Case Report

A persistent Retroperitoneal Synovial Sarcoma —Effect of Hyperthermia Alone—

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Abstract: An 8-year-old girl was admitted to hospital because of left hip and knee joint pain. We found a tumor in her left iliopsoas muscle, which was diagnosed as a synovial sarcoma. She received chemotherapy and radiotherapy at another hospital, but the tumor showed no response to the treatments. Metastatic humerus bone tumor developed, and she needed morphine derived analgesics. She was introduced to our hospital again, and we started hyperthermia treatment, after that her retroperitoneal tumor decreased in size. We have already performed hyperthermic therapy 27 times. She became not to ask for the analgetic drug and could go to school from her home. In this case, the significance of the treatment is that the tumor response was observed with hyperthermia alone.

Key words: Synovial sarcoma, hyperthermia, chemoresistant

Introduction

Synovial sarcoma is a relatively rare mesenchymal neoplasm. Because surgery combined with radiotherapy or chemotherapy is the main treatment method, there are no more than a few reports on the usefulness of hyperthermia.

We report our experience with one case of persistent retroperitoneal synovial sarcoma in a child treated with hyperthermia alone. Tumor shrinkage and remarkable improvement of activities of daily living (ADL) after the start of hyperthermia were observed, although it was inoperable and resistant to chemotherapy and radiotherapy.

Case Report

The patient was an 8-year-old girl. As pain started in the left hip and the knee joint about November, 2000, she was examined by a nearby doctor. No abnormality was pointed out, and the course

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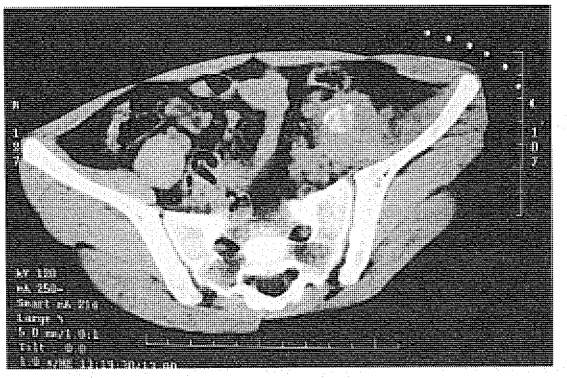

Fig. 1-1 Abdominal plain CT. A soft tissue mass accompanied by calcification in the left iliopsoas muscle

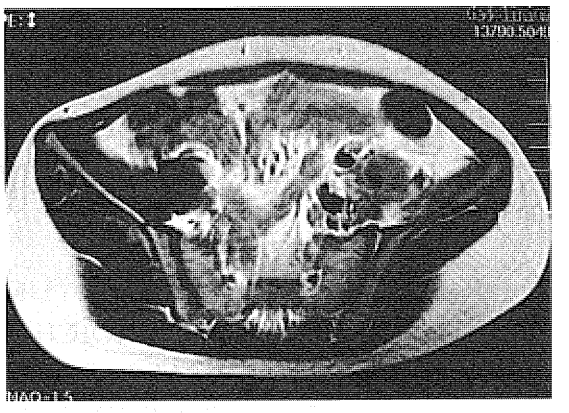

Fig. 1-2 Abdominal MRI. T1-weighted images with gadolinium showed a heterogeneously enhanced mass in this lesion.

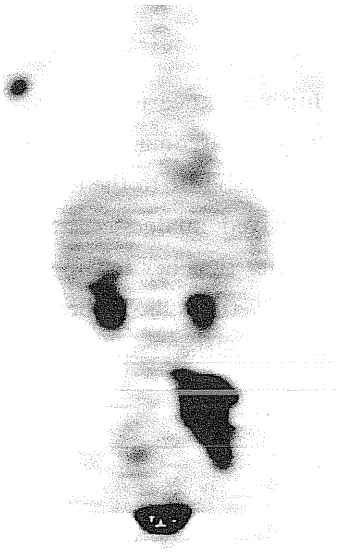

Fig. 1-3 18F-FDG-PET scan. An abnormal accumulation corresponding to the mass in the left iliopsoas muscle region and in the right humerus could be observed.

was palliatively observed. Although the symptom improved for a while, it was aggravated again and gait disturbances such as claudication became observable.

