Successful treatment of retroperitoneal giant cell-type malignant fibrous histiocytoma in a 5-year-old boy

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Malignant fibrous histiocytoma, usually seen in patients older than 10 years, is an aggressive soft-tissue sarcoma occurring mostly in the extremities and the trunk, but it is extremely rare in children. We report the clinical, radiological and pathologic features of a five-year-old boy who was diagnosed as a retroperitoneally originated malignant fibrous histiocytoma. The patient with unresectable mass was successfully treated with multidisciplinary approach, with chemotherapy, surgery and radiotherapy, by using combined chemotherapy consisting of vincristine, cisplatinum, adriamycin, cyclophosphamide, actinomycin D and dacarbazine.

Key words: giant cell-type malignant fibrous histiocytoma, retroperitoneal, children.

Malignant fibrous histiocytoma (MFH) was first introduced by Ozzello et al.[1] in 1963, and then more details of its histopathological appearance were described by O'Brien, Stout and Lattes[1,2]. Soft tissue sarcomas, malignant tumors of extra-skeletal connective tissues, which consist of rhabdomyosarcomas and non-rhabdomyosarcomas, are relatively rare in the childhood period[1-5]. Rhabdomyosarcoma is the most common soft tissue sarcoma in the childhood period[4]. Non-rhabdomyosarcoma soft tissue sarcomas (NRSTS), such as synovial cell sarcomas, MFH, fibrosarcomas, and malignant peripheral nerve sheath tumors, are rare and heterogeneous tumors sharing some biologic characteristics but differing in histology, and account for only 3% of all childhood malignancies[3-5].

Malignant fibrous histiocytoma of soft tissue origin, with the possibility of occurrence in the retroperitoneal region, is extremely rare in the childhood period[1-5]. Because this tumor is rare in the pediatric population, many treatment modalities of MFH are extrapolated from the adult experience[1-6]. The approaches to treatment of the disease and prognostic factors that affect survival in pediatric patients have not been well described in the literature[1-6].

In this report, we describe clinical, pathological findings and successful treatment of a five-year-old boy presented with retroperitoneal huge mass consisting of necrotic and calcified areas who was diagnosed as a giant cell-type MFH.

Case Report

A five-year-old boy with a two-day history of painless abdominal mass was referred to our department with no other symptoms. On physical examination, an abdominal mass with a diameter of 15x15 cm was palpated on the left side of the umbilicus extending to the pelvic aperture. No other remarkable findings on the physical examination were detected.

Laboratory studies revealed a white blood cell count of 13,400/mm^3, a hemoglobin level of 9.6 g/dl and a platelet count of 486,000/mm^3. Renal and liver function tests were within the normal limits, with a creatinine clearance of 113 ml/min/m^2. Diagnostic studies including radiographs of the lung and skeletal survey showed no evidence of disease. Abdominal ultrasonography demonstrated a solid mass 113x99 mm in size having cystic areas located on the whole left side of the

abdomen not involving surrounding visceral organs. Abdominal computed tomography (CT) demonstrated an 82x81x92 mm heterogeneous mass, which caused a lytic lesion on the corpus of L3 vertebra and consisted of calcified and necrotic areas, originating from the left retroperitoneal region and extending through the right side of the abdomen without infiltration of the left kidney or adrenal gland (Fig. 1). No abnormality was detected on the thorax tomography. Since the mass was unresectable, a tru cut biopsy was done for diagnosis. Bone marrow aspiration and biopsy revealed no infiltration and on the pathological evaluation no abnormality was found. Due to the limitation of the tru cut biopsy specimen, diagnosis could not be determined clearly so incisional biopsy was performed. The pathologic examination (Fig. 2a) revealed a tumor composed of a mixture of histiocytes, fibroblasts, foamy histiocytes and giant cells. Fibroblasts and histiocytes showed mild pleomorphism and mitotic activity. Two types of giant cells were observed: osteoclast-like giant cells and the malignant tumor giant cells with enlarged and hyperchromatic nuclei. There were no osteoid foci. No lipoblast was observed. The tumor was infiltrating the mature bone tissue at the periphery of the lesion. Immunohistochemically, tumor cells were negative for cytokeratin, HMB45, desmin, alpha-smooth muscle actin, myoglobin, mdm2 and cdk4. Positivity for S-100 and CD68 was observed in histiocytes and giant cells. Tumor cells were diffusely positive for vimentin[7-10].

