

Case Report

Carcinosarcoma of the gallbladder: a case report and review of the literature

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Abstract: Carcinosarcoma of the gallbladder is a rare malignancy characterized by malignant epithelial and mesenchymal components. The disease usually presents at an advanced stage, and as a result, curative resection is uncommon. This report describes a case that underwent curative resection. We herein declare the case of a patient in a 62-year-old male, with carcinosarcoma of the gallbladder with chondroid differentiation. The patient is treated by a simple cholecystectomy, a wedge resection of the underlying liver tissue and the pericholedochal lymph nodes for a tumor which occupied the entire gallbladder. Histologically, the epithelial component of the tumor was composed of adenocarcinoma and the mesenchymal component was composed of fibrosarcoma. The tumor was identified as extend to the serosa tissue and to have metastasized to no lymph node. The prognosis of carcinosarcoma of the gallbladder remains poor despite curative resection, and thus, the authors recommend that effort should be made to improve surgical outcomes. The patient survived 13 months and is still alive today.

Keywords: Gallbladder, carcinoma, carcinosarcoma, curative treatment, prognosis

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 [1-3]. Carcinosarcomas of the gallbladder are uncommon. Up to now, < 100 cases have been reported in the English literature. The invasive nature and aggressive biology of carcinosarcoma of gallbladder adequately explains the limited number of respectable cases. Here, we report a case of carcinosarcoma of gallbladder treated by curative radical cholecystectomy.

Case report

A 62-year-old man, with the complaints of intervallic pain before admission, presented with a 5 months of abdominal pain in the upper right quadrant. There was not any history of fever, vomiting, anorexia or weight loss. The patient reported a past medical history of chronic cho-

lecystitis, hypertension and diabetes mellitus. A physical examination illustrated tenderness in the right upper quadrant of the abdomen. A laboratory analysis revealed haemoglobin of 98 g/L, a normal leukocyte count. The tumor marker, serum carcinoembryonic antigen, carbohydrate antigen 19-9 and α -fetoprotein (AFP) levels were normal. Liver function tests revealed that total cholesterol levels were increased to 5.22 mmol/L. Abdominal computed tomography (CT) revealed a intraluminal polypoid mass with no demonstrable lymph nodes in the pericholecystic and upper abdominal regions (**Figure 1**), and magnetic resonance imaging (MRI) showed irregular wall thickening with enhancement of the fundus of the gallbladder (**Figure 2**). The preliminary diagnosis was gallbladder cancer. During the surgery, the frozen examination revealed that it was a malignant mesenchymal tumor. A simple cholecystectomy, with a wedge resection of the underlying liver tissue and the pericholedochal lymph nodes were performed. The specimens were sent for histopathology. The macroscopic examination of the specimen showed a 5 × 4 cm



Figure 1. Abdomen computed tomography showed an intraluminal polypoid masses possible gallbladder cancer.

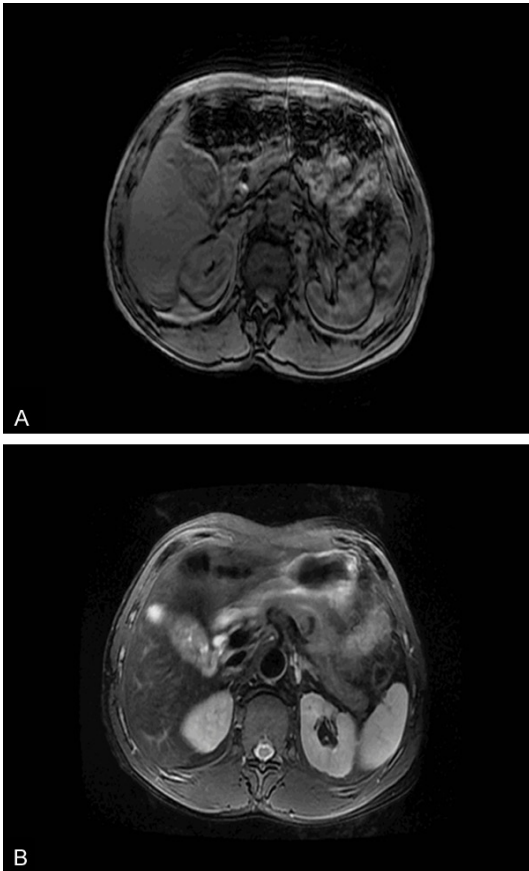


Figure 2. The abdominal magnetic resonance imaging (MRI) showed irregular wall thickening with enhancement of the body of the gallbladder (A, B).

