

BRIEF ARTICLES

## Surgical management of gallbladder sarcomatoid carcinoma

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### Abstract

**AIM:** To study the behavior as well as optimal treatment of gallbladder sarcomatoid carcinoma, we reviewed the results of treatment of gallbladder sarcomatoid carcinoma from Chang Gung Memorial Hospital.

**METHODS:** From 1987 to 2005, six patients were diagnosed with gallbladder sarcomatoid carcinoma and treated at our institution. Tumor staging was based on 2002 revised tumor-node-metastasis (TNM) staging for gall bladder cancer from the American Joint Committee on Cancer. The clinical presentation, laboratory data and preoperative workup were reviewed retrospectively.

**RESULTS:** Five patients were female and one was male. The age ranged from 51 to 66 years (median, 58 years). Surgical procedures included three curative resections, two palliative resections and one biopsy. There were two surgical complications (33.3%) and one case of surgical mortality (16.7%). The follow-up time ranged from 30 d to 5 mo. The median survival was 2.5 mo. The prognosis was extremely poor, even after curative resection and postoperative chemotherapy.

**CONCLUSION:** The prognosis of gallbladder sarcomatoid carcinoma was not dependent on TNM stage and was always dismal. The clinicopathological features were different from those of gall bladder cancer.

### INTRODUCTION

Primary gallbladder carcinoma is the fifth most common gastrointestinal tract malignancy and the most common malignancy in the biliary tract<sup>[1,2]</sup>. Despite improvements in imaging modalities and therapeutic facilities, the prognosis of gallbladder carcinoma is still poor. Tumors that possess epithelial and mesenchymal components are so-called sarcomatoid carcinomas. Gallbladder sarcomatoid carcinoma is a rare and atypical subset of gallbladder carcinoma, and only 44 cases have been described in the English-language literature worldwide<sup>[3-18]</sup>. All of these have been case reports and have little information about the clinical behavior and optimal treatment of these tumors. In order to define the behavior and prognosis of gallbladder sarcomatoid carcinoma, we reviewed retrospectively the data of six patients from Chang Gung Memorial Hospital (Taoyuan, Taiwan).

### MATERIALS AND METHODS

From 1987 to 2005, six patients were diagnosed with gallbladder sarcomatoid carcinoma and treated at our institution. The histology was confirmed in all patients by tissues taken from either surgical or biopsy specimens. In total, there were 141 patients diagnosed with gallbladder cancer who received surgical treatment during this period. Among them were 124 with adenocarcinoma (87.9%), eight with adenosquamous carcinoma (5.7%), six with sarcomatoid carcinoma (4.3%), two with squamous cell carcinoma (1.4%), and

Table 1 Clinical features, operative methods and survival of six patients with gallbladder sarcomatoid carcinoma

	Age/sex	Jaundice	Operative method	Pathological staging	Chemotherapy	Survival
Case 1	51/F	No	Curative resection	T3N1M0 (II b)	Yes	3 mo
Case 2	66/M	Yes	Palliative	T4NxM0 (IV)	No	2 mo
Case 3	60/F	No	Palliative resection	T3N0M0 (II a)	No	2 mo
Case 4	65/F	No	Curative resection	T3N1M0 (II b)	No	20 d <sup>1</sup>
Case 5	56/F	No	Curative resection	T2N1M0 (II b)	Yes	5 mo
Case 6	53/F	Yes	Palliative resection	T3N1M1 (IV)	Yes	5 mo

F: Female; M: Male; <sup>1</sup>Surgical mortality.

one with neuroendocrine carcinoma (0.7%). Tumor staging was based on the 2002 revised tumor-node-metastasis (TNM) staging for gallbladder cancer from the American Joint Committee on Cancer (AJCC)<sup>[19]</sup>. The clinical presentation, laboratory data and preoperative workup, including abdominal sonography, computerized tomography (CT), magnetic resonance imaging (MRI) and endoscopic retrograde cholangiopancreatography (ERCP) were reviewed retrospectively. Extensive surgery was defined as cholecystectomy combined with one or more of the following procedures: liver resection of the involved gallbladder fossa, common hepatic artery lymph nodes and hepatic proper artery lymph nodes, and resection of the extrahepatic bile duct, or other organs invaded by tumor directly. Cholecystectomy was defined as cholecystectomy alone without other extensive surgical procedures. Palliative surgery included cholecystectomy, drainage of biliary obstruction or biopsy of tumor only.

