Case Report

Long-term Tumor Control of a Fibrosarcoma in the Left Lower Extremity after Thermoradiotherapy and Limb-sparing Surgical Resection

KAZUSHIGE ATSUMI[1], YOSHIYUKI SHIOYAMA[1]*, SATOSHI NOMOTO[1], SAIJI OHGA[1], TADAMASA YOSHITAKE[1], TAKASHI TOBA[1], KAYOKO OHNISHI[1], HIROMI TERASHIMA[2], KAZUHIRO TANAKA[3], SHUICHI MATSUDA[3], KATSUMASA NAKAMURA[4], YUKIHIDE IWAMOTO[3], HIROSHI HONDA[1]

[1]Department of Clinical Radiology, Graduate School of Medical Sciences, Kyushu University, 3-1-1, Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

[2]School of Health Sciences, Kyushu University, 3-1-1, Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

[3]Department of Orthopedic Surgery, Graduate School of Medical Sciences, Kyushu University, Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

[4]Department of Radiology, Fukuoka University, 8-19-1 Nanakuma, Jonan-ku, Fukuoka 814-0180, Japan

Abstract : This case report describes a 40 year old man with a fibrosarcoma arising from the left lower extremity. The tumor was seated deeply in the left lower extremity and the tumor size was 13 cm in diameter and 24 cm in length. The patient was treated with a preoperative combination of hyperthermia and radiotherapy followed by a limb-sparing surgical resection. Radiation therapy was delivered using a Linac 6-MV Xray with two opposed beams. The dose was 3 gray (Gy) per fraction, 5 times per week, for a total dose of 30 Gy. Hyperthermia was given twice a week, and started within 15 minutes after irradiation. Hyperthermia was performed using a Thermotron RF-8, and applied for approximately 40 minutes to achieve a temperature of over 42°C in the tumor. Limb-sparing surgical resection was performed eight days after the completion of radiotherapy and hyperthermia. No local recurrence was observed after 67 months. Furthermore, no serious complications were observed after surgery, and the function of the limb has been completely preserved.

A combination of preoperative thermoradiotherapy and marginal resection for fibrosarcomas arising in the lower extremities may offer a useful therapy for preserving function and for local control. This report describes a fibrosarcoma case arising from a lower extremity which was successfully treated by thermoradiotherapy and limb-sparing surgical resection.

Key Words : fibrosarcoma, lower extremity, preoperative therapy, thermoradiotherapy

Received 1 August, 2007, Accepted 27 August, 2007. *Corresponding author ; Tel, +81-92-642-5695 ; Fax, +81-92-642-5708 ; e-mail, shioyama@radiol.med.kyushu-u.ac.jp
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Introduction

Surgical treatment is considered to be a basic approach for the treatment of soft tissue sarcomas. However, local recurrences occur in a significant fraction (35-70%) of patients who are treated with surgery alone[1]. Therapeutic goals include local control of sarcomas with maximal functional preservation, especially for the tumors in extremity regions, as well as a reduction in the risk of distant metastases. Consequently, combination therapy with surgical resection, radiotherapy, and/or hyperthermia has been used for soft tissue sarcomas in an attempt to improve treatment outcomes[1-5].

Fibrosarcoma represents only about 10% of musculoskeletal sarcomas. A strongly preferred treatment method with a high curability rate for fibrosarcoma is radical resection, which is also used for other histological types of soft tissue sarcomas. However, it is difficult to preserve function if the tumor is deeply seated in the limb, especially in a region adjacent to a critical organ (e.g., the neurovascular band). An adjuvant therapy such as radiation could improve local control and might reduce the incidence of clinically evident metastatic disease. Radiation therapy has been used in conjunction with surgery for soft-tissue sarcoma. However, high-dose irradiation often causes severe complications such as wound healing delays, skin ulceration, and fractures after surgery[2,6].

A combination of preoperative thermoradiotherapy and marginal resection for soft tissue sarcomas arising in the lower extremity has been reported to be a useful therapy for both preserving function and local control[1-5]. This report describes a fibrosarcoma case arising from a lower extremity which was successfully treated with thermoradiotherapy and limb-sparing surgical resection.

