Palliation of recurrent myxofibrosarcoma with radiotherapy and hyperthermia

Ichinohe K, Kobayakawa M

ABSTRACT

Soft tissue sarcomas are rare biologically and histologically heterogeneous neoplasms that may arise throughout the body. The preferred treatment is total resection with a sufficient margin. Radiotherapy with or without chemotherapy offers another treatment option, but its effectiveness is limited. Hyperthermia, a treatment method that heats tumour tissue by exposing the target tissues to conductive heat sources or non-ionising radiation, is known to enhance the effect of radiotherapy. We report a case of an elderly man with a second recurrent myxofibrosarcoma in the left groin, who responded well to radiotherapy in combination with hyperthermia. This combination treatment was effective in maintaining the patient's quality of life during his remaining years.

Keywords: contralateral lymph node, hyperthermia, myxofibrosarcoma, palliative radiotherapy, recurrence

Singapore Med J 2010;51(11):e187-e190

INTRODUCTION

Soft tissue sarcomas are biologically and histologically heterogeneous neoplasms that are rare and may develop throughout the body. The preferred treatment is surgery, but the prognosis is poor due to the high rate of local recurrence and distant metastases.[1] Radiotherapy offers another treatment option for primary tumours and local recurrence, but its effectiveness is limited.[2] Hyperthermia, a treatment method that heats tumours by exposing the target tissue to conductive heat sources or non-ionising radiation, is known to enhance the effect of radiotherapy.[3] We report a case of an elderly man with local recurrence of myxofibrosarcoma who was not a candidate for resection or chemotherapy. He was treated with radiotherapy in combination with hyperthermia. This combined treatment was effective in maintaining the patient's quality of life (QOL) during his remaining years.

CASE REPORT

A 90-year-old man with a past history of cardiac infarction from six years before first presented at our hospital in May 2002 with a large tumour in his right thigh (Fig. 1). At presentation, he was not on any medication other than those for insomnia. Preoperative examination indicated no nodal or distant metastases. The tumour was then resected at our hospital. Histology revealed a high-grade myxofibrosarcoma with a questionable margin, but the patient did not give his consent for adjuvant therapy.

Fifteen months after the resection, the tumour recurred in the right inguinal region (Fig. 2). The patient was then referred to a provincial cancer centre, where he underwent a second resection with curative intent after preoperative irradiation of 25.0 Gy in ten fractions. The postoperative margins were negative.

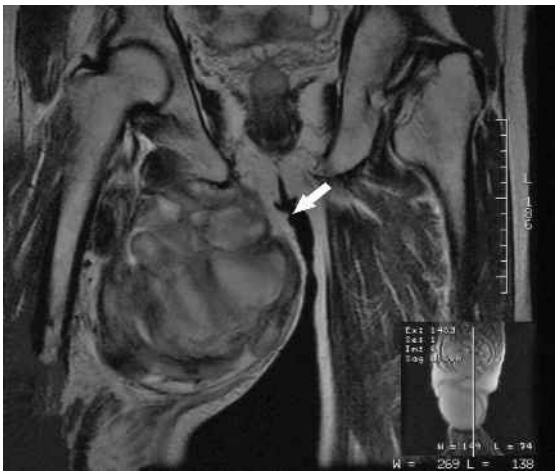

Fig. 1 Coronal T2-W MR image of the patient at first presentation shows a large tumour in the right thigh (arrow).

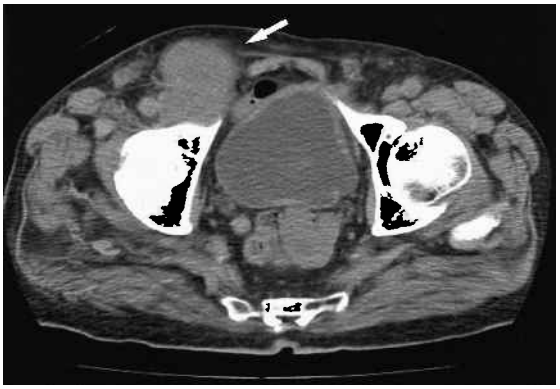

Fig. 2 Non-contrast CT image, performed 15 months after the resection of the primary lesion, shows a recurrent tumour in the right inguinal region (arrow).