The patient was referred to the Department of Orthopaedic Surgery at Gunma University Hospital in May, 2001. There was no notable finding in the family history or the patient's previous history except repeated otitis media. The findings at the first examination included hamstring contracture in the left hip joint and mild exaggeration of deep tendon reflex in the legs. Muscle atrophy was not clearly noted. Abdominal CT revealed a soft tissue mass accompanied by calcification in the left iliopsoas muscle (Fig. 1-1). Abdominal MRI detected a mass that showed an equal signal to muscles in the T1-weighted image and a heterogenous high signal in the T2-weighted image. T1-weighted images with gadolinium showed a heterogeneously enhanced mass in this lesion (Fig. 1-2). ^{18}F-FDG-PET revealed an extensive abnormal accumulation corresponding to the mass in the left iliopsoas muscle region (Fig. 1-3). An abnormal accumulation was also found in the right humerus, which showed osteolytic change on radiography.

Because these image findings strongly suggested malignant tumors, a CT-guided biopsy of the left iliopsoas muscle region was performed. Pathological findings in the biopsy specimen are shown in Fig. 2. Tumor cells with round to oblong nuclei and short spindle-shaped cytoplasms proliferated densely. Lymphocyte infiltration with a small amount of collagen fibers were observed in the interstitium. On immunostaining, tumor cells were positive to vimentin and negative to desmin, actin and S-100. The findings indicated a malignant soft tissue tumor, but discrimination of synovial sarcoma from fibrosarcoma was necessary. In addition to histological findings, genetic examination was performed, but no particular finding was

observed. Finally, synovial sarcoma (monophasic) was highly likely considering the clinical course and histological findings.

Radical treatment seemed to be difficult, but her parents asked the National Cancer Center for a second opinion. As for treatment, chemotherapy was started in July, 2001 at the Cancer Center. The patient received 4 courses consisting of a high-dose administration of ifosfamide at 14 g/m^2 for 5 consecutive days and alternative therapy with vincristine at 1.5 mg/m^2 and cyclophosphamide at 900 mg/m^2 for 2 days and doxorubicin at 30 mg/m^2 for 2 days. But the therapy showed no response. Subsequent radiotherapy at 50 Gy in the iliopsoas muscle region which started in October, 2001 also showed no response. After the treatment, she always needed a wheel chair, and morphine was used for pain control.

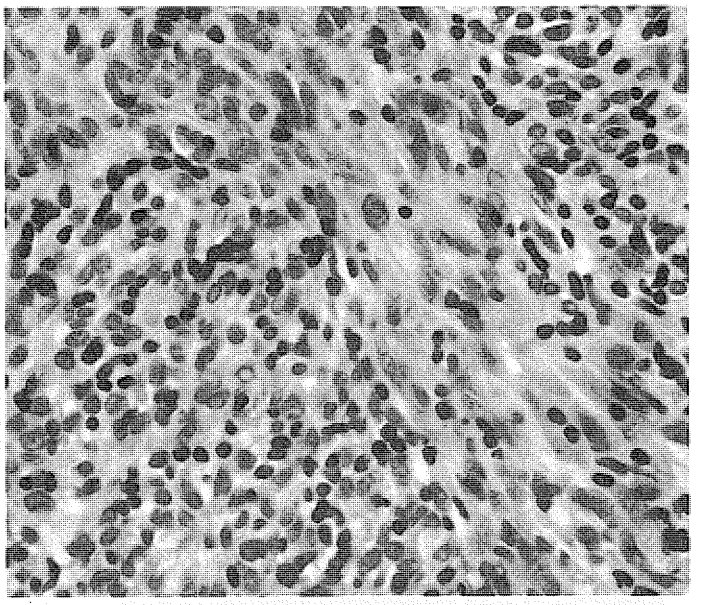

Fig. 2 Pathological findings in the biopsy specimen. Tumor cells with round nuclei and short spindle-shaped cytoplasms proliferated densely. Synovial sarcoma was highly possible.

