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Case Report

A Large Retroperitoneal Malignant Solitary Fibrous Tumor

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We report on a large, retroperitoneal, malignant, solitary fibrous tumor (SFT) with high proliferation activity. A 43-year-old man was admitted to our department complaining of a palpable mass. Computed tomography (CT) and magnetic resonance imaging (MRI) revealed a large retroperitoneal tumor occupying the entire abdominal cavity. A laparotomy was performed for diagnosis and treatment, which revealed a tumor in the retroperitoneum but with no invasion to the surrounding organs, thereby allowing safe macroscopic excision. Histologically, the tumor was composed of spindle-shaped cells with patternless pattern and a hemangiopericytomatous appearance. Moreover, immunohistochemical staining was positive for CD34, vimentin, Bcl-2, and CD99 and negative for desmin, S-100p, and smooth muscle actin (AMA). The tumor exhibited high cellularity, moderate mitotic activity, pleomorphism, necrosis, and hemorrhagic changes. In addition, the Ki-67 labeling index was 37%. These findings confirmed the diagnosis of malignant SFT with high proliferation activity. Subsequently, adjuvant doxorubicin plus ifosfamide chemotherapy was performed. No signs of recurrence were observed 12 months after the surgery.

Key words: Malignant solitary fibrous tumor – Retroperitoneum – Ki67

Solitary fibrous tumors (SFTs) constitute a heterogeneous group of rare spindle-cell tumors, which includes both benign and malignant neoplasms. They usually develop in the pleura, and approximately 30% of them arise in extrapleural tissues[1] including retroperitoneum.[2] The treatment for usual pleural SFTs remains the large en bloc resection, and adjuvant treatments (radiotherapy and chemotherapy) are not usually employed.[3] But the treatment for retroperitoneal SFT is uncertain. We report a retroperitoneal malignant SFT with high proliferation and reference the recent strategy for soft tissue sarcoma.

Case Report

A 43-year-old male was referred to our hospital with a palpable mass in his abdomen. On physical

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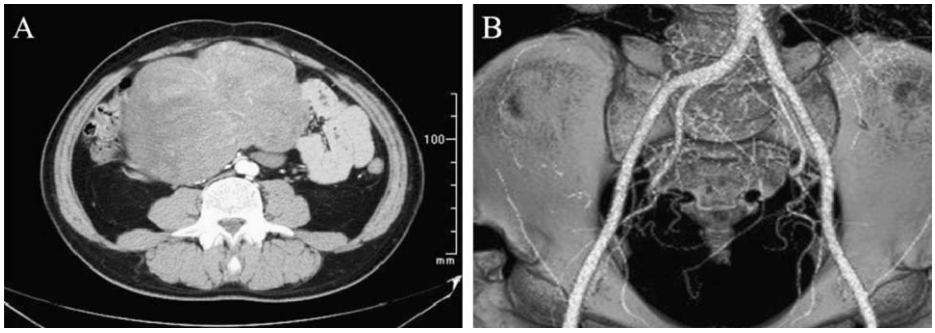

Fig. 1 (A) Abdominal contrast-enhanced CT demonstrated the presence of a solid encapsulated mass, which was heterogeneously enhanced. (B) CT angiography suggested that the tumor feeding was supplied by the branch of the right internal iliac artery and many uncertain vessels.

examination, a large mass occupying the lower abdomen was observed by palpation. No mass was palpable on digital rectal examination. Abdominal contrast-enhanced computed tomography (CT) revealed a large, solid, encapsulated mass, which was heterogeneously enhanced (Fig. 1A), and the tumor surface was surrounded by several vessels. Moreover, CT angiography suggested that the tumor was supplied by a branch of the right internal iliac artery and several indeterminate vessels (Fig. 1B). Subsequently, magnetic resonance imaging (MRI) demonstrated a large tumor with a relatively smooth margin in the retroperitoneum, which demonstrated high intensity on T1-weighted images and low intensity on T2-weighted images. Furthermore, neither lymph node swelling nor distant metastasis could be detected by CT. On the basis of these findings, the lesion was suggestive of a soft tissue retroperitoneal tumor, and a surgery was planned; however, biopsy was not performed considering the risk of bleeding from the tumor.

At laparotomy, a smooth-surfaced and lobulated large tumor occupied the retroperitoneal space (Fig. 2A). Most of the tumor was encapsulated and, thus, was resected sharply along the tumor capsule with division of the feeding vessels. The tumor was supplied by a branch of the right internal iliac artery and the right gonadal artery. The urinary bladder was preserved, and complete macroscopic resection was performed (Fig. 2B). Macroscopic findings revealed an encapsulated, elastic, hard tumor, 17 $\times$ 10 $\times$ 13 cm in diameter (Fig. 3A) and 2.8 kg in weight.

