An unresectable retroperitoneal malignant fibrous histiocytoma: A case report

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Abstract. Malignant fibrous histiocytoma (MFH) is most commonly observed in the extremities and the trunk but rarely in retroperitoneum. The present case report documents a 64-year-old man who was admitted with an abdominal palpable mass for 6 months. After a thorough investigation, a tumor of the retroperitoneum was identified adhered to adjacent organs and vessels. The patient experienced mild hydronephrosis and hydroureter as a result of the tumor compression. A number of previous surgeons considered the tumor unresectable and suggested palliative treatment. *En bloc* resection of the tumor was attempted but incomplete surgery was performed initially as the tumor was friable and prone to bleeding. Therefore, a biopsy of the tumor was performed and a double J ureteral stent was set for hydronephrosis. Histopathological examination confirmed the tumor was an MFH. The patient received neo-adjuvant chemotherapy with 4 cycles of mesna, doxorubicin, ifosfamide, and dacarbazine (MAID). A computed tomography scan demonstrated that the tumor had reduced in size following chemotherapy. E*n bloc* resection of the tumor was arranged again 6 months later. The tumor exhibited a complete response to neo-adjuvant chemotherapy after the formal pathological evaluation. The patient survives without tumor recurrence >5 years without recurrence.

Introduction

Malignant fibrous histiocytoma (MFH), which is also termed undifferentiated pleomorphic sarcoma or pleomorphic spindle cell sarcoma (PSCS), is a type of malignant sarcoma that occurs most frequently in patients aged between 50 and 70 years (1). MFH occurs most commonly in the extremities and the trunk, and it is extremely rare in the retroperitoneum (1,2). The majority of retroperitoneal MFH cases are asymptomatic. Compression of nearby organs in the abdomen may elicit symptoms, including anorexia, abdominal discomfort, nausea and the sensation of an abdominal mass with abdominal girth enlargement (3). Chemotherapy is employed for advanced disease, however, large trials have not demonstrated a significant benefit (4,5). Recent insights into the neo-adjuvant chemotherapy of MFH provide exciting avenues for future research. A review of the clinical literature on this topic supports the management that was taken in the present case.

Case report

A 64-year-old male with an unremarkable medical history presented with a 6-month history of abdominal fullness at the China Medical University Hospital (Taichung, Taiwan) in April 2012. On abdominal physical examination, a painless mass was palpated in right abdomen. After thorough investigation, a tumor measuring ~20x12x8 cm in size was identified in the retroperitoneum. The right internal and external iliac vessels were adhered to the tumor and medial deviation. Right mild hydronephrosis and hydroureter was observed in computed tomography (CT) scan due to external compression (Fig. 1).

The patient had previously sought medical opinion and palliative treatment was suggested by the majority of those consulted. Instead, the patient was admitted to our a tertiary referral hospital (China Medical University Hospital, Taichung, Taiwan) in April 2010. The patient underwent an exploratory laparotomy for removal of the tumor in May, 2012. The tumor was not completely removed due to a severe hemorrhage during the surgery when the tumor surface was approached. However, excisional biopsy of the tumor was performed and a double J stent for the right hydronephrosis was inserted.

A diagnosis of MFH (grade 3/3 based on the Fédération Nationale des Centres de Lutte Contre le Cancer soft tissue tumor grading system) was confirmed by a pathologist. Immunohistochemical analysis was performed by incubation with the following primary antibodies: Monoclonal mouse anti-human cytokeratin (CK; low molecular weight; AE1; dilution, 1:800; catalog no., Z2269; Zeta Corp., Sierra Madre, CA, USA),

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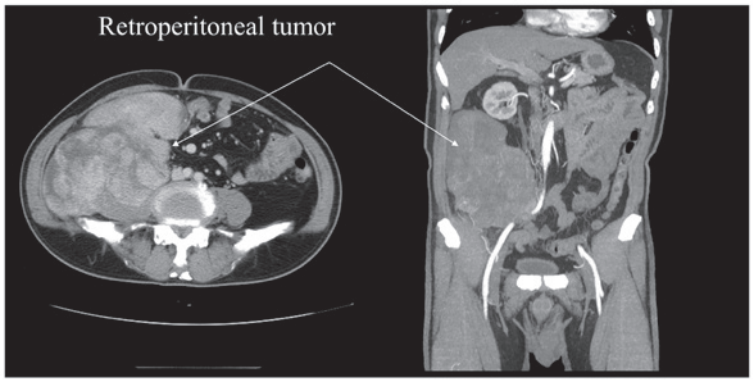