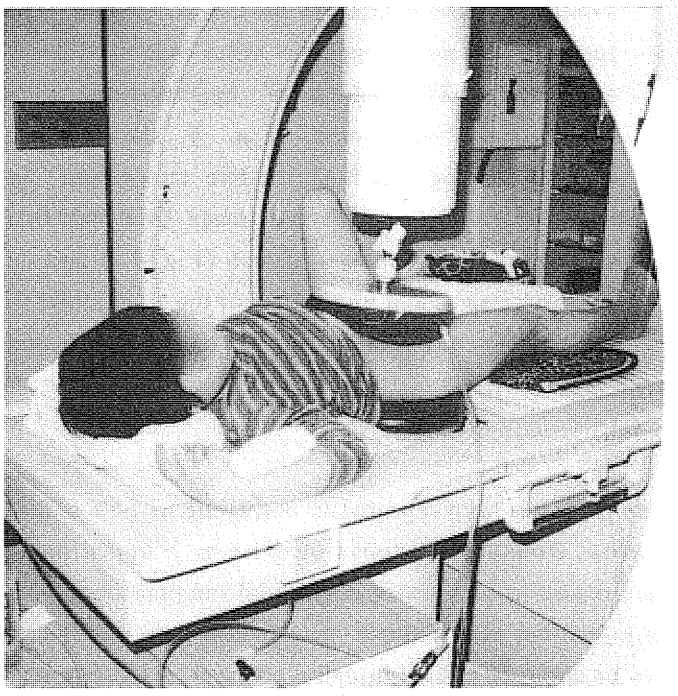

Fig. 3 The treatment scene for hyperthermia

She was examined again at our hospital, where close to her house she received supportive care. She was referred to the Department of Radiation Oncology for palliative treatment after a period of 7 months from the first examination. Radiotherapy to the humerus bone was firstly recommended for prevention of bone fracture, but in view of a strong desire by the patient's parents, it was decided to apply hyperthermia to the retroperitoneal mass.

Fig. 3 shows the treatment scene for hyperthermia. The instrument used was a deep-heating system, Thermotron RF-8 (Yamamoto Binita Co. Ltd., Osaka, Japan), and heating was performed mainly with a pair of electrodes 21 cm in diameter and a circulating water temperature of 5 °C.

Fig. 4　MRI Findings during the hyperthermic treatments

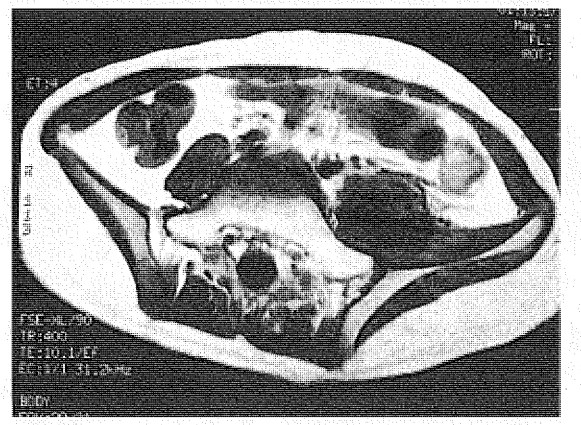

Fig. 4-1 Before treatment

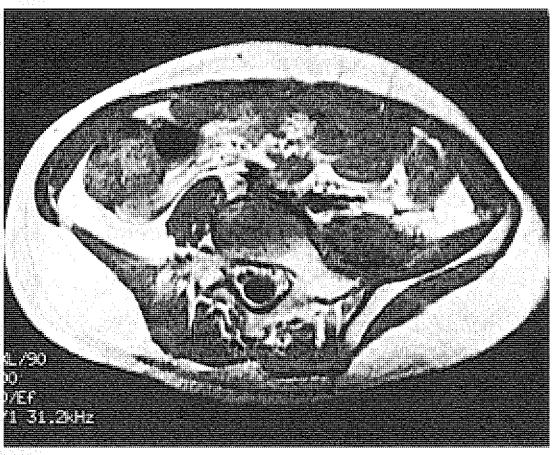

Fig. 4-2 After the treatment with hyperthermia (six times)

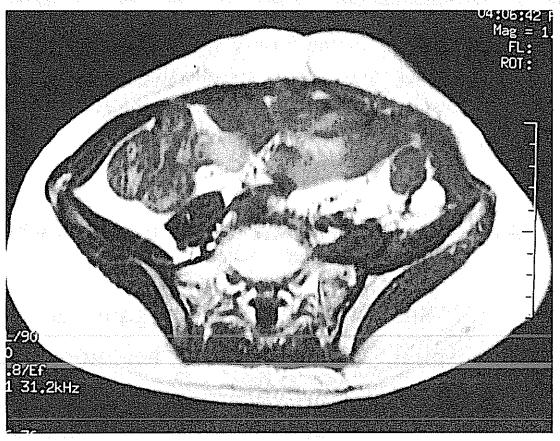

Fig. 4-3 After the treatment with hyperthermia (twenty-two times)