## RESULTS

Five patients were female and one was male. The age ranged from 51 to 66 years (median, 58 years). Table 1 displays the clinical features, operative methods and survival of the six patients with gallbladder sarcomatoid carcinoma. Abdominal pain (83%) was the most frequent complaint in these patients, and two (33.3%) were found to have jaundice. No patient had anemia. Except in patients with jaundice, the liver function tests were all normal. Carcinoembryonic antigen (CEA) level was elevated in one patient and carbohydrate antigen 19-9 (CA19-9) level was elevated in two patients. Five patients were diagnosed with gallbladder cancer preoperatively and one was diagnosed with gallstones with chronic cholecystitis. All six patients underwent surgical procedures, including three curative resections and three palliative procedures. Four patients underwent extensive surgery, including three cholecystectomies with partial resection of the gallbladder bed of the liver, and one cholecystectomy with right hemicolectomy for direct tumor invasion of the hepatic flexure of the colon. One patient underwent laparoscopic cholecystectomy only, after preoperative diagnosis with gallstones and chronic cholecystitis. The remaining patient received laparotomy and biopsy of the tumor only as a result of peritoneal seeding during operation. There were two surgical complications (33.3%) including one

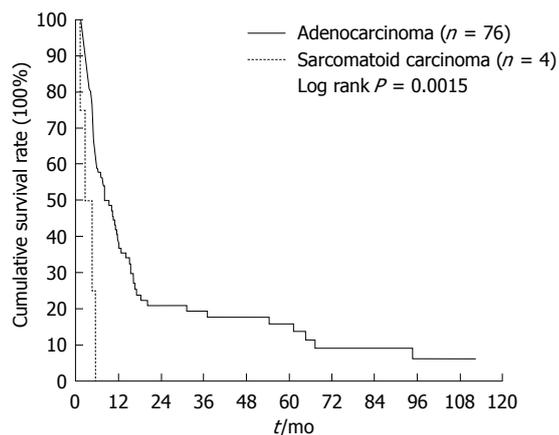
postoperative hematoma and one case of postoperative sepsis caused by bile leakage. One case of surgical mortality (16.7%) was encountered after bile leakage. Three patients received fluorouracil-based chemotherapy postoperatively. Pathological staging was one stage II a, three II b, and two stage IV.

The follow-up time ranged from 30 d to 5 mo. Except for the case of surgical mortality, all patients died within 5 mo from tumor recurrence or disease progression. The median survival was 2.5 mo. The prognosis was extremely poor even, after curative resection with or without postoperative chemotherapy.

## DISCUSSION

The most common histological type of gallbladder cancer is adenocarcinoma, and sarcomatoid carcinoma is extremely rare<sup>[2-18]</sup>. Chao *et al.*<sup>[11]</sup> have reported the incidence of sarcomatoid carcinoma from gallbladder cancer as 4.1%. It has been described that sarcomatoid carcinoma arises from totipotent stromal stem cells<sup>[8]</sup> and is composed of epithelial and mesenchymal components that contain undifferentiated spindle or stellate cells<sup>[3,4,6,8,9,11,14-18]</sup>. The cancer was first reported by Landsteiner in 1907, and until now, only 44 cases have been reported in the English-language literature, with an age range of 45-91 years<sup>[2-18]</sup>. However, in our review, patient age was limited to the sixth and seventh decades of life. At our institution, the female-to-male ratio for gallbladder cancer was about 2:1, which was similar to the ratio for gallbladder sarcomatoid carcinoma reported in the literature<sup>[1,2,4]</sup>. In the present study, the female-to-male ratio was 5:1.

