Malignant fibrous histiocytoma in a child

A case report and review of the literature

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Malignant fibrous histiocytoma (MFH) is the most common soft tissue sarcoma of late adult file. It is extremely rare in children, though, and its existence in the pediatric population remains controversial. Although the most common site of tumor in children is the extremities, which is similar to findings of adults' series, different sites have been reported in children. Because of the rarity of this tumor in childhood, the approach to treatment of MFH is based primarily on the experience with adults.

We present the clinical and pathologic features of an eight-year-old boy with MFH located on his left retroperitoneum and also review the literature.

Key words: children, malignant fibrous histiocytoma, non-rhabdomyosarcoma soft tissue sarcoma.

Malignant fibrous histiocytoma (MFH) was first described as a distinct histological type of sarcoma in 1964, by O'Brien and Stout[1]. Although MFH is the most common soft tissue sarcoma of late adult life, it is extremely rare in children and its existence in the pediatric population remains controversial[2,3]. Several reports of large series note that three to 10 percent of all patients with MFH are less than 20 years old at the time of diagnosis and two to six percent of childhood soft tissue sarcomas have been reported as MFH[4,5]. Because MFHs are rare in children, the natural history of these tumors and prognostic factors that affect survival have not been well described[4].

We present the clinical and pathologic features of an eight-year-old boy with MFH located on his left retroperitoneum and also review the literature.

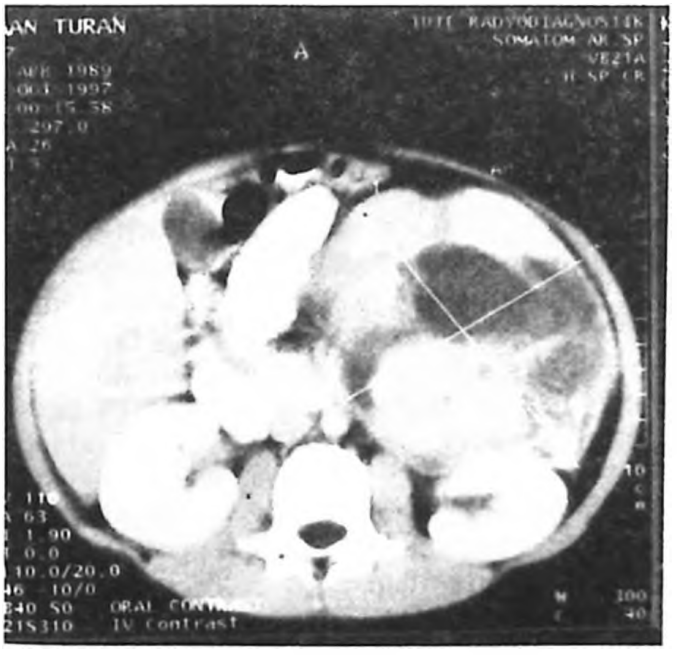
Case Report

An eight-year-old boy was admitted to our hospital with fever, fatigue, weight loss, palor, and painless upper left abdominal mass. Physical examination showed high fever (38.5 °C, axillary), pallor, and a painless left upper abdominal mass (diameter of 10x15 cm with irregular shape). The other physical findings were normal. Significant laboratory findings included decreased hemoglobin level (8.0 g/dl) and an elevated erythrocyte sedimentation rate (90 mm/h). Spot urine vanillylmandelic acid, alpha-fetoprotein, and β human chorionic gonadotropin levels were normal. The chest roentgenogram was also normal. Abdominal ultrasonography demonstrated a huge (8x20x12 cm) solitary lobulated echogenic mass with cystic areas located in the upper left abdomen. Its margins could not be seen clearly. Abdominal computed tomography showed a huge heterogeneous mass with cystic and necrotic areas located in the left hypochondrium and extending to the pelvis aperture (Fig. 1a). A surgical approach was undertaken but, owing to the size of the mass, complete excisional surgery could not be performed and only a partial excision was done. According to the postoperative staging system used in the Intergroup Rhabdomyosarcoma Studies, he was staged as a Group III disease[6]. Pathological examination revealed a solid tumor 8x10x5 cm with irregular contours infiltrating the pancreas. Histologically the tumor was highly cellular and consisted mainly of vacuolized atypical mesenchymal cells (Fig. 2). The mitotic rate was high, with more than 10 mitotic figures per 10 high power fields. Atypical mitotic figures were also seen. A wide necrosis was observe throughout the tumor. Immunohistochemical studies revealed the positivity of vimentin in the tumor tissue.