Case description

The patient was a 40-year-old male who was diagnosed with a malignant soft tissue tumor of the left thigh. In August 2001, He noticed a mass on his left thigh and went to a local hospital. In September, 2001, he was admitted to another hospital, and pathological examination of the specimen obtained by an open biopsy revealed a Spindle cell sarcoma. The case surgeon in the hospital diagnosed this case, and

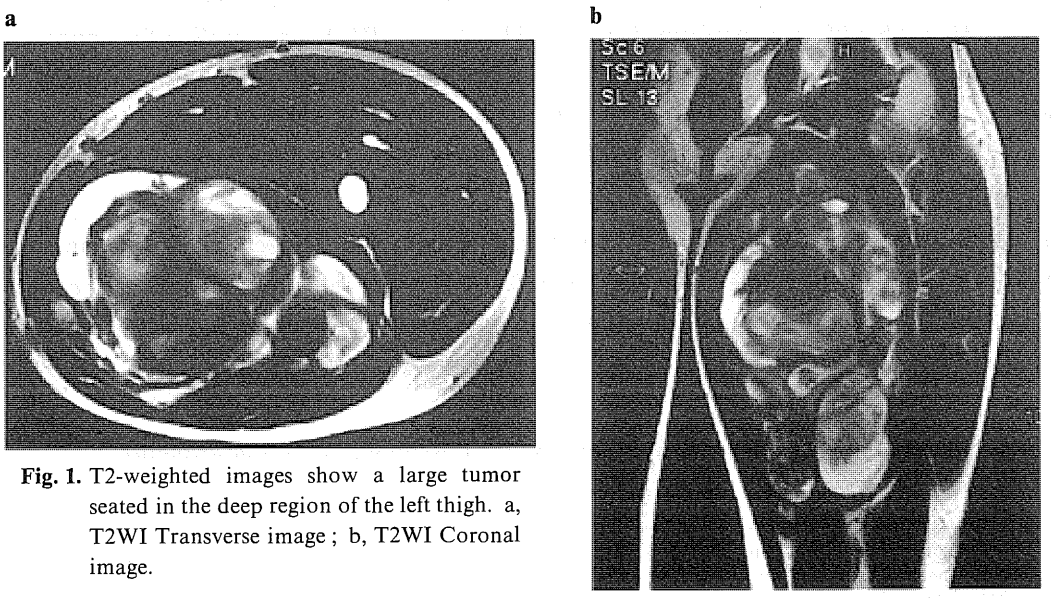

Fig. 1. T2-weighted images show a large tumor seated in the deep region of the left thigh. a, T2WI Transverse image ; b, T2WI Coronal image.

the patient was told that the left limb could be amputated. The patient hoped to preserve his limb, and he was presented to the department of orthopedic surgery at Kyushu University Hospital for treatment in October 2001. Magnetic resonance imaging (MRI) revealed the tumor was seated in the deep lower extremity, and that the tumor size was 13 cm in diameter and 24 cm in length (Fig. 1). In November 2001, he was treated with a preoperative combination of thermoradiotherapy and limb-sparing surgical resection.

Radiation therapy was delivered with a Linac 6-MV Xray machine with two opposed beams. A dose of 3 gray (Gy) per fraction, 5 times per week, for a total dose of 30 Gy was used. Hyperthermia was given twice a week, and started within 15 minutes after irradiation. Hyperthermia was delivered with a Thermotron RF-8, and applied for approximately 40 minutes to produce temperatures over 42°C in the tumor. Temperatures were monitored during treatment at the skin surface and in the central part of the tumor during one treatment session (Fig. 2). MRIs taken after thermoradiotherapy showed that the tumor size was not significantly changed, but contrast within the tumor was decreased when compared to previous images (Fig. 3). Limb-sparing surgical resection was performed eight days after the completion of radiotherapy and hyperthermia. The portion of the tumor adjacent to a neuro-vascular

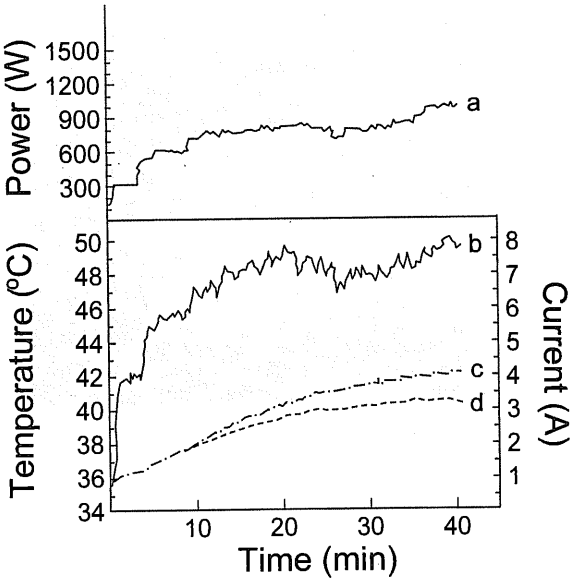

Fig. 2. Temperature was monitored during treatment in the central part of the tumor in one treatment session. Hyperthermia was applied for approximately 40 minutes, and temperatures of over 42°C were generated in the tumor. The graph-a, -b, -c, and -d shows power; current; temperatures in the central part of the tumor; and temperatures at the skin surface, respectively.