tumor with a polypoid structure, which originated from the body of the gallbladder and filled the entire gallbladder lumen. The tumor was a

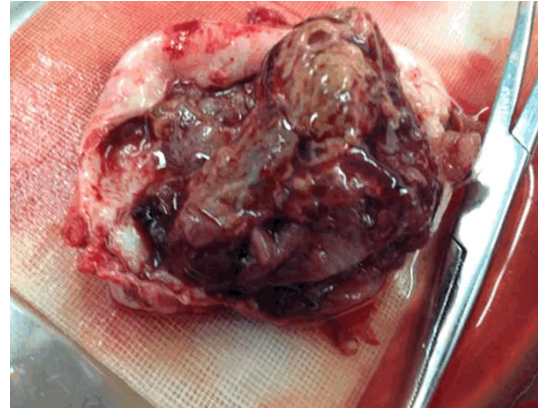


Figure 3. The gross examination of carcinosarcoma of the gallbladder revealed a 5 × 4 cm tumor with a polypoid structure, which originated from the body of the gallbladder and filled the entire gallbladder lumen. The tumor was a solid mass with hemorrhagic and necrotic foci.

solid mass with hemorrhagic and necrotic foci (**Figure 3**). Histologically, the tumor was formed of two distinct components, namely moderately-differentiated tubular adenocarcinoma and sarcomatous tissue with fibrosarcoma differentiation (**Figure 4A** and **4B**). An immunohistochemical examination demonstrated positive staining for cytokeratin and epithelial membrane antigen (EMA) in the epithelial areas (**Figure 5A, 5B**), vimentin in the mesenchymal component (**Figure 5C**). Staining for smooth muscle actin (SMA) and S-100 was negative. This gallbladder carcinoma was classified as stage II (T2N0M0) using the classification of the International Union Against Cancer (UICC). The patient survived 13 months and is still alive today.

Discussion

The first case of a carcinosarcoma of the gallbladder was reported by Landsteiner in 1907 [4]. Up to now, < 100 cases have been reported in the English literature. Carcinosarcomas of the gallbladder consist of both epithelial and mesenchymal components. The diagnosis requires the presence the two histological components. The epithelial component usually consists of adenocarcinoma, although an element of squamous cell carcinoma is also occasionally observed. The mesenchymal component typically consists of undifferentiated spindle or satellite cells, and is occasionally accompanied by various proportions of heterogenous ele-

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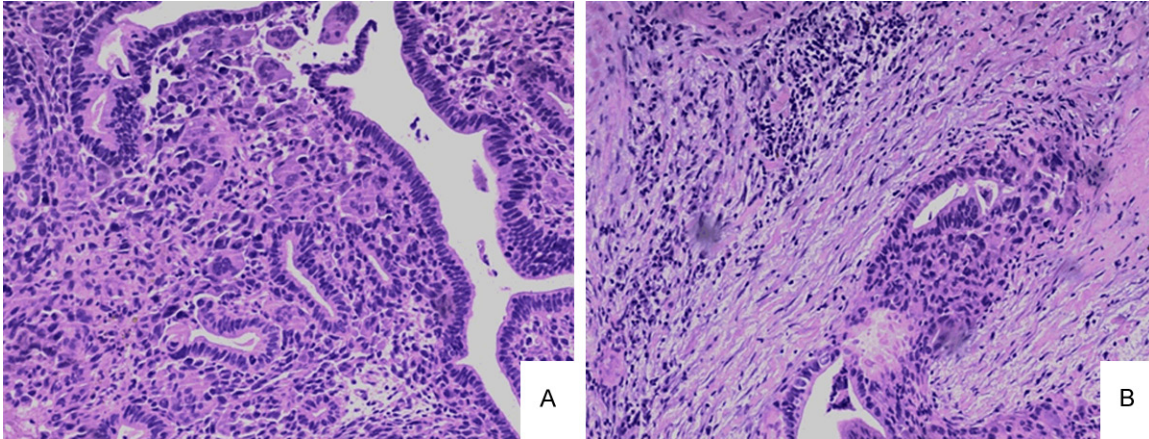


Figure 4. Histologically, the tumor contains two distinct components: a well to moderately differentiated adenocarcinoma (A) and fibroid differentiated sarcomatous tissue (B) (H & E stain, original magnifications: 100 ×).

ments, including chondrosarcoma, osteosarcoma, rhabdomyosarcoma and leiomyosarcoma [5]. Zhang et al [6] reported that adenocarcinoma was the most common epithelial component (79.2%) while squamous cell carcinoma was the least common (9.4%). Spindle cell type was the most common mesenchymal component (44.6%) when compared with osteoid, which was the least common (5.4%). In the case presented, the epithelial component of the tumor was composed of adenocarcinoma and the mesenchymal component was composed of fibrosarcoma. An immunohistochemical examination demonstrated that the epithelial component was positive for cytokeratin, while the mesenchymal component was positive for vimentin.

