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

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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 hypo-volemic 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 her gallbladder revealed an acute hemorrhagic and chronic cholecystitis with cholelithiasis. The patient's postoperative phase was uneventful and she was discharged from the hospital four days after surgery. Two months later, the patient suddenly developed severe abdominal pain and was readmitted to the hospital. Her abdominal computed tomography scan revealed free intraperitoneal blood and a

L'hémangiosarcome de la vésicule biliaire : Un rapport de cas et une analyse bibliographique

Une femme blanche de 62 ans aux antécédents médicaux quelconques s'est présentée avec une cholécystite aiguë. Une cholécystectomie a été exécutée et a révélé une cholécystite hémorragique aiguë et chronique associée à des calculs biliaires. Deux mois après l'opération, la patiente a développé un hémopéritoine massif et est morte d'un choc hypovolémique. À l'autopsie, un hémangiosarcome de 5 cm de diamètre a été découvert dans le foie, au foyer de la fossette cystique. On a découvert de nombreuses métastases hépatiques, spléniques, ovariennes et péritonéales ainsi qu'un hémopéritoine massif composé de 8 L de sang et de caillots sanguins. L'examen des coupes tissulaires de la vésicule biliaire de la patiente a confirmé la présence d'une cholécystite hémorragique aiguë et chronique et révélé des foyers résiduels d'hémangiosarcome. L'analyse de huit cas déjà publiés d'hémangiosarcome de la vésicule biliaire est également présentée.

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

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Figure 1) A Histological section from a metastatic nodule of an angiosarcoma with an epithelioid pattern revealing sheets of cuboidal, pleomorphic cells forming lumens containing red blood cells. An intra-cellular lumen containing a red blood cell is observed (arrow). **B** A smaller component of the tumour consists of irregular vascular spaces lined by prominent, spindle-shaped endothelial cells (hematoxylin and eosin stain, original magnification $\times 400$)

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 μ m 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 (5). 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
Summaries of eight reported cases of gallbladder angiosarcoma and the present case

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

*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).

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