Pathologic examination revealed that the tumor was composed of spindle-shaped cells with patternless pattern and a hemangiopericytomatous appearance (Fig. 3B). In addition, the tumor exhibited high cellularity, moderate mitotic activity [3 mitoses per 10 HPF], pleomorphism, necrosis, and hemorrhagic changes. Immunohistochemical staining was positive for Bcl-2, CD34, vimentin, and CD99 and negative for desmin, S-100p, and SMA (Fig. 3C and 3D). The Ki-67 labeling index was 37%, thereby confirming the diagnosis of malignant SFT of the retroperitoneum with high proliferation activity. The patient had an uneventful postoperative course and was discharged 9 days after the surgery. Because the tumor was diagnosed pathologically as a malignant SFT, we initiated adjuvant doxorubicin plus ifosfamide chemotherapy. No signs of recurrence were observed 12 months after the surgery.

Discussion

SFTs are soft tissue tumors categorized in the intermediate group (rarely metastasizing) along with hemangiopericytomas in fibroblastic or myofibroblastic tumors, according to a recent World Health Organization (WHO) classification.[4] Histologic characteristics of SFTs comprise the so-called "patternless pattern" characterized by a haphazard, storiform arrangement of spindle cells and a "hemangiopericytoma-like appearance" with prominent vascularity.[5] In addition, immunohistochemical staining is generally helpful for establishing the diagnosis; while diffuse positive expressions of CD34, Bcl-2, and CD99 and negative expressions of cytokeratin, SMA, S-100, CD31, and c-kit are useful in confirming the diagnosis.[6,7] In particular, Hasegawa *et al*[8] reported that 75% of extrapleural SFTs revealed positive reactivity for Bcl-2, which suppresses apoptosis, thereby supporting the view that

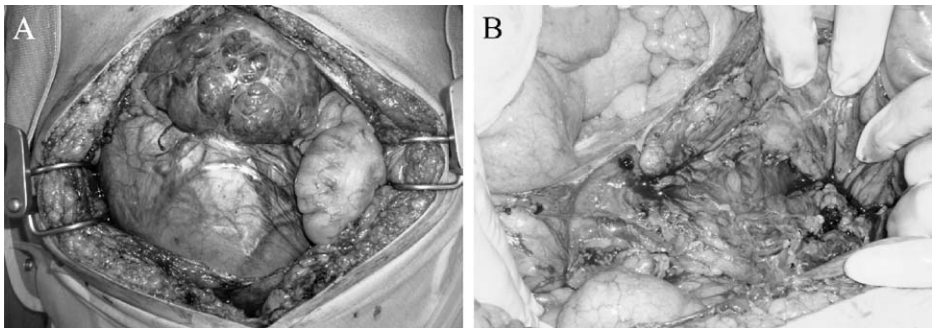

Fig. 2 (A) At laparotomy, a smooth-surfaced and lobulated large tumor occupied the retroperitoneum. (B) Macroscopic complete resection could be performed.

Bcl-2 expression can be used along with CD34 expression in confirming the diagnosis of SFTs.

England *et al*[9] have described the pathologic criteria for malignancy: high cellularity, high mitotic activity (more than 4 mitoses per 10 HPF), pleomorphism, necrosis, and hemorrhagic changes. Recently, Sun *et al*[10] reported that Ki-67 and basic fibroblast growth factor (bFGF) are relevant when assessing the malignant potential of SFTs, and these markers are potentially useful for predicting the prognosis of SFTs. In particular, Ki-67 is a well-known tumor proliferation marker, which is expressed in G1, S, G2, and M phases as assessed by cell-cycle analysis; in addition, they reported that the mean Ki-67 labeling index is 1.9% for benign SFTs and 6.11% for malignant SFTs. These markers are believed to play a role in the differentiation of benign and malignant phenotypes in SFTs, thereby suggesting the usefulness of immunoreactivity in the diagnosis of clinically malignant SFTs. In our case, only the Ki-67 label index was measured and was determined to be 37%. Thus, the tumor had the capacity for a high degree of proliferation as a malignant tumor. On the