Although recent studies suggest some causative factors, such as multistep genetic alterations, the precise mechanisms of gallbladder carcinogenesis have not been clearly elucidated. At present, two opposing theories have been hypothesized to account for the origin of these morphologically diverse tumors. The multiclonal theory regards a carcinosarcoma as a collision tumor composed of the derivatives of two or more stem cells of separate epithelial and mesenchymal origin. The monoclonal theory proposes that carcinomatous and sarcomatous elements are derived from a single pluripotential stem cell that subsequently develops divergent differentiation along separate epithelial and mesenchymal pathways [7]. Dacic et al [8] found identical allelic losses shared by each tumor component, without discordant losses.

This was consistent with the hypothesis that the carcinomatous and sarcomatous components of this neoplasm were derived from a single pluripotential stem cell and that the tumor was monoclonal.

The symptoms and signs of gallbladder carcinosarcoma are non-specific. Representative clinical symptoms include right upper abdominal pain and masses, loss of appetite, weight loss, general fatigue, jaundice, and vomiting. In addition, 66.7%-83% [9, 10] of the cases presented with simultaneous cholecystolithiasis.

Zhang et al [6] reported that tumors which were smaller than 5 cm had a longer survival and that therefore, the tumor size should be considered as a major component in the future staging system. They also indicated that the presence of gallstones, epithelial and mesenchymal component types, age and sex were of little prognostic value. The most common treatments are surgery. There is no successful treatment reported with radiotherapy or chemotherapy [11].

The prognosis of this disease is normally poor. Most cases present with locally advanced disease. Liver metastasis and peritoneal dissemination are widespread in these cases. Adrenal glands, pancreas, diaphragm, and lower thoracic vertebrae are the other metastatic sites reported in the literature. Regional, retroperitoneal, and para-aortic lymph nodes may be involved. The mean survival time after diagnosis is usually only a few months [12-14]. We

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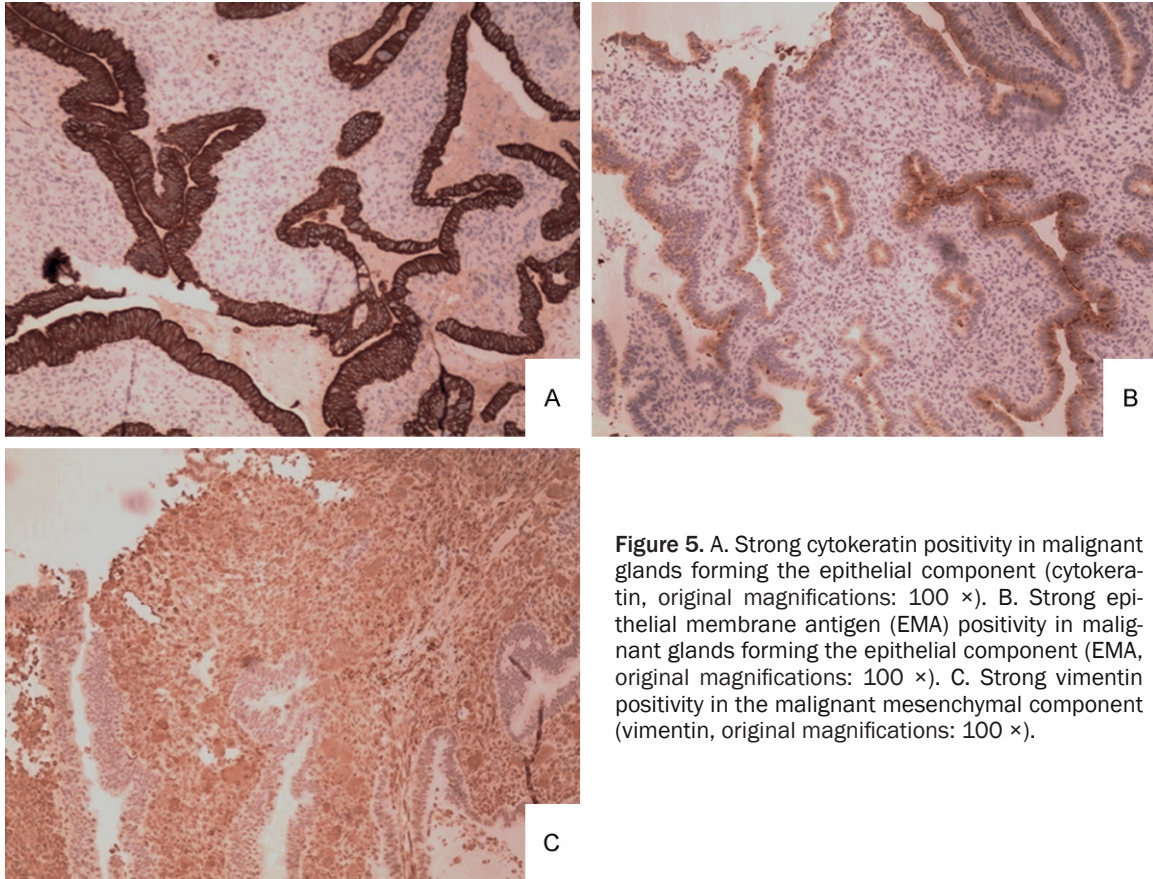


