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CASE REPORT

Primary leiomyosarcoma of gallbladder

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Malignant mesenchymalneoplasms of the gallbladder are extremely rare with only 105 cases of primary gallbladder sarcoma having been described. It has a very aggressive behavior and is usually diagnosed at advanced stages. Therefore, curative surgical management may not be possible. We performed a radical cholecystectomy (S4b + S5 segmentectomy), omentectomy and small bowel resection in a 54-year-old patient with locally invasive leiomyosarcoma of the gallbladder. Further studies are needed to confirm the benefit of aggressive treatment for patients with leiomyosarcoma of the gallbladder.

Key Words: Leiomyosarcoma, Gallbladder neoplasms

INTRODUCTION

Adenomatous hyperplasia of gallbladder is the most common benign mesenchymal proliferation, accounting for more than 40% of tumor-like lesions of the organ [1,2]. The malignant degeneration of adenomatous hyperplasia is rare. Malignant mesenchymal neoplasms of the gallbladder are extremely rare and only 105 isolated cases of primary gallbladder sarcoma have been reported. A variety of tumor types have been reported (such as leiomayosarcoma, rhadomyosarcom, angiosarcoma, Kaposi's sarcoma, malignant fibrous histiocytoma, and synovial sarcoma). Leiomyosarcoma is the most common type of primary gallbladder sarcoma. Leiomyosarcomas are usually diagnosed at an advanced stage therefore surgical management is not a therapeutic option. Consensus about the management of leiomyosarcomas is limited due to limited experience with to this type of tumor. We present a case of leiomyosarcoma of the gallbladder treated by radical cholecystectomy and small bowel resection.

CASE REPORT

A 54-year-old male patient presented to the outpatient clinic with complaints of a palpable mass in the right upper quadrant of the abdomen, nausea and some weight loss. On physical examination, a firm and fixed mass was found in the abdomen. The levels of hepatic and biliary enzymes were normal. The tumor markers (carcinoembyonic antigen, carbohydrate antigen 19-9, alpha-fetoprotein) were also normal. Endoscopic ultrasound examination revealed a gallbladder mass without direct invasion of liver parenchyma and duodenum (Fig. 1). Abdominal com-

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puted tomography (CT) and magnetic resonance cholangiopancreatography (MRCP) demonstrated a 9-cm mass lesion that was attached to the small bowel and abdominal wall, but had not invaded the liver parenchyma (Figs. 2, 3). The stage of tumor using the standard tumor-node-metastasis staging system was T4N0M0. An anomalous union of the pancreatobiliary duct was not demonstrated on MRCP. The 18F-fluorodeoxyglucose positron emission tomography/CT that was performed to check for distal metastasis revealed a hypermetabolic lesion (maximum standardized uptake value [SUVmax] 14.5) in the entire gallbladder (Fig. 4).

We performed a simultaneous radical cholecystectomy (S4b + S5 segmentectomy), omentectomyand small bowel segmental resection. We also did dissection of lymph nodes around the hepatoduodenal ligaments and the celiac

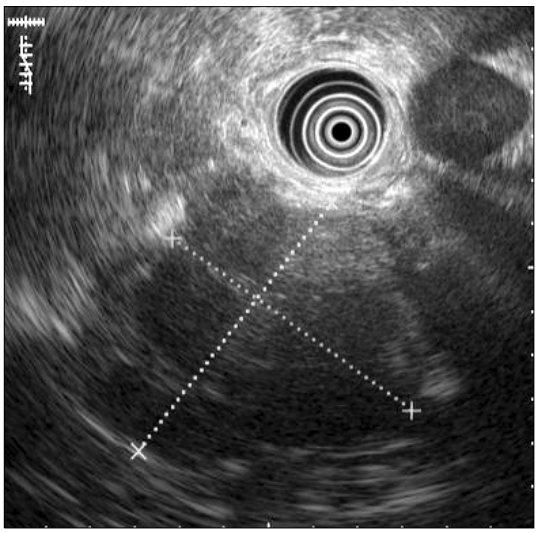

Fig. 1. Endoscopic ultrasound shows 6.7 × 7.1 cm-sized huge mass on gallbladder body extended to omentum but not invaded into duodenum.