Department of Radiotherapy, Fukuroi Municipal Hospital, 2515-1 Kunou, Fukuroi, Shizuoka, Japan

Ichinohe K, MD
Radiation Oncologist

Department of Orthopaedics

Kobayakawa M, MD
Orthopaedist and Chief of Hospital

Correspondence to:
Dr Kenji Ichinohe
Tel: (81) 538 43 2511
Fax: (81) 538 43 5576
Email: koya@moon.odn.ne.jp

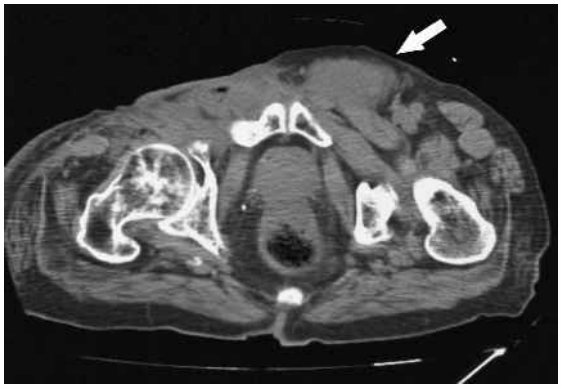

Fig. 3 Non-contrast CT image, performed ten months after resection of the recurrent tumour in the right inguinal region, shows a recurrent tumour in the left inguinal region (arrow).

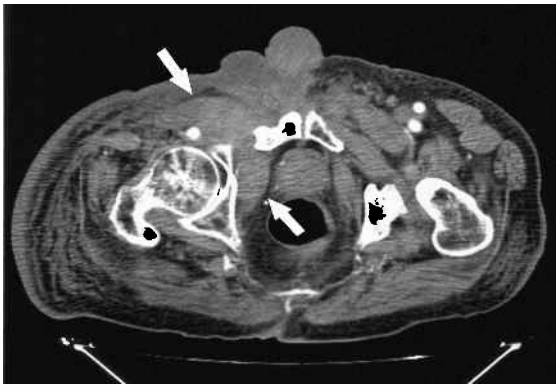

Fig. 4 Post-contrast CT image, performed six months after initiation of radiotherapy and hyperthermia of the tumour in the left inguinal region, shows a recurrent tumour in the right inguinal region (arrows), with no left inguinal tumour seen.

Approximately ten months after the second resection, the patient noticed a painful nodule in the left inguinal region. A computed tomography (CT) examination (Fig. 3) was performed, which revealed a left-sided inguinal tumour. It was diagnosed as a recurrence by biopsy. The patient was again referred to the provincial cancer centre, but no curative treatment was proposed because of the higher risks associated with a third resection in an elderly man with a comorbidity of prior infarction. In addition, neither the patient nor his family wanted any invasive treatments. Hence, he returned home to spend his remaining time with his family for as long as possible, receiving palliative care at our nearby hospital.

On his first follow-up visit to our hospital, the patient looked quite well. His Karnofsky's QOL index was 60%, and there were no visceral metastases on the radiological examination for restaging. As local tumour control seemed to have maintained his QOL, radiotherapy was proposed with adjuvant local hyperthermia on an outpatient basis. With the consent of both the patient and his family, he received an anterior 4-MV X-ray irradiation of 50.0 Gy in 25 fractions and an additional 15 MeV electron irradiation of 20.0 Gy in ten fractions, totalling 70.0 Gy in 35 fractions over 57 days. On CT, the irradiation field was confined to the tumour, with a 1-cm margin. Hyperthermia was started once a week for an hour with a 13.56 MHz radiofrequency apparatus, using two opposed 20 cm ϕ electrodes at 100–200 W shortly after each irradiation. During hyperthermia, the tumour temperature was measured three times directly by CT-guided tumour puncture, and the maximum tumour temperature was 40.0°C, 41.2°C and 40.1°C at each measurement. Although the patient occasionally complained of a hot sensation or pain at the heating site during hyperthermia, these complaints remitted with control of the heating power or heating devices.