Figure 1. Abdominal computed tomography scan prior to mesna, tetrahydropyranyl adriamycin, ifosfamide and dacarbazine treatment. The tumor measured ~20x12x8 cm and was situated in the retroperitoneum. The tumor caused right internal, external iliac arteries and right ureter medial displacement, mild hydronephrosis and hydroureter.

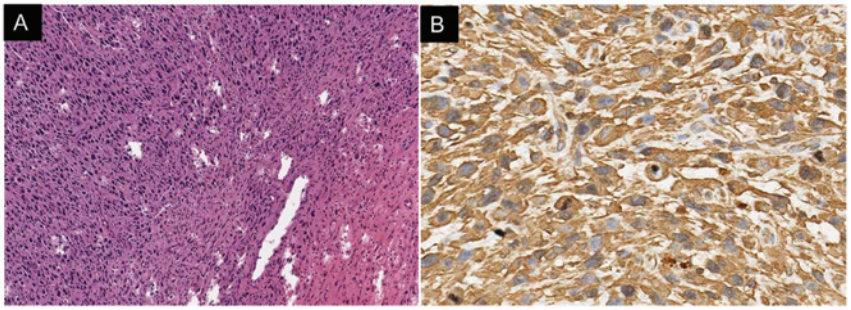

Figure 2. Microscopy and photomicrography of the tumor prior to chemotherapy. (A) Microscopic examination revealed the tumor was composed of a mixture of spindle cells in a storiform pattern and polygonal or rounded cells (hematoxylin and eosin staining; magnification, x100). (B) Immunohistochemical staining revealed the tumor cells were positive for vimentin (magnification, x400).

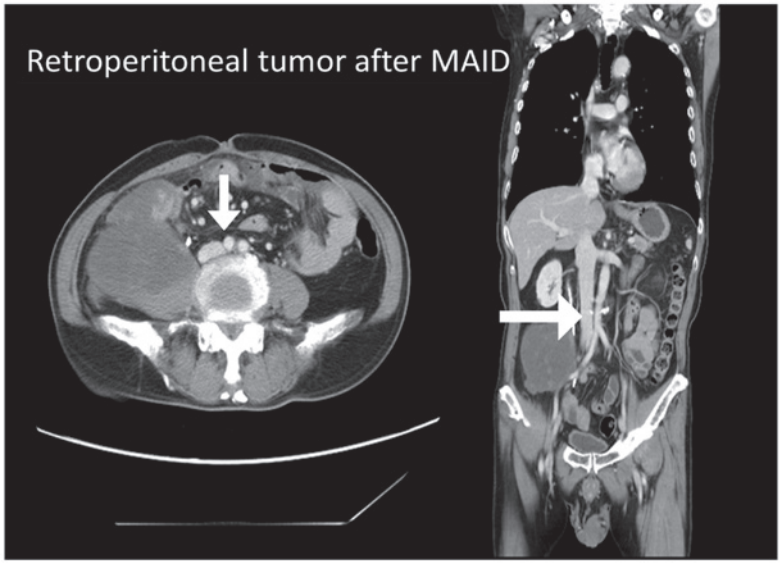

Figure 3. Abdominal scan following MAID treatment. The mass was decreased in size and had reduced levels of necrosis compared with the previous CT scan. White arrows indicate the inferior vena cava. CT, computed tomography; MAID, mesna, tetrahydropyranyl adriamycin, ifosfamide and dacarbazine.