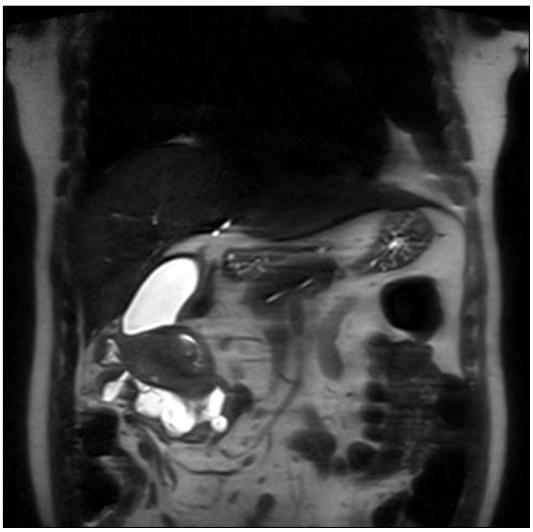

Fig. 3. Coronal T2WI shows 9 cm-sized well-defined and heterogenousexophytic mass lesion in gallbladderaccompanied by invasion into surrounding tissues.

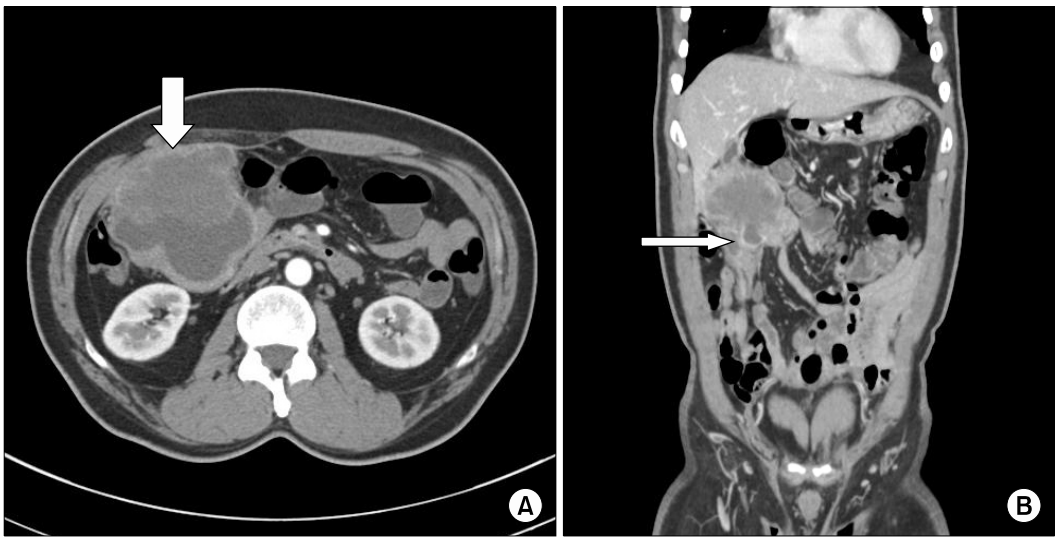

Fig. 2. Computed tomography (CT) image with intravenous contrast shows 9 cm-sized exophytic gallbladder mass that invaded abdominal wall (A, thick arrow) and small bowel (B, thin arrow).

trunk. The size of the tumor was 7.0 × 5.5 cm. Histopathology showed a malignant spindle cell tumor consisting of leiomyosarcoma with marked nuclear atypia and mitosis (62/10 high-power fields [HPFs]) (Fig. 5). The neoplastic cells infiltrated the muscularispropia layers of the small bowel and the soft tissue of the abdominal wall. The tumor cells showed positive immunoreactivity for smooth muscle actin (SMA) (Fig. 6A) and vimentin (Fig. 6B). There was negative immunoreativities for the following markers; caldesmon, cytokeratin (CK) 7, CK19, CK20, CD31, CD34, c-kit, calponin, desmin, myoglobin, HMB45, high molecular weight cytokeratin (HMWCK), PanCK, and S100. Necrosis was observed in 5% of the tumor. Of the 22 resected lymph nodes, a metastatic lymph node was not contained.