Although no change in tumour size was noted on completion of the treatment regimen, the patient did not complain of pain in the left inguinal region or report any symptoms associated with the treatments. Four months later, his family noticed a right-sided inguinal nodule. CT imaging was performed (Fig. 4), which revealed a recurrent tumour in the right inguinal region but complete remission of the left inguinal tumour. On biopsy of the right inguinal tumour, it was diagnosed as a recurrence, and the patient was again referred to the provincial cancer centre. Keeping in mind his previous history of preoperative radiotherapy for the first recurrence of the right inguinal lesion, radiotherapy or invasive treatments were not proposed. Therefore, only observations were continued at the patient's home. 12 months after completion of the treatments, a final follow-up CT imaging was performed, which showed an increase in the size of the right inguinal tumour, but no tumour was found in the left inguinal region. The patient finally died of an intestinal obstruction caused by pelvic extension of the right recurrent inguinal tumour in January 2006, three-and-a-half years after the first operation. From the beginning of radiotherapy with hyperthermia until the final follow-up CT study (a 14-month period), the patient's QOL remained almost unchanged, with no remarkable complications associated with these treatments. An autopsy was not performed.

DISCUSSION

The primary treatment for a soft tissue sarcoma is surgery, which has a five-year survival rate of less than 25%.[1] When surgery is contraindicated, radiotherapy with or without chemotherapy is an alternative, but its effectiveness for curative treatment

is limited.[2] However, hyperthermia is known to enhance not only the effect of radiotherapy, but also that of chemotherapy.[3] In the treatment of locally advanced, high-grade soft tissue sarcomas, hyperthermia has been shown to improve response and survival when combined with chemotherapy.[4] In this case study, an elderly man with a second recurrent myxofibrosarcoma, and who was not a candidate for resection or chemotherapy, was treated effectively with only radiotherapy and hyperthermia. To the best of our knowledge, there have been no other cases in which recurrent myxofibrosarcoma was treated with only radiotherapy and hyperthermia.

At presentation for palliative care at our hospital, the patient had no lesions other than the left inguinal tumour. Therefore, we believed that more effective tumour control could have maintained the patient's QOL for a longer period during his remaining years. As invasive treatments such as resection or systemic chemotherapy may degrade his QOL, we decided to irradiate the tumour as locally as possible. In previous studies, patients with soft tissue sarcomas were treated with a dose of 20.0–70.0 Gy by various irradiation techniques.[5] More recently, a dose greater than 64.0 Gy has been recommended with radiotherapy alone for local control of soft tissue sarcoma.[2] Therefore, considering the dose limits of the skin and underlying soft tissue, the patient was irradiated with a total of 70.0 Gy in 35 fractions for tumour control. Furthermore, we thought that our elderly patient would receive maximum benefit from this treatment because he had already undergone two risky operations (once with preoperative irradiation) with curative intent. Thus, local hyperthermia was used concurrently with radiotherapy to maximise the probability of controlling a local relapse.

During hyperthermia, the tumour temperature was not increased to as high as 43.0°C, as the patient complained of a hot sensation or pain at the heating site. On completion of the treatment regimen, there was no change in tumour size; however, the tumour began shrinking thereafter and finally disappeared four months after completion of the treatments, as shown in the CT images. In general, hyperthermia at temperatures exceeding 43.0°C is known to be effective for killing tumour cells.[3] Therefore, hyperthermia in this case seemed unlikely to control the tumour. However, mild hyperthermia, in which the tumour temperature is not greater than 42.0°C–43.0°C, is known to enhance the radiation sensitivity of malignant disease.[6] Hyperthermia in combination with radiotherapy in this case was thus believed to be effective for the control of the recurrent myxofibrosarcoma.

