Leiomyosarcoma of the Gallbladder

A Case Report and Review of the Literature

David A. Zeig, Muhammed A. Memon, David R. Kennedy, Suzette A. Woodward and Robert J. Fitzgibbons, Jr

From the Department of Surgery (D. A. Zeig, M. A. Memon, D. Kennedy), Department of Pathology (S. A. Woodward), and the Division of General Surgery (R. J. Fitzgibbons, Jr), Creighton University School of Medicine, Omaha, Nebraska

Correspondence to: Dr Muhammed A. Memon, 228S Maple No. D, Oak Park, IL 60302, USA. Tel/Fax: +1 708 449 2633. E-mail: mmemon@rush.edu

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Primary sarcoma of the gallbladder is an extremely rare neoplasm that was first described in detail by Landsteiner in 1904 (1). In 1982 Willen & Willen (2) published a comprehensive review on primary gallbladder sarcomas and reported a total of 124 cases, 16 of which were reported as leiomyosarcoma. Since then, only a handful of cases of primary gallbladder sarcomas have been reported in the English literature (3–6). We therefore add to this rare type of neoplasm another case report of primary leiomyosarcoma of the gallbladder.

Case report. A 67-year-old Caucasian male was admitted to our surgical service with a history of severe right upper quadrant (RUQ) pain, jaundice and shock. Past history was significant for gallbladder disease (non-functioning gallbladder). Physical examination revealed an acutely ill, deeply jaundiced elderly man with a diffuse tender mass, 7 cm × 7 cm, occupying the whole RUQ. Rectal examination revealed black tarry stools. Examination of other systems failed to reveal any abnormality. Laboratory workup showed a decreased hemoglobin and hematocrit and an elevated bilirubin and alkaline phosphatase confirming the clinical suspicion of obstructive jaundice. Ultrasound scan of the liver revealed a mass in the right lobe of the liver and a liver scan disclosed a 7 cm oval, cold, solid area in the region of the porta hepatis. The diagnosis of hepatobiliary malignancy was entertained and the patient was prepared for exploratory laparotomy.

At laparotomy, a markedly inflamed gallbladder containing multiple stones was found embedded in the omentum and neighboring jejunum. Furthermore, the patient had a mass arising from the porta hepatis, representing either metastasis or an extension of the primary tumor. This was causing external compression of the common hepatic duct leading to a collapsed distal common bile duct. The remaining abdominal organs were normal to palpation. A palliative cholecystectomy and a choledochostomy with insertion of a T-tube were performed.

Postoperatively, the patient's pain and jaundice improved and he was discharged 12 days later to the referring hospital. The patient died 8 days later of advanced metastatic disease.

Histopathogical findings. Macroscopic appearance. The gallbladder measured 9 × 4 × 3 cm and contained numerous, multifaceted calculi. The external surface was irregular with multiple fibrous adhesions and an irregular mass on one side measuring 2 × 2 × 1.5 cm, was present, extending into the lumen. Microscopic examination revealed a malignant mass extending from the gallbladder lumen to the serosa.

Microscopic appearance. There were sheets and solid nests of tumor cells with abundant necrosis and focal areas of acute and chronic inflammation. Some areas had a vague fascicular pattern (Fig. 1A). The cells had moderate pleomorphism, ranging from round to oval nuclei with abundant cytoplasm to areas which had a spindle-like appearance, blunt-ended nuclei and scant cytoplasm (Fig. 1B). The chromatin was irregularly clumped and inconspicuous nucleoli were present. The original cytochemical stains performed included reticulin, trichrome, phosphotungstic acid hematoxylin (PTAH), and mucin. The reticulin stain revealed clumps of tumor cells surrounded by delicate bands of reticulin; trichrome stain showed that the tumor cells were surrounded by interlacing bands of fibrous tissue; PTAH was negative for cross-striations; and mucin was negative. On the basis of these histological examinations, the diagnosis of grade 4 spindle-cell sarcoma, probably of leiomyosarcoma type, was determined and confirmed by an outside consultation.