Figure 5. A. Strong cyokeratin positivity in malignant glands forming the epithelial component (cytokeratin, original magnifications: 100 ×). B. Strong epithelial membrane antigen (EMA) positivity in malignant glands forming the epithelial component (EMA, original magnifications: 100 ×). C. Strong vimentin positivity in the malignant mesenchymal component (vimentin, original magnifications: 100 ×).

Table 1. Twenty reported cases of surgical resection for carcinosarcoma of the gall bladder

Author	Year	Age (yr)	Sex	Pistion	Stone	Size (cm)	Depth	Stage	Survival (mo)
Mansori et al [15]	1980	81	M	Body	-	15	liver	IVa	1.5
Von Kuster et al [16]	1982	77	F	Fundus	-	3	mp	II	31 ¹
Inoshita et al [17]	1986	53	M	Neck	-	11	bd	IVa	17
Lumsden et al [18]	1988	81	F	Neck	-	5	mp	II	12 ¹
Ishihara et al [19]	1990	58	F	Fundus	-	8	mp	II	7 ¹
Fagot et al [20]	1994	83	F	Fundus	+	4.5	mp	II	12 ¹
Eriguchi et al [21]	1999	65	F	ND	+	10	mp	II	16 ¹
Ajiki et al [22]	2002	69	F	Body	+	6	liver	IVa	7
Kim et al [23]	2003	61	F	Neck	-	4.5	si	IVa	2 ¹
Sodergren et al [11]	2005	68	F	Neck	-	9	bd	IVa	5
Kubota et al [24]	2006	72	M	Body	-	7	liver, colon	IVa	8
Uzun et al [25]	2009	70	M	Fundus	-	10	mp	II	54 ¹
Shimada et al [26]	2009	69	M	Body	+	9	si	II	6 ¹
Okabayashi et al [27]	2009	72	F	Body	-	2.5	mp	II	60 ¹
Park et al [28]	2012	77	M	Fundus	-	8	mp	III	2.5
Kim et al [29]	2012	77	F	Fundus	-	6.5	ND	II	3 ¹
		81	M	Fundus	-	2	liver	III	4
Parreira et al [30]	2012	59	F	ND	-	5	ND	ND	6
Khanna et al [31]	2013	45	F	body	-	6	mp	II	6 ¹
Wang et al [32]	2013	68	F	Fundus	-	10	ND	II	ND
Present case	2015	62	M	Body	-	5	si	II	13 ¹

¹Alive patients; si: Serosal invasion; bd: Bile duct; mp: Muscularis propria; ND: Notdescribed; Stage: Classification according to UICC (International Union Against Cancer).

analyzed data from 20 patients recorded in the literature from 1980 to 2013 who underwent surgical management for carcinosarcoma of the gall bladder (**Table 1**). These patients consisted of 8 male and 12 female with a mean age of 65.2 years (range 45 to 83 years). Zhang et al [6] reported that for 68 patients with carcinosarcoma of the gallbladder, the mean survival time is 17.5 months, and the 1-year survival rate and 5-year survival rate are (19 ± 5)% and (16 ± 5)% respectively. As reported by Uzun MA, the longest survival time was 54 months [15]. In that case, a polypoid tumor of 2 cm in size protruded into the gallbladder lumen. A microscopic study showed that the tumor had infiltrated the surrounding connective and adipose tissue overlapping its primary site, but had not perforated the serosa nor invaded the liver. The patient was handled by a radical cholecystectomy and remained healthy for 54 months.

Disclosure of conflict of interest

None.

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