Angiosarcoma of the gallbladder: Case report and review of the literature

Alexandre N Odashiro MD1, Patricia Rusa Pereira MD1, Luciana N Odashiro Miiji MD1, Gia-Khanh Nguyen MD2

A 62-year-old white woman with an unremarkable past medical history presented with acute cholecystitis. A cholecystectomy was performed, revealing an acute hemorrhagic and chronic cholecystitis associated with cholelithiasis. Two months after the operation, the patient developed a massive hemoperitoneum and died by hypovolemic shock. At autopsy, an angiosarcoma measuring 5 cm in diameter was found in the liver, at the site of the gallbladder fossa. There were multiple hepatic, splenic, ovarian and peritoneal metastases and a massive hemoperitoneum consisting of 8 L of blood and blood clots. Review of the tissue sections from the patient’s gallbladder confirmed the presence of an acute hemorrhagic and chronic cholecystitis and also revealed residual foci of an angiosarcoma. A review of eight previously reported cases of gallbladder angiosarcoma is also presented.

Key Words: Angiosarcoma; Gallbladder

Gallbladder angiosarcoma (GA) is a very rare neoplasm with only eight reported cases in the literature (1-7). The present paper documents a case of GA that initially manifested clinically as acute cholecystitis. A brief literature review of this unusual neoplasm is also presented.

CASE PRESENTATION

A 62-year-old white woman with an unremarkable past medical history was admitted to the University of Alberta Hospital, Edmonton, Alberta because of sudden-onset epigastric pain associated with nausea and vomiting. She had no history of exposure to vinyl chloride, Thorotrast or arsenical compounds. Physical examination, routine blood work and diagnostic imaging suggested an acute cholecystitis and she underwent a cholecystectomy. At laparotomy, her gallbladder was found to be enlarged and diffusely hemorrhagic. The liver was of normal size and shape and showed a smooth capsule. It had a normal consistency and no tumour was palpable within the liver. Histological examination of the liver tumour at the gallbladder fossa revealed a malignant neoplasm that consisted of cuboidal and spindle-shaped cells forming lumens containing blood. Mitotic figures were abundant. The histological pattern of the lesion was in keeping with a predominantly epithelial angiosarcoma (Figure 1). The other tumour nodules in the liver, spleen, ovaries and peritoneal lesions were histologically similar to the mass at the former gallbladder fossa. An exploratory laparotomy was performed and revealed a massive hemoperitoneum consisting of approximately 12 L of blood and blood clots. There were several hemorrhagic nodular lesions on the parietal peritoneum and visceral serosa, ranging from 1 cm to 3 cm in diameter. The liver showed a hemorrhagic mass at the gallbladder fossa, measuring 5 cm in diameter. A few peritoneal lesions were excised for histological examination and a massive blood transfusion was instituted. The patient expired two days postsurgery due to hypovolemic shock, and a complete autopsy was performed.

At autopsy, 8 L of liquid blood and blood clots were found in the abdominal cavity, as well as a peritoneal carcinomatosis. There were multiple hemorrhagic tumour nodules on the peritoneal surface and in the liver, spleen and ovaries. The liver showed a 5 cm tumour at the gallbladder fossa and a few tumour nodules that measured from 1 cm to 2 cm in diameter, located 3 cm to 5 cm from the tumour at the gallbladder fossa. Histological examination of the liver tumour at the gallbladder fossa revealed a malignant neoplasm that consisted of cuboidal and spindle-shaped cells forming lumens containing blood. Mitotic figures were abundant. The histological pattern of the lesion was in keeping with a predominantly epithelial angiosarcoma (Figure 1). The other tumour nodules in the liver, spleen, ovaries and peritoneal lesions were histologically similar to the
angiosarcoma located at the gallbladder fossa. The liver tissue between the tumour nodules was histologically normal.

A review of the tissue sections from the surgically removed gallbladder confirmed the presence of an acute hemorrhagic and chronic cholecystitis. In addition, it showed an intraluminal mural hematoma with early organization. In some non-necrotic areas, the fibrotic gallbladder wall showed a residual angiosarcoma consisting of irregular vascular spaces lined by spindle-shaped endothelial cells with conspicuous nucleoli. In one small area, the tumour cells were cuboidal in shape, as seen in the above-described metastatic tumour nodules. The angiosarcoma was limited to the gallbladder wall and was not present on the surgical resection margins and serosa of the resected gallbladder. The rim of the liver tissue that had been resected with the gallbladder was histologically unremarkable. The presence of an organized mural thrombus suggested that the hemorrhagic acute cholecystitis had occurred a few days before the patient's presentation at the hospital emergency room. Gallbladder tissue sections 5 µm thick and one peritoneal angiosarcoma nodule were stained with cytokeratin AE1/AE3 and von Willebrand factor antibodies (Dako, USA), using the avidin-biotin complex technique. The tumour cell cytoplasm stained strongly positive with von Willebrand factor antibody only, further confirming the histological diagnosis of angiosarcoma. The original pathologist interpreted the vascular lesion in the gallbladder as reactive and proliferated capillary vessels in an acute hemorrhagic and chronic cholecystitis.

**DISCUSSION**

The pathological pattern of the liver in the present case indicated that the 5 cm liver tumour at the gallbladder fossa was a recurrent GA and that the other liver nodular lesions were metastatic in nature. The patient did not appear to have a hepatic angiosarcoma with gallbladder invasion; a situation in which the liver is usually diffusely and extensively involved by the tumour (8). Furthermore, at the time of cholecystectomy, only two months before the autopsy, the liver was macroscopically unremarkable and the rim of liver tissue removed with the gallbladder was also histologically benign.