Although a rare positivity was found with S-100, immunohistochemical stains of NSE, chromogranine, CD-68, and desmin were found to be negative. He was diagnosed as having malignant fibrous histiocytoma based upon the clinical, laboratory and histopathological findings. Following surgery he was put on a combined chemotherapy consisting of vincristine (1.5 mg/m^2, day 1,8,15,22,43), ifosfamide (3 g/m^2, day 1,2,22,23,43,44) with mesna, cisplatinum (90 mg/m^2, day 3,24) and adriamycin (40 mg/m^2, day 43). After two courses of combined chemotherapy, he showed a good response to the treatment with more than 50 percent shrinkage of the tumor (Fig. 1b). It is planned that the will undergo a second operation for complete surgical removal of the residual tumor. After the operation, radiotherapy willbe given to the residual tumor.

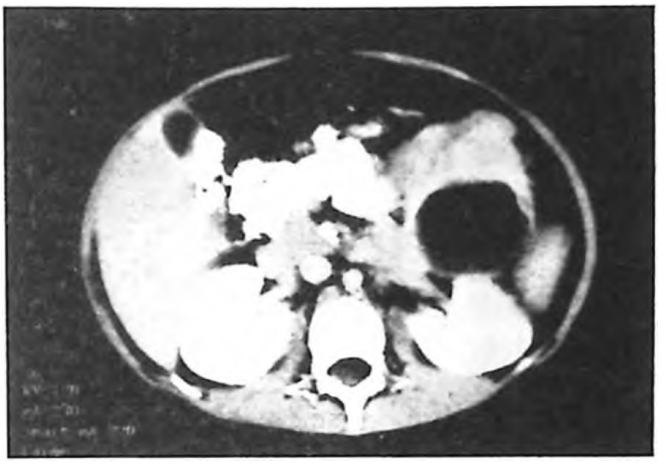
Discussion

Malignant fibrous histiocytoma is rare in childhood, and patients younger than 20 years of age have rarely been reported by investigators[4,5]. A male predominance has been noted in most pediatric series[4,5]. Although the most comon site of the tumor was the extremity, which is similar to findings of adults'



(a)

Fig. 1. The computed tomographic appearance of the tumor at the time of diagnosis (a) and after 2 cycles of chemotherapy (b).



(b)

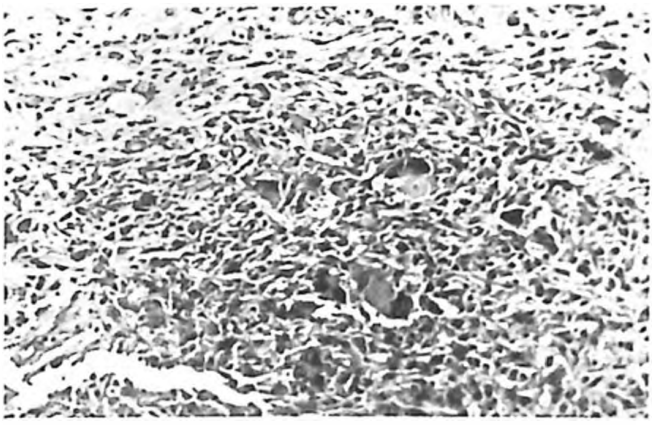


Fig. 2. Histological appearance of malignant fibrous histiocytoma consisting of pleomorphic neoplastic cells with some inflammatory response (H E x 200).

series, different sites have been reported in children[7-14]. Moreover, MFH is one of the most common radiation-induced sarcomas[4,15].

Cole et al.[5] reported that clinical presentation and physical findings of malignant fibrous histiocytoma are similar in children and adults. The diagnosis of MFH is made using histopathological and clinical findings. Berardo et al.[16] reported that although fine-needle aspiration in soft tissue lesions remains controversial, it is important in the initial triage of patients with soft tissue tumors, and is particularly accurate for confirming recurrent or metastatic disease. The tumors of MFH are solitary, multilobulated, fleshy masses that frequently involve deep muscle and are often larger than 5 cm at the time of diagnosis[5]. Most lesions occur as painless lumps in the extremities or retroperitoneum[5]. In our case, the lesion was painless and was located in left the patient's retroperitoneum.