With the diagnosis of giant cell-type MFH, he was put on a combined chemotherapy started with an induction period consisting of vincristine (1.5 mg/m^2, day 1), cisplatinum (90 mg/m^2, day 1), adriamycin (30 mg/m^2, days 1,2) and cyclophosphamide (10 mg/kg, days 1,2,3) every three weeks and then maintenance period including vincristine (1.5 mg/m^2, day 1), cyclophosphamide (10 mg/kg, days 1,2,3), and actinomycin D (15 γ/kg, days 1,2,3,4) alternating with cisplatinum (90 mg/m^2, day 1), adriamycin (45 mg/m^2, day 1) and dacarbazine (400 mg//m^2, days 1, 2) every four weeks[2-4]. At the end of the induction period (four courses), he showed a minimal response with only 20% decrease in size and enlargement of necrotic areas of the tumor with no difference in the vertebral lytic lesion. Gross total resection of abdominal mass and removal of a part of vertebral corpus with lytic lesion were done. On the evaluation of the CT and F-18FDG whole body positron emission tomography (PET), a residual disease on the L3 vertebra was detected with absence of abdominal mass (Fig. 3a). On the further

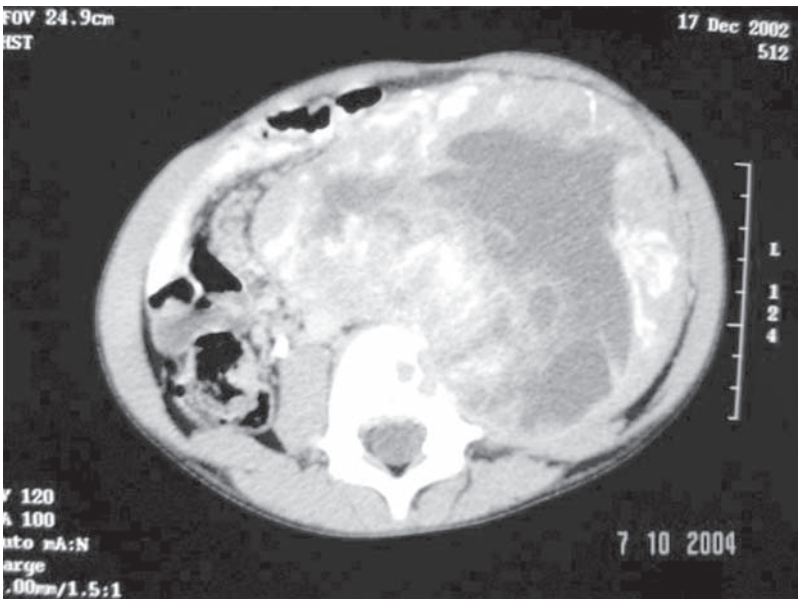

Fig. 1. Computerized tomography findings on admission.

pathologic examination (Fig. 2b), tumor tissue was mostly necrotic and calcified. The non-necrotic areas of the tumor showed similar features with the incisional biopsy material.

The patient received radiotherapy on the left hemi-abdomen with a total dose of 4000 cGy and on the local area of L2-L3-L4 with an additional dose of 1040 cGy. After 12 courses of combined chemotherapy (4 courses of induction period and 8 course of maintenance period) completed in one year, no viable residual lesion was detected on CT or PET (Fig. 3b). He was off treatment for 20 months without any evidence of disease.