GA is an exceedingly rare tumour. A review of the English-language literature revealed only eight cases reported by 1994 (1-7). The clinical data of these eight cases and that of the present case are shown in Table 1. The average age of seven patients with GA, including our patient, was 71.7 years (range 54 to 87 years). Among these patients there were three men and three women (2,4-7), with the sex of one patient unreported (3). Both the age and sex of the two patients cited by Vaittinen (1) were not documented. Four of the patients had abdominal pain localized in the right hypochondrium, suggesting an acute cholecystitis was present (2-4) and a palpable abdominal mass was noted in five patients (2,4,6,7). In five patients, the duration of the abdominal pain varied from three to eight weeks before their GAs were confirmed histologically (2,3,6,7). An abdominal ultrasound confirmed the presence of a gallbladder mass lesion in five patients (2-4,6,7). In four patients, the GA was found at an advanced stage when first detected, with the tumour spreading to adjacent organs and the peritoneum, and in five patients a cholelithiasis was present (2-4,6). In two patients, including the present, the disease appeared to be limited to the gallbladder when diagnosed (7). Two patients survived four and five months after the operation, respectively (3,4). One patient with a squamous cell carcinoma and angiosarcoma limited to the gallbladder was alive with no evidence of tumour recurrence or metastasis five years after his gallbladder surgery (7). In the present case, the disease was rapidly progressive with multiple intra-abdominal metastases, and the patient died two months after cholecystectomy. The case reported by Kumar et al (7) was unusual in terms of

**TABLE 1**

<table>
<thead>
<tr>
<th>Reported cases (reference)</th>
<th>Age/sex</th>
<th>Clinical presentation</th>
<th>Follow-up data (causes of death)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaittinen, 1972 (1)*</td>
<td>NA</td>
<td>NA</td>
<td>Died after 28 days of hospitalization (hepatorenal syndrome, renal failure)</td>
</tr>
<tr>
<td>Rosansky and Mullens, 1982 (2)</td>
<td>59/M</td>
<td>AP + PAM</td>
<td>Died 4 months after cholecystectomy (cause of death not stated)</td>
</tr>
<tr>
<td>Kawai et al, 1989 (3)</td>
<td>73/M</td>
<td>AP + PAM</td>
<td>Died 4 months after cholecystectomy (cause of death not stated)</td>
</tr>
<tr>
<td>Kumar et al, 1989 (4)</td>
<td>56/M</td>
<td>PAM</td>
<td>Died 5 months after cholecystectomy (multiple metastases)</td>
</tr>
<tr>
<td>Hittmair et al, 1991 (5)</td>
<td>87/NA</td>
<td>Fatigue, black stools</td>
<td>Died 4 days after cholecystectomy (cause of death not stated)</td>
</tr>
<tr>
<td>White and Chan, 1994 (6)</td>
<td>81/F</td>
<td>AP + PAM</td>
<td>Died 2 weeks after cholecystectomy (sepsis)</td>
</tr>
<tr>
<td>Kumar et al, 1994 (7)</td>
<td>54/M</td>
<td>PAM</td>
<td>Alive 5 years after cholecystectomy</td>
</tr>
<tr>
<td>Present case</td>
<td>62/F</td>
<td>AP</td>
<td>Died 2 months after cholecystectomy (multiple metastases, massive hemoperitoneum and hypovolemic shock)</td>
</tr>
</tbody>
</table>

*Vaittinen (1) reported two cases of gallbladder angiosarcoma. AP Abdominal pain; F Female; M Male; NA Not available; PAM Palpable abdominal mass
survival because GAs usually pursue a highly aggressive course resulting in the death of the patient within a few months (3-6). We wonder if the patient reported by Kumar et al (7) suffered from a squamous cell carcinoma of the gallbladder associated with pseudoangiomatous change, because abnormal proliferation of capillary blood vessels is not an uncommon finding in carcinomas arising from different anatomical sites (9).

From a pathological point of view, three GAs were of the epithelioid type and the histological subtype of the other five GAs were not reported (1-7). The gallbladder tumour in our patient was an angiosarcoma showing a focal epithelioid pattern and its metastatic deposits were predominantly epithelioid in type. The histological diagnosis of angiosarcoma can be challenging because a well-differentiated tumour may mimic a hemangioma (10) or an organizing hematoma, especially in small biopsy samples. The presence of endothelial cells with nuclear atypia, abundant mitotic figures and necrosis indicate the possibility of a malignant vascular tumour (10).

In cases of epithelioid angiosarcoma, immunostaining with CD31 and von Willebrand factor antibodies is helpful (10) because histologically the tumour may mimic a poorly differentiated carcinoma (6). It is important to note that cells of an epithelioid angiosarcoma express cytokeratin in approximately one-third of patients (10). Electron microscopy may also provide useful information in the diagnosis of epithelioid angiosarcoma, revealing characteristic intracytoplasmic Weibel-Palade bodies (11).

In general, postoperative radiotherapy and adjuvant chemotherapy proved to be beneficial to patients with soft tissue angiosarcoma (10), but the effects of these two therapeutic modalities on GA is unknown. Currently, the only therapeutic option for this rare cancer is a complete surgical resection of a GA that is still limited to the gallbladder. Unfortunately, early diagnosis of this GA is difficult, and in most reported cases (2-6) the tumour was found to be at an advanced stage when detected.

REFERENCES