Patients with gallbladder sarcomatoid carcinoma usually present with abdominal pain, jaundice, nausea, and poor oral intake, and some may present with a palpable abdominal mass and weight loss. Symptoms may persist from several days to years. Liver function tests are normal, except in patients with obstructive jaundice caused by tumor invasion of the biliary tract<sup>[3-18]</sup>. Most cases have been reported to have normal CEA and CA19-9 levels, and in our series, the CEA level was elevated in one case and CA19-9 level was elevated in two cases. Mass lesions can be identified by abdominal sonography and CT. Sonographic studies have shown an echogenic mass, with or without areas of necrosis occupying the gallbladder lumen, and the wall may be diffuse, localized or irregular. The



**Figure 1** Survival curve of adenocarcinoma and sarcomatoid carcinoma of the gallbladder (excluding stage I, biopsy only and surgical mortality patients).

characteristics of gallbladder sarcomatoid carcinoma are similar to those of adenocarcinoma of the gallbladder, and it is difficult to distinguish between these two tumors. However, if there is speckled calcification within the tumor upon CT, gallbladder carcinoma with calcification, calcified gallstones, porcelain gallbladder and ossifying sarcomatoid carcinoma should be the in differential diagnosis of the tumor<sup>[6,13,16]</sup>. Other associated findings, including gallstones, liver invasion or metastasis, retroperitoneal organ invasion or lymph node enlargement along the hepatoduodenal ligament, can be identified by CT. In our series, five patients (83.3%) were diagnosed preoperatively with gallbladder cancer, and the remaining one was diagnosed with a 1.5-cm gallstone.

T and N stages are important prognostic factors in gallbladder cancer<sup>[20]</sup>. However, there are no prognostic factors determined in gallbladder sarcomatoid carcinoma. Surgery is suggested as the only recognized treatment for gallbladder sarcomatoid carcinoma; either radiotherapy or chemotherapy has no benefit on survival<sup>[8]</sup>. However, even after curative extensive surgery with combined gallbladder/liver bed resection or combined resection of involved organs, many patients die shortly after surgery from recurrence or metastasis. After excluding stage I gallbladder adenocarcinoma, biopsy only and surgical mortality patients, the survival rate for gallbladder sarcomatoid carcinoma and stage II-IV gallbladder adenocarcinoma is shown in Figure 1. One-year survival rate for gallbladder sarcomatoid carcinoma *vs* adenocarcinoma was 0% *vs* 38.2%  $\pm$  5.57% ( $\chi^2$ ,  $P < 0.05$ ). Among the 44 cases reviewed in the literature, the mean survival time was 2 mo and only two patients have survived for  $> 1$  year<sup>[11,12]</sup>. In our series, the median survival time was 2.5 mo and the longest survival was only 5 mo. Apart from the one case of surgical mortality, all patients died from cancer recurrence or disease progression.

In conclusion, better survival of gallbladder cancer was seen in patients with early-stage disease. However, the prognosis of gallbladder sarcomatoid carcinoma was not dependent on TNM stage, and was always dismal. The

clinicopathological features were different from those of gallbladder cancer, and will be necessary to accumulate additional reports of such patients to clarify these issues.

## COMMENTS

### Background

Gallbladder cancer is the most common malignancy in the biliary tract. Sarcomatoid carcinoma of the gallbladder is a rare and atypical subset of gallbladder carcinoma, and only 44 cases have been described in the English-language literature worldwide.

### Research frontiers

Little information about the clinical behavior and optimal treatment of these tumors has been reported. In this study, the authors retrospectively reviewed clinical presentation and treatment results of six patients from Chang Gung Memorial Hospital Taoyuan, Taiwan.

### Innovations and breakthroughs

Only case reports have been described before. This is believed to be the first series of patients diagnosed with gallbladder sarcomatoid carcinoma in a single institution.

### Applications

Tumor staging was based on the 2002 revised tumor-node-metastasis (TNM) staging for gallbladder cancer from the American Joint Committee on Cancer. The clinical presentation, laboratory data and preoperative imaging workup were reviewed. Surgical procedures, postoperative chemotherapy and survival rate after treatment were discussed by the authors.

### Terminology

Sarcomatoid carcinoma arises from totipotent stromal stem cells, and is composed of epithelial and mesenchymal components that contain undifferentiated spindle or stellate cells.

### Peer review

The authors emphasized that the prognosis of gallbladder sarcomatoid carcinoma was not dependent on TNM stage, and was always dismal. The clinicopathological features are different from those of gallbladder adenocarcinoma.

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