Histological examination shows varying proportions of spindled fibroblastic-type cells and plumper histiocytic type cells lacking light microscopic features of differentiation other than collagen production. Some tumors contain a predominantly histiocytic pattern, others a predominantly fibroblastic pattern, and often there is a mixture of both patterns[5]. A number of histological subtypes are defined including storiform-pleomorphic, myxoid giant cell, inflammatory and angiomatoid. Immunohistochemical staining with alpha-1-antitrypsin, alpha-1-antichymotrypsin, and lysozyme, and ultrastructural features of myoblastic and histiocytic differentation suggest an origin of undifferentiated mesenchymal cells[5]. Pathological examination in our case showed that histopathology of the tumor was highly cellular and consisted mainly of vacuolized atypical mesenchymal cells. The mitotic rate was high, with more than 10 mitotic figures per 10 high power field. Atypical mitotic figures were also seen. A wide necrosis was observed throughout the tumor. Immonuhistochemical studies supported the diagnosis of MFH.

The most common site of metastasis is the lung, although metastases to the brain and other sites are also seen[5]. Local recurrence is common because the tumor often grows along fascial planes, forming a pseudocapsule that is often infiltrated[5]. Although lungs are the most common site of metastasis, primary MFH of the lungs has also been reported[9,11]. However, primary MFH of the lungs in children is extremely rare and frequently fatal[11].

Cytogenetic analysis of short-term cultures has revealed chromosomal abnormalities in MFH. The chromosome bands most frequently affected are 19p13, 11p11, 3p12, and 1q11[2,15]. It has been observed that tumors with 19p+ have a pronounced tendency to recur both locally and systemically[15]. Palmer et al.[3] demonstrated that cytogenetic and molecular genetic evidences of pediatric and adult MFHs are histologically related entities. Unfortunately, cytogenetic examination of the tumor tissue could not be done in our case.

Because of the rarity of this tumor in childhood, the approach to treatment of MFH is based primarily on the experience with adults[15]. Surgery is the mainstay of therapy, but there is a high rate of local recurrence even with wide local excision or amputation[5]. Because there is a low incidence of lymph node metastasis, lymph node resection is not recommended with the initial resection[5]. Although complete surgical excision remains the most effective therapy for MFH, several investigators have discussed the role of adjuvant chemotherapy and radiation therapy[4]. Zagars et al.[17] reported that patients with myxoid tumors do not require systemic therapy. Patients with nonmyxoid disease exceeding 5 cm are at significant risk for metastases, and the development of effective adjuvant treatment is an important research tool. Chemotherapy with vincristine, dactinomycin, and cyclophosphamide with or without doxorubicin has produced objective tumor regressions in children with advanced disease[15]. A study in adults suggests that ifosfamide may be a more effective agent against soft tissue sarcomas than cyclophosphamide[15]. Further, studies in adult patients with advanced disease have demonstrated a higher response rate after ifosfamide was added to the regimen. For this reason, we put our patient on a combined chemotherapy regimen consisting of vincristine, adriamycin and ifosfamide. The treatment of angiomatoid MFH is different from that for classic adult-type MFH. Because the risk of metastasis is very low, adjuvant chemotherapy is not indicated. However, this tumor does ocasionally metastasize. Radiation therapy with moderate doses (4000-6000 rad) has been shown to improve survival in various soft tissue sarcomas and substantially reduced the recurence rate in adults with MFH[5]. radiation therapy may be used in cases of an initially inoperable tumor or in patients in whom incomplete resection cannot be avoided[4].

Relatively few studies have examined the prognostic factors associated with MFH. According to the "Pediatric Oncology Group Non-Rhabdomyosarcoma Soft Tissue Sarcoma" grading system, angiomatoid MFH is classified as a low-grade (grade 1) tumor, and the remandier of MFH are intermediate or high-grade (grade 2) tumors. The survival rate of children with MFH described was somewhat better than that of several series of adult patients[4]. Corpron et al.[4] demonstrated that large tumor size (diameter > 5 cm) is predictive of a poorer prognosis. Tumor size has also been found to be a significant prognostic factor for adults with MFH[4].

Although MFH is rare in childhood, it should be kept in mind in the differential diagnosis of a child presenting with painless abdominal mass.

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