Although we could not obtain histological confirmation of lymph node metastasis using specimens from both the inguinal regions, the recurrent tumour in the left inguinal region in our patient was thought to be contralateral nodal metastasis, which occurred via the lymphatic system from the right inguinal nodal metastasis of the primary lesion. On the other hand, cases of contralateral nodal metastases have been reported for breast[7] and vulval[8] cancers. This phenomenon has been attributed to the rerouting of the lymphatic drainage by ipsilateral nodal metastases[9] or postoperative/post-radiation collateralisation of the lymphatic system.[10]

Finally, the third recurrence occurred near the primary site, and the patient died of the disease three years and six months after the initial resection. During the radiotherapy and hyperthermia treatment regimen, he visited our hospital every day but was able to spend almost the entire day at home. Furthermore, from completion of the treatment regimen till the final follow-up CT study, the patient was able to live fairly well with his family. The 14-month interval between initiation of radiotherapy in combination with hyperthermia and the last visit for the follow-up CT study constituted over one-third of his survival from the first operation. We believe that effective local control can prolong life and maintain the QOL of patients for a relatively long duration, and that radiotherapy with hyperthermia is an option to control the local recurrence of soft tissue sarcoma without degrading the patient's QOL.

ACKNOWLEDGEMENTS

We wish to thank Tetsuo Nishimura, MD, Division of Radiation Oncology and Mitsuru Takahashi, MD, Division of Orthopaedics, from Shizuoka Cancer Centre, for their assistance with the preparation of this manuscript.

REFERENCES

1. Gutierrez JC, Perez EA, Franceschi D, et al. Outcomes for soft-tissue sarcoma in 8249 cases from a large state cancer registry. J Surg Res 2007; 141:105-14.
2. Tepper JE, Suit HD. Radiation therapy alone for sarcoma of soft tissue. Cancer 1985; 56:475-9.
3. Jones EL, Samulski TV, Vujaskovic Z, Prosnitz LR, Dewhirst MW. Hyperthermia. In: Perez CA, Brady LW, Halperin EC, Schmidt-Ullrich RK. Principles and Practice of Radiation Oncology, 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2004: 699-735.
4. Issels RD, Lindner LH, Verweij J, et al. Neo-adjuvant chemotherapy alone or with regional hyperthermia for localised high-risk soft-tissue sarcoma: a randomised phase 3 multicentre study. Lancet Oncol 2010; 11:561-70.
5. McNeer GP, Cantin J, Chu F, Nickson JJ. Effectiveness of radiation therapy in the management of sarcoma of the soft somatic tissues. Cancer 1968; 22:391-7.
6. Song CW, Park H, Griffin RJ. Improvement of tumor oxygenation

by mild hyperthermia. Radiat Res 2001; 155:515-28.
7. Wellner R, Dave J, Kim U, Menes TS. Altered lymphatic drainage after breast-conserving surgery and axillary node dissection: local recurrence with contralateral intramammary nodal metastases. Clin Breast Cancer 2007; 7:486-8.
8. Jackson KS, Das N, Naik R, Lopes A, Monaghan JM. Contralateral groin node metastasis following ipsilateral groin node dissection in vulval cancer: a case report. Gynecol Oncol 2003; 89:529-31.
9. Leijte JA, van der Ploeg IM, Valdés Olmos RA, Nieweg OE, Horenblas S. Visualization of tumor blockage and rerouting of lymphatic drainage in penile cancer patients by use of SPECT/CT. J Nucl Med 2009; 50:364-7.
10. Milardovic R, Castellon I, Mills C, et al. Scintigraphic visualization of an epigastric sentinel node in recurrent breast cancer after lumpectomy and postoperative radiation therapy. Clin Nucl Med 2006; 31:207-8.