The patient developed a high fever and tarchycardia on the 3rd postoperative day. A pulmonary thromboemolism in the upper left anterior lobe's segmental branch was revealed in a chest CT therefore, the patients received thrombolysis followed by heparin anticoagulation therapy. The patient was discharged from the hospital on the 12th postoperative day.

Multiple liver metastasis and seeding metasitasis on the peritoneum were found in an abdominal CT 1 month postoperatively. The patient subsequently underwent adjuvant chemotherapy composed of mesna, adriamycin,

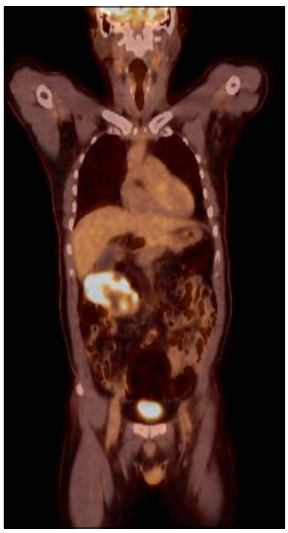

Fig. 4. A hypermetabolic lesion (maximum standardized uptake value [SUVmax] 14.5) in entire gallbladder was shown on 18F-fluorodeoxyglucose positron emission tomography/computed tomography.

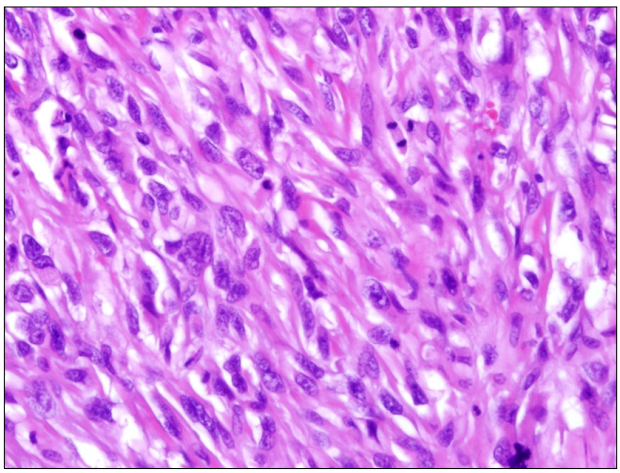

Fig. 5. Higher magnification of spindle cell component displaying marked nuclear atypia and mitosis (62/10 high-power fields [HPFs]; H&E, ×400).

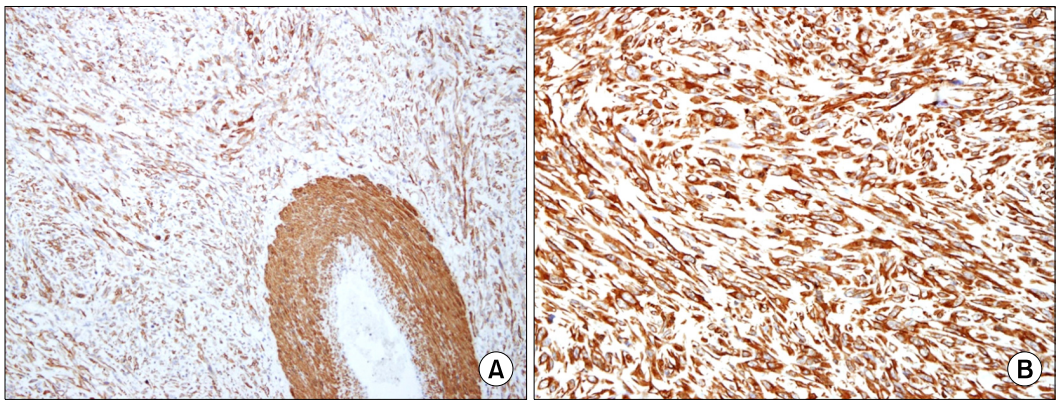

Fig. 6. (A) Tumor cells showed positive immunoreactivity for smooth muscle actin (A, ×200) and vimentin (B, ×400).

ifosfamide and dacarbazine (MAID) for 3 months.