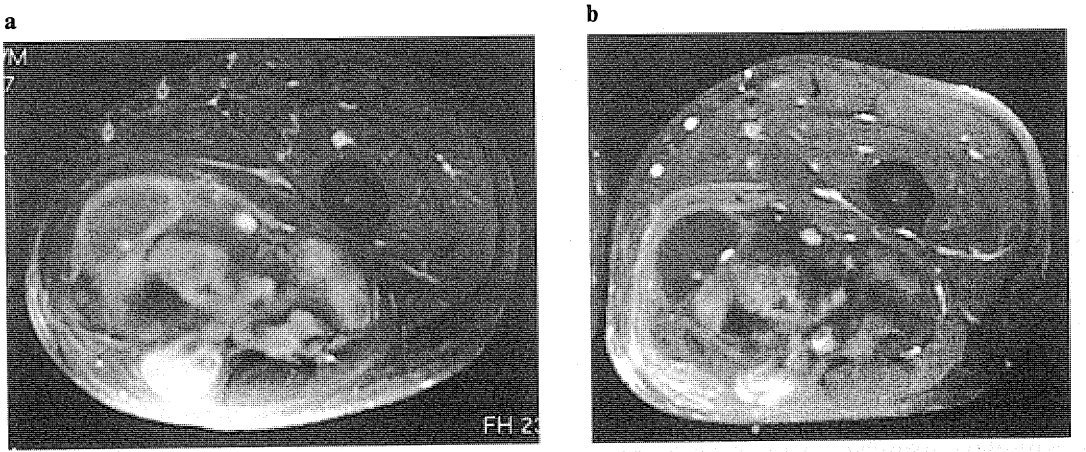

Fig. 3. Post-contrast fat-suppression T1-weighted MRI images before (a) and after (b) preoperative thermoradiotherapy. The tumor's size has not significantly changed, but contrast within the tumor in (b) has decreased in comparison to the earlier image in (a).

bundle was resected marginally. Finally, pathological examination of the specimen obtained by surgical resection revealed that in the fibrosarcoma, necrotic tissues were seen predominantly in the peripheral regions of the tumor (Fig. 4). The surgical margin adjacent to the sciatic nerve was affected by tumor cells.

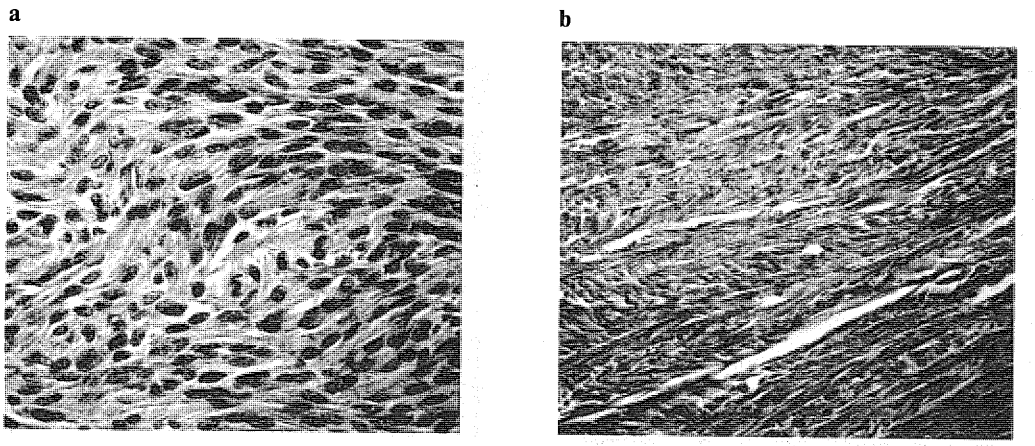

Fig. 4. Pathological examination of the specimen obtained by surgical resection revealed fibrosarcoma. a) a proliferation of spindle-shaped or fusiform cells arranged in fascicles and in a haphazard fashion : b) a necrotic portion seen predominantly in the peripheral region of the tumor.

No local recurrence or distant metastasis was observed after 67 months. Furthermore, no serious complications were observed after surgery. The function of the limb has been completely preserved, and the patient is walking freely and sitting erectly.