monoclonal mouse anti-human CK (high molecular weight; AE3; dilution, 1:800; catalog no., Z2267; Zeta Corp.) monoclonal mouse anti-human smooth muscle actin (dilution, 1:100; catalog no., NCL-SMA; Leica Biosystems, Wetzlar, Germany), monoclonal mouse anti-human desmin (dilution, 1:200; catalog no., DES-DERII-CE; Leica Biosystems), monoclonal mouse anti-human vimentin (dilution, 1:400; catalog no., 61-0066; Genemed Biotechnologies, Inc., San Francisco, CA, USA), monoclonal mouse anti-human melan-A (dilution, 1:50; catalog no., NCL-MelanA; Leica Biosystems), monoclonal

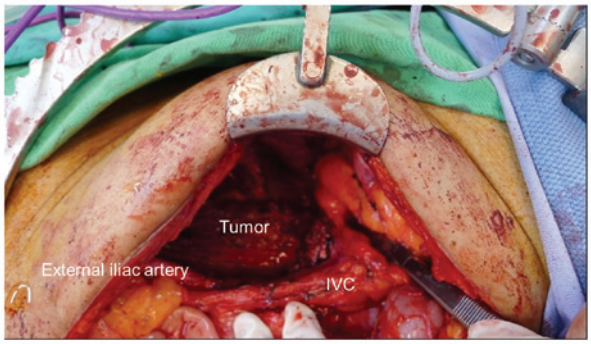

Figure 4. The tumor adhered to the right gonadal vein, adjacent to right common iliac, internal and external iliac arteries, anterior to the IVC and medial to the right ureter, below the right kidney and ascending colon.

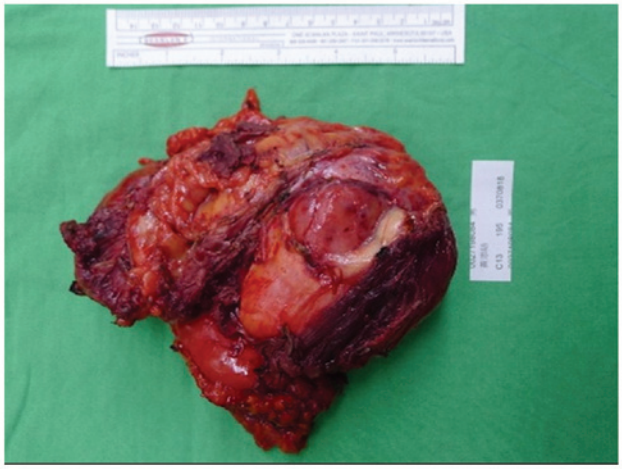

Figure 5. Complete resection of the tumor: The tumor size was 13.3x8.8x5.7 cm.

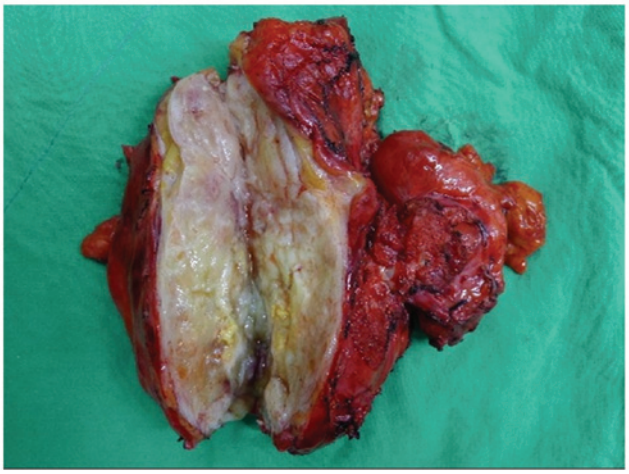

Figure 6. Dissection revealed that the interior of the tumor was a yellow-white color, with necrotic tissue.

