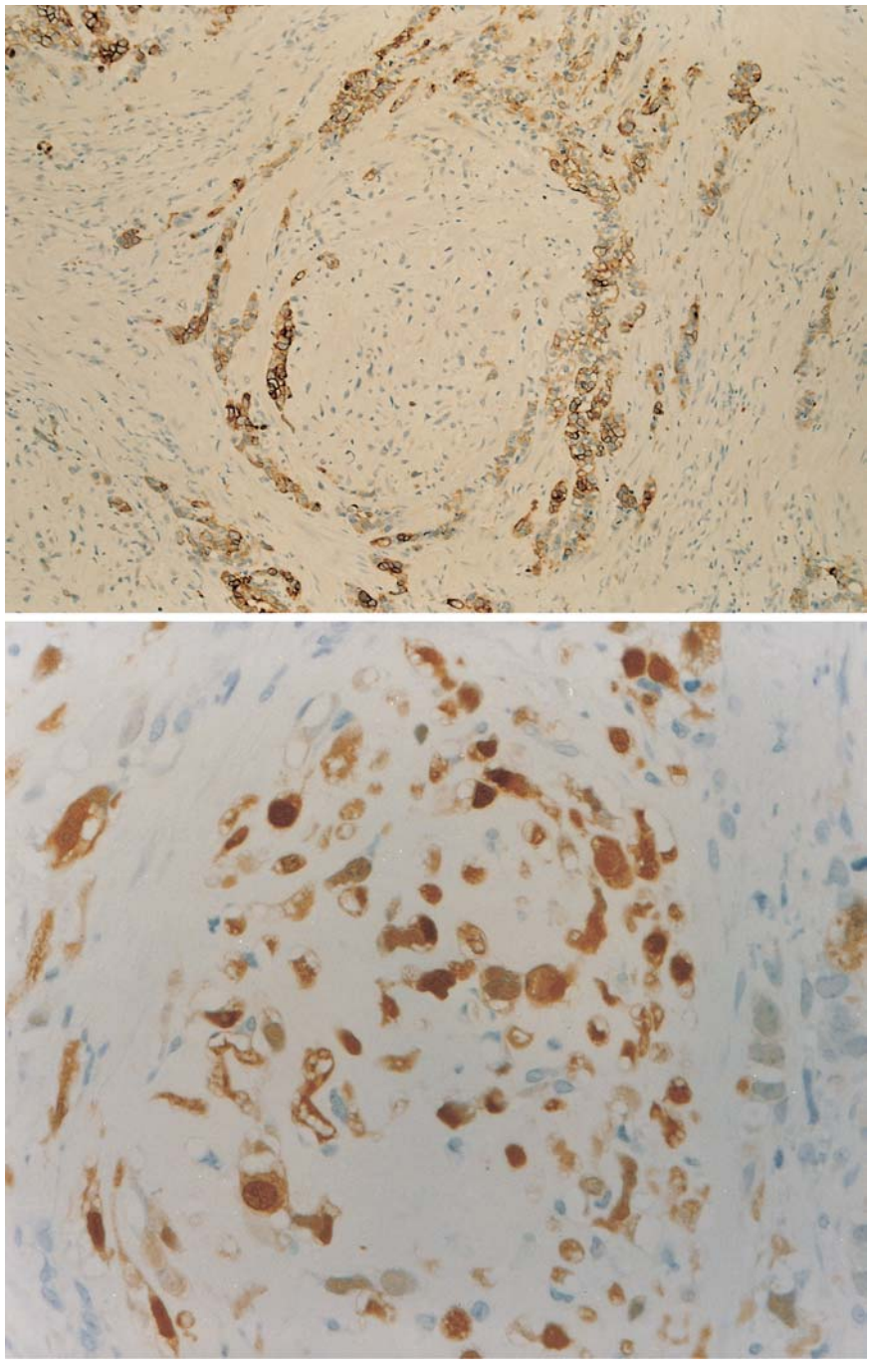

Fig. 4. **a** Immunohistochemical staining shows that the chondromatous sarcomatoid portions are focally positive for keratin and **b** strongly positive for S-100 **a** $\times 50$; **b** $\times 100$

apparent sarcomatous differentiation, there were some cases that included several differentiated cell types in one tumor. In particular, three of five cases with rhabdomyosarcomatous differentiation also possessed various other differentiated elements, including chondroid and osteoid differentiation. The mean ages and male-to-female ratios of the patients did not differ significantly between the groups (Mann-Whitney U-test). Follow-up data were reported in 10 patients with chondroid differentiation, 5 with osteoid differentiation, 3 with rhabdomyosarcomatous differentiation, and 18 with spindle-cell carcinoma. There was no significant difference in prognosis among any of these groups (Kaplan-Meier method with generalized Wilcoxon test). In only 8 patients were recurrent forms reported after surgery.[26,29,30,33–35,38] Liver metastasis was reported in 3 patients, peritoneal dissemination in 1 patient, and local recurrence in 2 patients. In addition, liver, peritoneal, and lymph-node recurrence was reported in 1 patient. The prognosis of gallbladder carcinosarcoma was

Table 2. Mesenchymal cell characteristics of carcinosarcoma of the gallbladder: a review of the literature[6–45]

	Mesenchymal elements			
	Chondro-sarcoma	Osteo-sarcoma	Rhabdomyo-sarcoma	Spindle-cell carcinoma
Number of cases[a]	18	9	5	29
Age (mean; years)	70.3	64.4	64.3	68.5
Sex (M/F)	5/13	2/7	1/4	5/24
Median postoperative survival (months)[b]	4	4	NC	6

NC, Median survival could not be calculated
[a]Repetition exists
[b]Restricted to cases mentioned in the follow-up data

very poor in every histologically differentiated type, and our patient died 7 months after surgery, from peritoneal dissemination.

The histogenesis of carcinosarcoma of the gallbladder is unclear. The tumor in our patient was composed of both adenocarcinomatous and sarcomatous elements with chondroid differentiation. The sarcomatous elements existed adjacent to the carcinomatous elements, and blended with them. Moreover, the sarcomatous cells were focally positive for keratin, an epithelial marker. From the histologic findings, it is possible that the sarcomatous element arose from invading carcinomatous elements. However, the histogenesis of this tumor is still difficult to determine, as is the histogenesis of carcinosarcomas of other organs. Thompson et al.[46] mentioned that the carcinomatous and sarcomatous components may be monoclonal in origin and derived from a single stem cell. Genetic analysis is one possible solution to this problem, as reported in esophageal carcinosarcoma.[3]

The only recognized treatment for gallbladder carcinosarcoma is surgery, and there were no reports of effective chemotherapy or radiotherapy for this tumor. However, the preoperative diagnosis of this tumor was often gallbladder cancer, and in spite of aggressive surgical resection of gallbladder carcinosarcoma, the prognosis of this tumor was very poor. Although, in gallbladder cancers, T or N-stage are important prognostic factors,[47] we have yet to clearly determine prognostic factors in gallbladder carcinosarcoma. In this study, we examined the mesenchymal differentiation of these tumors, which has been mentioned in most reports on gallbladder carcinosarcoma; however, each group had a poor prognosis, possibly because reported numbers of recurrent cases are small, thus making the evaluation of prognostic factors difficult. Moreover, there have been no previous reports showing early lesions or significant prognostic factors of gallbladder carcinosarcoma. Because the sarcomatous component is often recognized in the invasive area, as in our patient, the detection of early lesions of gallbladder carcinosarcoma may be difficult. The accumulation of more clinicopathological data and further examinations are necessary to analyze prognostic indicators and the histogenesis of gallbladder carcinosarcoma.

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