Discussion

Malignant fibrous histiocytoma, with an incidence of 2-7% of all soft tissue sarcomas in the pediatric population, is mostly reported in the fifth and sixth decades as an adult malignancy in the literature[1-14]. Male predominance with a 2 to 1 male to female ratio has been reported[1-2]. MFH has a typical origin of subcutis and deep dermal layer of the body with a most frequent occurrence in the extremities followed by the retroperitoneum in adult age, in contrast to the head and neck regions in pediatric patients. However, data on the etiology of MFH is limited; exposure to

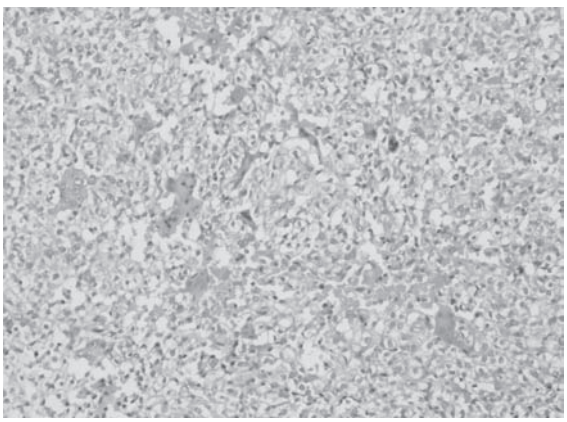

Fig. 2a. Tumor composed of giant cells, fibroblasts and histiocytes (hematoxylin and eosin-HE, X200).

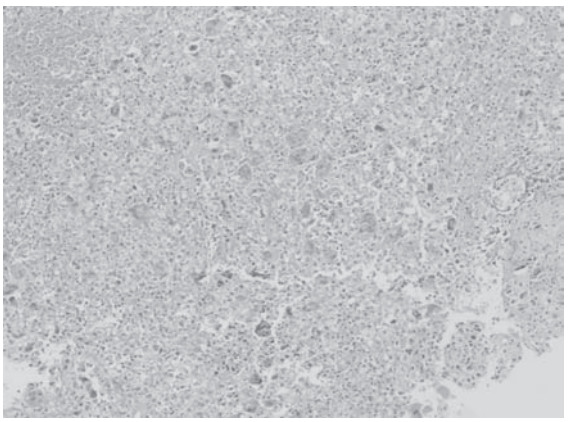

Fig. 2b. Tumor with necrotic and calcified areas with numerous giant cells after chemotherapy (HE X100).

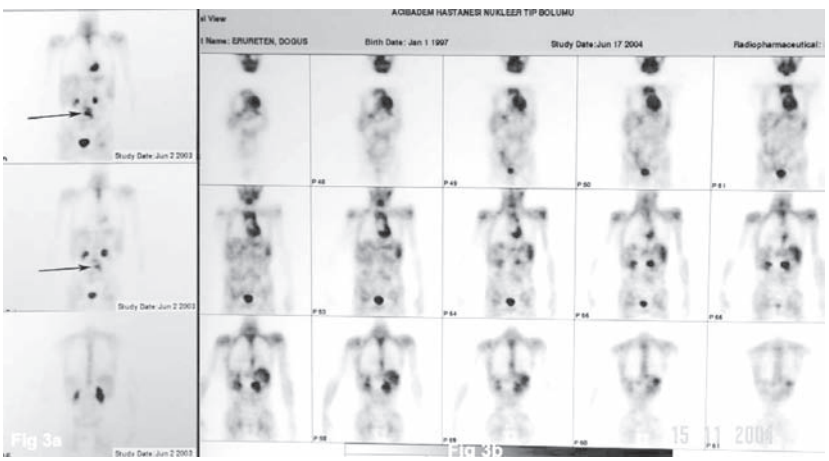

Fig. 3a-b. Positron emission tomography (PET) findings of the patient.

ionizing radiation, xeroderma pigmentosum, burn scars, scarring dermatosis, chronic ulcers and previously diagnosed hematopoietic diseases including Hodgkin's lymphoma, melanoma multiplex and malignant histiocytosis have been described as etiologic factors of MFH in some reports[1,2,6].