Although temperature measurement was not performed, treatment was given at 300-550 W output for 40-60 minutes while observing the patient's condition. The leg position was supported by folded towels because of difficulty in stretching from the left hip joint. After six weekly sessions of hyperthermia, pain and gait disturbance were alleviated. A distinct reduction in the size of the tumor was also detectable on the abdominal MRI images. As the therapeutic effect was considered satisfactory, 27 sessions of hyperthermia were subsequently performed. Fig. 4 shows MRI findings during the hyperthermic treatments. At the first hyperthermia session, the mass rather showed increasing size in the image from the first examination, but tumor shrinkage was significantly observed in the images after 6 (Fig. 4-2) and 22 sessions (Fig. 4-3) of hyperthermia. Analgesics were not necessary, and alleviation of the contracture in the leg enabled the patient to walk on her own. She can now go to school from home after 1 year and 8 months from the start of hyperthermia.

Discussion

While synovial sarcoma is a relatively rare tumor, it has been reported to constitute to 7-8% of soft tissue sarcomas in children [1]. The tumor often develops around limb joints (lower limbs > upper limbs) but it may develop in the trunk and head and neck region in some cases. Synovial sarcoma sometimes develops not only distant metastases to lungs and bones, but also frequent metastases to regional lymph nodes. The five year survival rate was reported to be about 60% [2]. Although a relatively good five year survival rate of 70-80% has been shown for occurrence of the tumor in the limbs in recent reports, it has

also been reported that the prognosis is poor in cases with tumor sizes exceeding 5 cm, with infiltration in the surrounding tissues, with occurrence in inoperable regions in the trunk or with distant metastases [1) 3) 4)]. Prognosis in cases with distant metastases is particularly poor and the five year survival rate is reported to be only about 10% with median survival for about 1 year [1) 3) 4)]. For diagnosis, chromosomal translocation, t (X, 18) (p11, q11), and high specificity for SYT-SSX fusion gene transcript have been known recently [4) 5)]. In our case, although the result of genetic diagnosis by RT-PCR could not detect chromosomal translocation (SYT-SSX1, SYT-SSX2), sensitivity for SYT-SSX gene was reported to be 85-100% in synovial sarcoma. Moreover, as a sublocation of SSX4 is present for translocation of SSX[5)], the result of genetic diagnosis in our case could not deny synovial sarcoma. In this case, the genetic marker of fibrosarcoma, ETV6-NTRK3, was examined at the same time, but the result was also negative.

Concerning treatments for synovial sarcomas, the efficacy of surgery and postoperative radiotherapy has often been reported. Some reports demonstrated the efficacy of chemotherapy [6) 7)], but there are also negative opinions [1)]. Opinion is divided because of the overall small number of cases and the absence of a prospective study [3) 4)]. Only a few case reports have been found concerning the efficacy of hyperthermia [8)]. A direct antitumor effect of hyperthermia was unknown also in our case, because measurement of the temperature was impossible. In another mechanism of hyperthermia, activation of the antitumor immunological system mediated by heat shock proteins was reported [9)], but this hypothesis is also unproven in this case.

In conclusion, although it is unknown how much direct antitumor effect was attributable to hyperthermia, it has become at least one hope for the child patient and her family. In this case, the tumor response was significantly observed with hyperthermia alone. Because there is no other effective treatment, we are considering to continue hyperthermia for this patient.

References

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難治性の後腹膜滑膜肉腫
—ハイパーサーミア単独の効果—

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要　　旨：症例は8歳，女児．左股関節，膝関節痛の精査加療目的に当院を紹介された．左腸腰筋に腫瘍が認められ，生検にて滑膜肉腫と診断された．他院にて化学療法と腸腰筋部の放射線治療が施行されたが腫瘍の縮小は認められなかった．上腕骨への転移も出現し，疼痛管理のためモルヒネ製剤を使用する状態となった．その後，当院を再度受診，温熱療法を開始した．この治療開始後から腫瘍の縮小傾向が認められたため，現在までに計27回の温熱療法を施行した．鎮痛薬は不要となり，現在は自宅から元気に通学が可能である．本症例では，温熱療法単独により著明な腫瘍縮小が認められた．