DISCUSSION

Sarcomas of the gallbladder are rare and represent about 1.5% of all malignant gallbladder diseases. A variety of tumor types have been described including leiomyosarcoma, rhabdomyosarcoma, angiomyosarcoma, Kaposi's sarcoma, malignant fibrous histiyocytoma, and synovial sarcoma [2]. Leiomyosarcoma of the gallbladder is an especially rare malignant tumor. By 1984, 105 cases of primary sarcomas of the gallbladder had been reported, with primary leiomyosarcomas accounting for 7% of them [3].

The diagnoses were established in accordance with the new World Health Organization classifications for soft tissue tumors and the most recent soft tissue criteria published. Leiomyosarcoma is defined as a malignant tumor composed of cells showing distinct smooth muscle features. In the macroscopy, leiomyosarcoma typically forms a fleshy mass, with colors varying from grey to white to tan. Large examples often display hemorrhage, necrosis or a cystic change. The typical histopathologic pattern of leiomyosarcoma is that of intersecting, sharply marginated groups of spindle cells. In the immunophenotype, desmin, h-caldesmon, and SMA were positive in a great majority of leiomyosarcomas. None of these are absolutely specific to smooth muscle and positivity for two of these markers were more supportive of leiomyosarcoma than positivity for one alone. Immunostains may be focally positive on CD34, epithelial membrane antigen (EMA), keratin and S100. A diagnosis should be made on the appropriate morphologic features, not only on the immunostains. In this case, immunopositive staining was strong for SMA and vimentin but the typical histopathologic pattern of leiomyosarcoma had appeared in the hematoxylin and eosin stain. Therefore other types of the sarcoma were excluded from the diagnosis.

Leiomyosarcoma is more frequent in women between the ages of 50 and 75 years and usually has a poor prognosis. The presence of gallstones are invariable and the symptoms presented are those of chronic cholecystitis [4]. Histopathologically, the majority of these tumors are high grade and display an epithelioid morphology; but cases with features of well-differentiated leiomyosarcoma have been described.

According to the National Comprehensive Cancer Network clinical practice guideline in oncology ver. I. 2011, patients with a resectable intraabdominal sarcoma should undergo immediate surgical treatment with a grossly negative margin and and possible interoperative radiation therapy. The postoperative margin status was the most important factor contributing to long-term disease free survival [5]. Postoperative treatment options were dependent on the surgical outcomes and clinical, or pathological finding following surgery. Postoperative radiation therapy should be considered in patients with pathological findings of high grade disease following a negative margin resection (R0 resection) or for microscopic positive margins (R1 resection). For patients with unresectable or disseminated recurrences, preoperative RT and/or chemotherapy should be considered after a biopsy. Combination regimens with activity in soft tissue sarcoma include AD (doxorubicin, dacarbazine), AIM (doxorubicin, ifosfamide, mesna), MAID, and so on [6,7]. The single agents include dacarbazine, doxorubicin, epirubicin, gemcitabine, ifosfamide, liposomal doxorubicin and temozolomide [8,9].

The prognosis of sarcoma and leiomyosarcomas of the gallbladder is dismal, the five year survival rate being less than 5%. This is due to the fact that at the time of the diagnosis or surgery. Almost 75% of cases involve the liver [10]. Our patient was also diagnosed at an advanced stage, but he had no distant organ metastasis. Because R0 resection is expected in this case, an aggressive surgical approach was attempted. However, soon after, multiple liver metastasis and peritoneal seeding metastasis were detected in postoperative evaluations. Therefore additional aggressive multimodality treatments such as surgery with chemotherapy are the only way to increase the survival rate.

In conclusion, the five year survival rate of leiomyosarcoas of the gallbladder is less than 5%. However for young and healthy patients with leiomyosarcomas of the gallbladder, aggressive surgical treatment followed by adjuvant chemotherapy should increase the survival rate despite high mortality and morbidity. Because of limited ex-

perience with this disease, there is no consensus about management. Further studies are needed to confirm the benefit of aggressive treatment for patients with leiomyosarcoma of the gallbladder. Also surgeons will have to tread very carefully in selection of candidates for surgical treatments.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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