Discussion

Surgery is considered to be a basic approach in the treatment of soft tissue sarcomas. However, local recurrences occur in a significant portion (35-70%) of the patients who are treated with surgery alone[1]. This high incidence of local recurrence has been considered to result from daughter lesions around the tumor and/or insufficient resection margin adjacent to critical organs. Consequently, a sufficiently wide resection margin and/or adjuvant treatments such as radiotherapy have been used in an attempt to reduce the risk of local recurrence. Most major medical centers have reported local control rates of 70 to 90% with limb-sparing surgery and radiation for soft tissue sarcomas[7]. L.R. Prosnitz *et al.* reported that preoperative thermoradiotherapy provided excellent local regional control (95%) for aggressive high-grade soft tissue sarcomas[7]. In this particular case, necrotic sections were seen in the tumor after thermoradiotherapy, and no local recurrence was observed for more than 5 years, despite the fact that the surgical margin adjacent to the sciatic nerve was affected by tumor cells. The result in this case may suggest that preoperative thermoradiotherapy played an important role in long-term tumor control. A multidisciplinary treatment with surgical resection, radiotherapy, and/or chemotherapy was shown to achieve favorable local control rates in previous studies in which various soft tissue sarcomas were included[2–5]. Considering that 50 Gy or more of irradiation has usually been thought to be necessary to

control single cancer cells or small numbers of cancer cells in all except for a few kinds of malignancies (e.g., lymphoma, seminoma)[5], the combination of hyperthermia with radiation might have compensated for the lower radiation dose used in this case.

When considering the use of radiotherapy in combination with other treatment modalities, it has not yet been clarified whether pre- or postoperative irradiation is better as an adjuvant therapy for soft tissue sarcomas. Previous studies have suggested no evidence for differences in disease outcome attributable to the use of either pre- or post-operative radiotherapy[9]. Preoperative radiotherapy has been reported to have several advantages, such as lower irradiation doses and smaller irradiated field, over postoperative radiotherapy[1,3,4]. However, preoperative radiotherapy often increases the risk of complications such as wound healing delays, skin ulcerations, and fractures after surgery[2,6]. That there were no serious complications seen after surgery in this patient might be attributed primarily to the relatively low irradiation dose used. Consequently, the excellent local control found in this case suggests that marginal resection combined with preoperative thermoradiotherapy may offer a useful treatment method comparable to extended radical resection.

Previous studies have suggested the possibility that distant metastasis is promoted by hyperthermia[8,9]. To date, however, the role of hyperthermia in the development of distant metastasis is still unclear. In fact, Marmor *et al.* reported an inhibitory effect of hyperthermia on the development of distant metastasis[10]. The relationship between hyperthermia and distant metastasis remains to be defined yet.

This report described a case of fibrosarcoma arising in the lower left extremity which was successfully treated with thermoradiotherapy and limb-sparing surgical resection. A combination of preoperative thermoradiotherapy and marginal resection for fibrosarcoma arising in the lower extremity can be considered as a useful therapeutic approach for both, preserving function and for local control.

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Abstract in Japanese

術前温熱併用放射線療法および患肢温存手術にて根治しえた下肢原発線維肉腫の1例

渥美和重[1]・塩山善之[1]・野元　諭[1]・大賀才路[1]・吉武忠正[1]
鳥羽隆史[1]・大西かよ子[1]・寺嶋廣美[2]・田仲和宏[3]・松田秀一[3]
中村和正[4]・岩本幸英[3]・本田　浩[1]

[1]九州大学大学院医学研究院・臨床放射線科学
[2]九州大学医学部保健学科・放射線技術学科
[3]九州大学大学院医学研究院・整形外科学
[4]福岡大学医学部・放射線科

要　　旨: 40歳男性，下肢原発の線維肉腫の症例．大腿深部に径 24×13cm の腫瘤として認められた．術前の温熱治療，放射線治療の併用療法後，引き続き，患肢温存手術が行われた．放射線治療は，リニアック 6MV X 線を用い，前後対向2門照射，1回 3Gy，週5回法で総線量 30Gy で行われた．温熱療法は，照射期間中に放射線照射後 15 分以内に開始することを原則として，週2回併用された．温熱療法はサーモトロン RF-8 を使用し，腫瘍内温度 42°C以上，加温時間 40 分で行われた．患肢温存手術は温熱併用放射線療法終了 8 日後に行われた．術後に特記すべき副作用もなく，患肢機能も温存された．治療後 67ヶ月，無病生存中である．

下肢原発の線維肉腫に対し，術前温熱放射線治療と温存手術は，患肢機能温存および局所制御の両面で有用と考えられた．我々は，術前温熱放射線療法および患肢温存手術にて根治しえた下肢原発線維肉腫を経験したので報告する．