At the time of the diagnosis, MFH is mostly manifested as an enlarging painless soft tissue mass and is typically larger than 5 cm in diameter[1,2]. Most lesions occur in the extremities, with the possibility of remaining painless for several years, or in the retroperitoneum with constitutional symptoms including fever, malaise and weight loss[1,2,13]. Retroperitoneal disease may cause expansion, distension, hernia, varicocele with a mass effect and hormonal abnormalities such as hyperglycemia and hyperinsulinemia as a result of insulin-like substance produced by tumor cells.

The histogenetic origin of MFH is supposed to be either primitive mesenchymal stem cells or primitive fibroblastic or histiocytic cells[1,2,5,14]. MFH can be confused with pleomorphic rhabdomyosarcoma, extrarenal rhabdoid tumor, liposarcoma, large cell lymphoma and anaplastic carcinoma[1,7,10]. It is very difficult to differentiate the subtypes of MFH and distinguish it from other malignant tumors[7,8]. Specially five histologic subtypes of MFH are defined, including storiform-pleomorphic type as the most common form, myxoid type, giant cell type with usually multinodular morphology, inflammatory type as frequently retroperitoneally originated, and angiomatoid type, which is mainly seen in children and young adults located more superficially than other variants[1-6,11,14].

It is reported that a retroperitoneal poorly differentiated sarcoma resembling MFH or fibrosarcoma should be investigated for a liposarcoma component histologically and for immunohistochemical positivity for mdm2 and cdk4 to exclude a diagnosis of dedifferentiated liposarcoma[9,10]. We eliminated the diagnosis of dedifferentiated liposarcoma as the tumor did not contain lipoblasts and the tumor cells were negative for mdm2 and cdk4. The possibility of rhabdomyosarcoma was also excluded as the skeletal muscle markers were negative immunohistochemically.

Metastatic disease is demonstrated in 0-43% of childhood MFH and 5-41% of adult MFH[4]. The highest metastasis ratio among the MFH subtypes is 50% in giant cell subtypes[6]. The most common site of metastasis is lung (90%), followed by the lymph nodes (35%), bones (8%), and liver (1%), although spreading to peritoneum, brain and other organs can be seen[1-6,11-14]. The survival rate of illness depends on some prognostic factors such as deepness, which is still controversial, size and grade of the tumor, localization, age of patient, adequacy of surgical margins and also cell types of the tumor[1-6,11-14]. Local recurrence is common in MFH due to the behavior of the tumor growing along facial planes, at a rate of 27% that increases to 43% if there is skeletal muscle involvement[1-6,11-14]. The five-year survival rates can vary depending on tumor size, such as smaller than 5 cm with 82%, 5-10 cm with 63% and above 10 cm with 51%[1-6,11-14]. According to the reported survival rates, children with MFH have a better prognosis than adults[2,4].

In many cases, the pediatric counterparts have a different clinical behavior and outcome. Because of the limited number of MFH cases in childhood, the approach to the treatment is extrapolated from the adult experience.

Although a high rate of local recurrence has been reported, the most acceptable treatment for MFH is a wide surgical excision[1,2,6,13,14]. It is demonstrated that lymph node involvement of the disease is very rare, so regional nodal dissection is not recommended except in the case of enlarged lymph nodes on examination or scanning[2,5,6,13,14]. In the literature, the effectiveness of adjuvant chemotherapy and radiation therapy in pediatric patients is not described clearly. As a result, their use is recommended in some conditions such as metastatic disease, disease of high metastatic potential or in large unresectable tumors[2,5,6,13]. Chemotherapeutic agents including vincristine, actinomycin D and cyclophosphamide with or without doxorubicin are mostly used in the treatment of the disease. Use of cisplatinum, ifosfamide, dacarbazine and VP-16 agents has also been reported in the treatment of the disease[2,3,5,14]. Moderate doses of radiation therapy have been revealed to improve the local control of inoperable or unresectable tumors and incompletely excised tumors.