Immunohistochemical stains. In light of our ability today to give a more definitive classification of sarcomas, immunohistochemical stains were performed on the original paraffin-embedded tissue using the avidin-biotin-peroxidase complex method. Vimentin (DAKO, Santa Barbara, CA) was strongly positive (Fig. 2); alpha smooth muscle actin (Bio Genex, San Ramon, CA) was positive (Fig. 3); and AE1:3 (broad spectrum keratin), (Boehringer Mannheim, Indianapolis, IN) was also positive. The following stains were negative: carcinoembryonic antigen (CEA) (DAKO, Santa Barbara, CA); desmin (DAKO, Santa Barbara, CA); S-100 (Bio Genex, San Ramon, CA); epithelial membrane antigen (EMA), (DAKO, Santa Barbara, CA); and Mak-6 (Triton Diagnostics, Alameda, CA).

Based on the histology and immunohistochemistry, the tumor was designated as a high-grade sarcoma arising within smooth muscle (a high-grade leiomyosarcoma).

Discussion. Primary sarcoma of the gallbladder is a rare entity with an estimated frequency of 1.4/1000 gallbladder malignancies (2). It occurs more frequently in females than in males by a ratio of 5 to 1 (7) The average age of patients with primary gallbladder sarcomas is 56 years, which is considerably less than the average age of 70 years for gallbladder carcinoma (7) Gallstones and chronic inflammatory changes have been suggested as the promoting factors in the pathogenesis of gallbladder sarcoma, although no proof exists (7–9).

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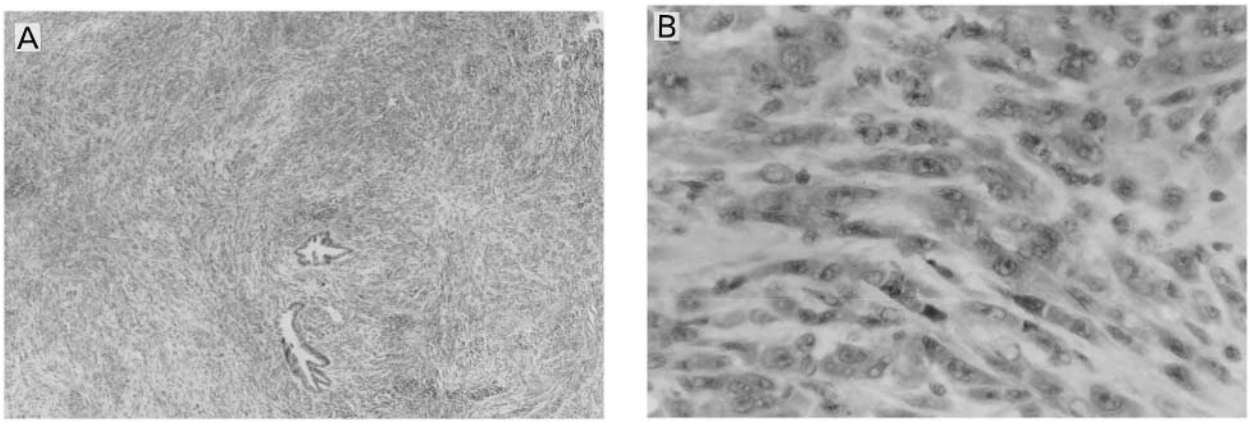

*Fig. 1*A) Hematoxylin and eosin staining showing sheets and solid nests of tumor cells. Some areas exhibit a vague fascicular pattern (H & E × 40). B) The cells are moderately pleomorphic, ranging from round to oval nuclei with abundant cytoplasm to areas which have a spindle appearance, blunt-ended nuclei and scant cytoplasm (H & E × 400).

The predominant signs and symptoms are those of hepatobiliary disease combined with malignancy and include right upper quadrant pain, fever, jaundice, palpable mass, hepatomegaly, weight loss, anorexia, nausea and vomiting. The symptoms resemble those of carcinoma of the gallbladder but are usually of shorter duration and occur earlier in the disease (9).

The diagnosis of primary gallbladder sarcoma is almost always made following histological examination of operative or necropsy specimen (2). However, with technological advances in B-mode real-time ultrasonography and computerized tomography, it may be possible to differentiate various types of gallbladder tumors preoperatively (3, 4).

Historically, there has been some skepticism concerning the accuracy of the histological diagnosis of primary gallbladder sarcoma and some have even questioned its existence (10, 11). Appleman & Coopersmith (11) have suggested two reasons for erroneous diagnosis of sarcoma: a) a tendency to consider any undifferentiated spindle-cell neoplasm as sarcoma, and b) the labile nature of the neoplastic epithelium which may change its shape and its pattern of growth rapidly. The use of electron microscopy (TEM) and immunocytochemical phenotyping has virtually eliminated these problems and it is now easier to differentiate between the most commonly confused histopathological diagnoses and primary gallbladder sarcoma (12). Furthermore, these two techniques have clearly established the existence of primary gallbladder sarcoma as a distinct entity.