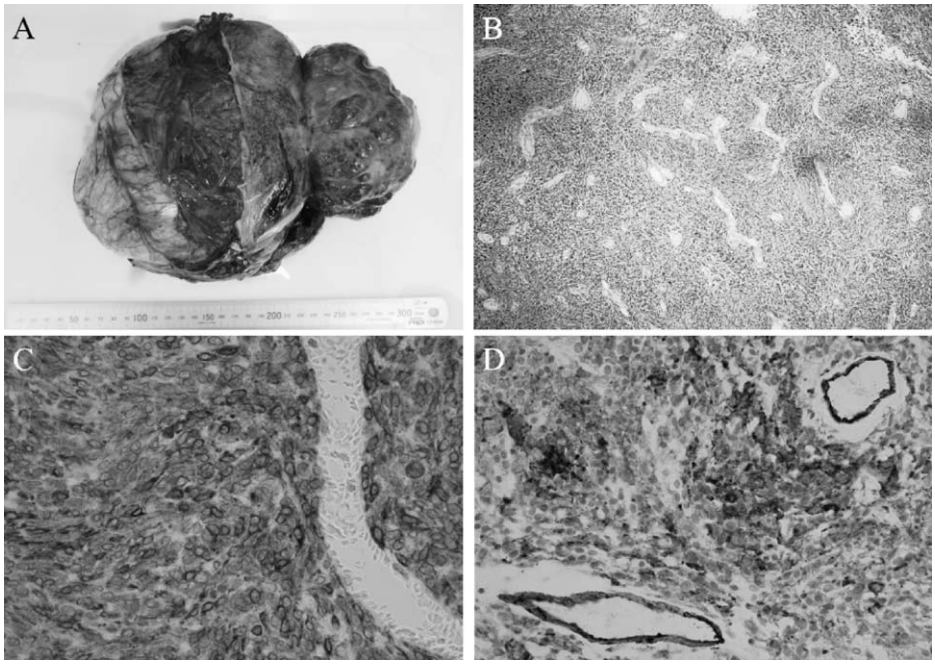

Fig. 3 (A) Macroscopic findings revealed an encapsulated elastic hard tumor, 17 × 10 × 13 cm in diameter and 2.8 kg in weight. (B) Pathologic examination revealed that the tumor was composed of spindle-shaped cells with patternless pattern and hemangiopericytomatous appearance (H&E stain; original magnification ×40). (C, D) Immunohistochemical staining was positive for Bcl-2 (C) and for CD34 (D), as well as for vimentin and CD99. All are ×40.

basis of these criteria, the specimen in our case was histologically considered to be a malignant SFT.

The basic treatment principle for soft tissue tumors including SFTs is resection with sufficient clear margins. Particularly in the case of limb sarcomas (malignant soft tissue tumors), it has been demonstrated that the resection of all gross tumor with a rim of normal muscle achieves better margins and better local control.[11] Recently, the European Society for Medical Oncology (ESMO) guidelines recommended a combined modality approach in limb sarcomas with preoperative and postoperative radiation therapy, rather than radical surgical procedures alone.[12] However, in the event of retroperitoneal sarcomas, effective treatment requires gross removal of all the diseased tissue, while sparing adjacent viscera that is not invaded by the tumor. Considering the difficulty in completely resecting these tumors with sufficient margins as well as the dose-limiting toxicity of high-dose radiation therapy on visceral organs, the prognosis for patients with high-grade retroperitoneal sarcomas is less favorable than for patients with tumors at other sites. In addition, complete compartmental surgery (en bloc tumor resection with uninvolved adjacent organs) for retroperitoneal sarcoma achieves better local control[13] than simple complete resection (shelling out of the tumor). Unfortunately, in some cases, complete compartmental surgery cannot be performed because of tumor size and/or location, as was the case in our patient.

In our case, the tumor was completely resected macroscopically (simple complete resection), but we failed to obtain sufficient margin because of the tumor size (17 × 10 × 13 cm in diameter) and location (retroperitoneum). In addition, the tumor exhibited pathologic malignancy and the capacity for a high degree of proliferation. Although the role of adjuvant chemotherapy for sarcoma is not as well defined as the role of radiation therapy, we initiated doxorubicin plus ifosfamide chemotherapy[14,15] considering the dose-limiting toxicity of high-dose radiation therapy on retroperitoneal organs.

In summary, we describe an unusual case of a large malignant retroperitoneal SFT. SFTs usually have a favorable prognosis after complete local excision, but they can hold the potential for recurrence or metastasis as well. Although the relationship between morphology and outcome with SFTs is poor, the pathologic findings should not be ignored when considering further therapy. This is particularly true in the event of large retroperitoneal SFTs, considering the difficulty in compartmentally resecting these tumors. In our opinion, the Ki67 label index is useful along with the traditional criteria in indicating the need for further therapy. With regard to retroperitoneal SFTs, even where simple complete resection is performed, the need for further therapy should be considered depending on the pathologic findings.

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