In our case, unresectable disease presenting with painless abdominal mass originating from the retroperitoneum in a pediatric patient without any metastasis was successfully treated with multidisciplinary approach. As described in the literature, after the chemo reduction of the disease, wide local excision and radiotherapy were done to decrease the local recurrence probability of the disease[2-4]. The patient is now 20 months into his follow-up for recurrence or metastasis of the disease. At the last follow-up he had no evidence of local recurrence or metastasis of the disease on the conventional methods and PET.

We suggest that abdominal tumors originating from the retroperitoneal region in pediatric patients should be evaluated more carefully.

REFERENCES

1. Repassy D, Csata S, Sterlik G, Hazslinszky P. Retroperitoneal malignant fibrous histiocytoma. Int Urol Nephrol 1999; 31: 303-311.
2. Köseoğlu V, Kürekçi AE, Kul M, Öztürk H, Günhan O, Özcan O. Malignant fibrous histiocytoma in a child. A case report and review of the literature. Turk J Pediatr 2000; 42: 72-75.
3. Pappo AS, Rao BN, Jenkins JJ, et al. Metastatic nonrhabdomyosarcomatous soft-tissue sarcomas in children and adolescents: the St. Jude Children's Research Hospital experience. Med Pediatr Oncol 1999; 33: 76-82.
4. Daw NC, Billups CA, Pappo AS, et al. Malignant fibrous histiocytoma and other fibrohistiocytic tumors in pediatric patients: the St. Jude Children's Research Hospital experience. Cancer 2003; 97: 2839-2847.
5. Belal A, Kandil A, Allam A, et al. Malignant fibrous histiocytoma: a retrospective study of 109 cases. Am J Clin Oncol 2002; 25: 16-22.
6. Rothman AE, Lowitt MH, Pfau RG. Pediatric cutaneous malignant fibrous histiocytoma. J Am Acad Dermatol 2000; 42: 371-373.
7. Brooks JS. Disorders of soft tissue. In: Mills SE (ed). Sternberg's Diagnostic Surgical Pathology (4th ed), Vol. 1. Philadelphia: Lippincott, Williams & Wilkins; 2004: 137-222.
8. Oliveira AM, Dei Tos AP, Fletcher CD, Naschimento AG. Primary giant cell tumor of soft tissues - a study of 22 cases. Am J Surg Pathol 2000; 24: 248-256.
9. Gebhard S, Coindre JN, Michels JJ. Pleomorphic liposarcoma: clinicopathologic, immunohistochemical and follow-up analysis of 63 cases: a study from the French Federation of Cancer Centers Sarcoma Group. Am J Surg Pathol 2002; 26: 601-616.
10. Coindre JM, Mariani OM, Chibon F, et al. Most malignant fibrous histiocytomas developed in the retroperitoneum are dedifferentiated liposarcomas: a review of 25 cases initially diagnosed as malignant fibrous histiocytoma. Mod Pathol 2003; 16: 256-262.
11. Barthel H, Wilson H, Collingridge DR, et al. In vivo evaluation of [18F]fluoroetanidazole as a new marker for imaging tumour hypoxia with positron emission tomography. Br J Cancer 2004; 90: 2232-2242.
12. Jadvar H, Fischman AJ. Evaluation of rare tumors with [F-18] fluorodeoxyglucose positron emission tomography. Clin Positron Imaging 1999; 2: 153-158.
13. Gambini C, Haupt R, Rongioletti F. Angiomatoid (malignant) fibrous histiocytoma as a second tumour in a child with neuroblastoma. Br J Dermatol 2000; 142: 537-539.
14. Shah SJ, Craver RD, Yu LC. Primary malignant fibrous histiocytoma of the lung in a child: a case report and review of literature. Pediatr Hematol Oncol 1996; 13: 531-538.