The differential diagnosis in our case included leiomyosarcoma, fibrosarcoma, pseudosarcomatous or spindle-cell carcinoma, and carcinosarcoma. On histology alone, this neoplasm did not have the mixed malignant epithelial and mesenchymal elements seen in carcinosarcomas (13). Separating the first three by the histology can be troublesome, but made easier by using the immunohistochemical results. The positive alpha smooth muscle actin helped to eliminate the fibrosarcoma and favor smooth muscle origin. Guo et al. (14) examined 21 cases of undifferentiated carcinoma of the gallbladder (5 were of the spindle-cell or pseudosarcomatous type) and found that all were positive for EMA, keratin and CEA. Our tumor was only focally positive for the keratin (AE1:3), which is not an unusual finding in leiomyosarcomas. Swanson (15) reported that cytokeratin was positive in 21% (43 out of 202) of the evaluated published cases of leiomyosarcomas. The vimentin and actin positivity was consistent with leiomyosarcoma (16). In our case, therefore, immunohistochemical stains clearly demonstrated that the tumor was a true sarcoma of smooth muscle origin.

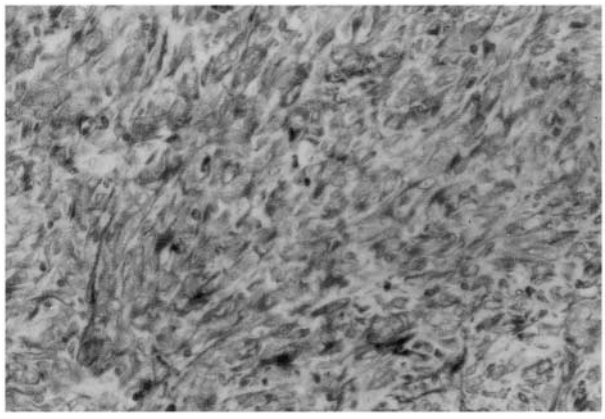

Fig. 2. Immunoreactive vimentin positive mesenchymal cells (× 200).

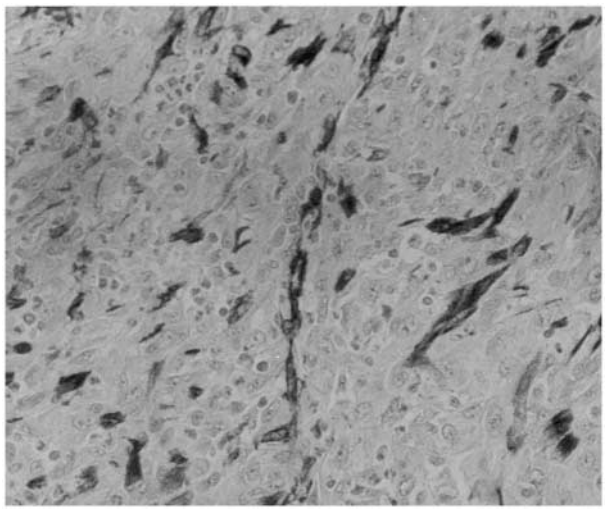

Fig. 3. Alpha smooth muscle actin positive cells (× 200).

The prognosis of the primary gallbladder sarcomas is dismal because of the highly malignant nature associated with rapid progression and early metastases. However, occasional long-term survivals have been described in the literature (9). Vaittinen (9) suggested that an early en bloc resection of the tumor and surrounding structures as devised for gallbladder carcinoma is the only way of curing this disease. The enthusiasm for radical surgery is not shared by other authors (11, 17) because of the advanced nature of the disease and the presence of distant metastases at the time of diagnosis.

In conclusion, these rare neoplasms can now be diagnosed confidently using immunohistochemical and TEM techniques, yet, on occasion, can still pose a diagnostic dilemma. At present, these tumors carry a dismal prognosis due to the delay in diagnosis and the advanced nature of the disease at presentation. Perhaps the only hope of improving the outlook for patients with these tumors lies in an early diagnosis and an aggressive, multimodality treatment approach.

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