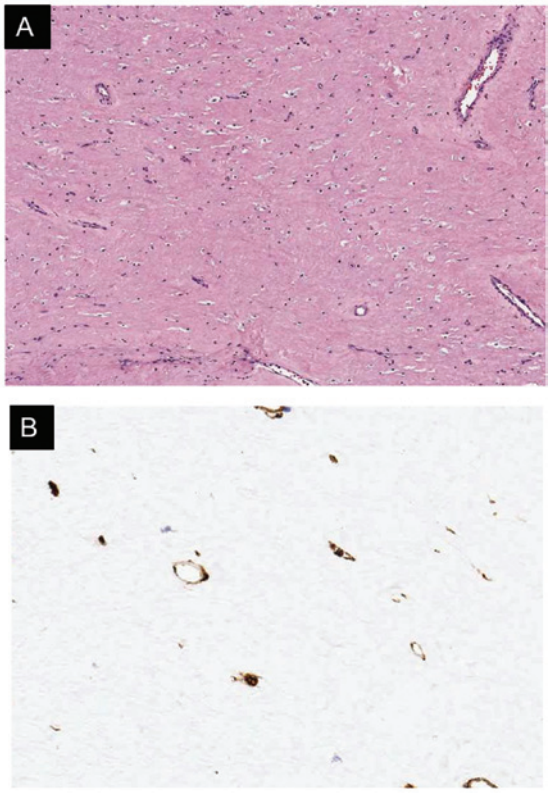

Figure 7. Microscopy and photomicrography of the tumor following chemotherapy. (A) Nuclear pleomorphism, tumor necrosis and degenerative foamy tumor cells with intracellular brown pigment deposition were present. Tumor cells responded well to chemotherapy with extensive tumor necrosis and fibrosis (hematoxylin and eosin staining; magnification, x100). (B) Immunohistochemical staining revealed that the vimentin positive tumor component was reduced following chemotherapy (magnification, x400).

rabbit anti-human S100 (1:400; catalog no, NCL-S100p; Leica Biosystems), monoclonal mouse anti-human cluster of differentiation (CD)68 (dilution, 1:800; catalog no., CD68-L-CE; Leica Biosystems) and monoclonal mouse anti-human HMB-45 (dilution, 1:100; catalog no., HMB45-L-CE; Leica Biosystems). Diaminobenzidine (Leica Biosystems) was used as a chromogen and Meyer's hematoxylin (Leica Biosystems) as a counterstain. An Olympus BX-50 microscope (Olympus Corp., Tokyo, Japan) with DP-20 digital camera (Olympus Corp.) was used to capture images at a magnification of x100 and magnification, x400 (vimentin immunostaining). Immunohistochemistry revealed positivity for vimentin; and negativity for CK, desmin, S-100 and CD117 (Fig. 2). Neo-adjuvant chemotherapy was suggested for palliative treatment. The patient received neo-adjuvant chemotherapy with 4 cycles of MAID [mesna 2,500 mg/m^2/6 h (days 1-3), tetrahydropyranyl adriamycin 20 mg/m^2/0. 5 h (days 1-3), ifosfamide 2,500 mg/m^2/6 h (days 1-3) and dacarbazine 300 mg/m^2/1 h (days 1-3)] (6) from June to October 2012. CT scan was arranged after undergoing 2 cycles of chemotherapy. The mass was reduced in size (minor response) with central necrosis components in comparison to the last CT scan (Fig. 3). Six months later, the patient underwent whole tumor resection in November 2012. The tumor was carefully removed from the right gonadal vein, right common iliac, internal and external iliac arteries. (Fig. 4) The tumor had also invaded the right psoas muscle and anterior longitudinal ligament of the lumbar spine. Part of the muscle and ligament were also therefore resected. *En bloc* resection was undergone successfully without any remaining tumor. The surgical specimen measured 13.3x8.8x5.7 cm in size and weighed 4.3 kg. (Fig. 5) The specimen had heterogeneous yellowish content and necrotic components inside. Extensive tumor necrosis

and fibrosis were noted microscopically (Fig. 6). Complete response of chemotherapy was observed following pathological review, where a pathological complete response was defined as 99-100% necrosis (7-9). Pathology composed of a mixture of spindle cells in a storiform pattern and polygonal or rounded cells. Nuclear pleomorphism and necrosis were present in the resected tumor. Degenerative foamy tumor cells with intracellular brown pigment deposition were observed inside the tumor. Tumor cells responded well to chemotherapy with extensive tumor necrosis and fibrosis. Immunohistochemistry demonstrated that the tumor cells were negative for cytokeratin, smooth muscle actin, desmin, S-100, and melan-A expression, but positive with diffuse cytoplasmic staining for vimentin, CD68, and HMB-45. The Fontana-Masson and iron stains were negative for intracellular pigments. The negative margin was also proven under microscopy (Fig. 7). The patient did not receive any further treatment and remained alive without tumor recurrence at the final follow-up appointment in February 2015.

Discussion

MFH was first described as soft-tissue sarcomas arising from fibroblasts and histiocytes in 1964 (5). MFH is generally divided into 5 histological types: Storiform-pleomorphic, myxoid, giant cell, angiomatoid and inflammatory subtypes (10). MFH presents with varied histology morphology, but the classic form is composed of spindle-shaped and round histiocytes arranged in storiform pattern as in the present case.

The primary treatment of retroperitoneal MFH is surgical resection (11). The main structures in the retroperitoneum are the aorta, vena cava, superior mesenteric vessels, celiac trunk, kidney, ureter and duodenum (12). Damage to these structures may cause severe post-operative complications such as hemorrhaging and fatalities (12). If the tumor is encased or adheres to these structures, the mortality and morbidity rate will be high during and following tumor excision surgery.

Although the 5-year survival rate of all MFH patients that receive surgical resection is 67.2% (13), the 5-year survival rate of patients with those unresectable MFH is <10% (14). To the best of our knowledge, no studies regarding the management of a marginally resectable or unresectable retroperitoneal MFH have been published. Retroperitoneal MFH may be shrunk following an initial course of chemotherapy. Multimodal therapy for extremity sarcoma has provided an inference for the role of chemotherapy in retroperitoneal lesions (2). There are certain survival benefits if the tumor can be removed after chemotherapy (15). Overall, the arguments for neo-adjuvant therapy are reasonable.

A study reported 70% of 63 patients underwent complete surgery after neoadjuvant chemotherapy of ifosfamide, cisplatin, adriamycin and mitomycin. But 65% of patients had disease relapsed and 34% of patients died of metastasis within 30 months following up. Median survival of patients was 30 months and median relapse-free survival was 13 months (16).

A meta-analysis study reported a slight advantage of 4% overall survival for the use of adjuvant chemotherapy to decrease the risk of death and recurrence in patients with high-grade lesions (17,18).

In the present study, a combination regimen of MAID was used for neoadjuvant chemotherapy. The regimen has been successful in neo-adjuvant programs for sarcomas of the extremities (19,20) compared with historical controls, yet less data are available with regard to other soft tissue sites. Bui-Nguyen *et al* (21) designed a randomized control trial that patients who had sarcoma of extremities received 4 cycles of standard dose and high dose of MAID. Their 3-year overall survival rate was 49.4 and 32.7%; the progression-free survival rate was 32.4 and 14.0%, respectively. Other studies have also indicated the benefit of MAID regimen; pre-operative MAID is effective in advanced adult soft tissue sarcomas (22,23). Elias *et al* (24) demonstrated that MAID treatment is effective for retroperitoneal sarcoma: The overall response rate was 47% (10% complete response CR). The majority of responses (~70%) were observed within 2 cycles, the median times to progression was 9 months; and the median survival was 16 months (24). Variations in chemosensitivity between different histological types have been observed (25). For example, response rates of >50% have been reported for synovial sarcoma (26) Similarly, myxoid liposarcomas are considered to be significantly more responsive than the majority of soft tissue sarcoma, although the evidence remains controversial (27,28) Limited data was reported for MFH type in retroperitoneal tumors. Therefore, further prospective randomized trials on special types of soft tissue sarcomas and on subtypes of MFH are needed in order to make a more conclusive evaluation.

In conclusion, palliative treatment is not the only option for a borderline resectable or unresectable MFH in retroperitoneum. The age and any comorbidity of the patient together with the histology of the tumor need to be taken into account. If the tumor is chemosensitive and adjacent to critical organs, chemotherapy may render the tumor suitable for radical surgery. However, patients with MFH exceeding 5 cm are at a significant risk of developing metastases. The present study provides evidence that neo-adjuvant chemotherapy for those high grading or unresectable retroperitoneal tumor may lead to the possibility to perform complete resection or an improvement in prognostic outcome.

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