



Case report

Carbon ion radiotherapy for unresectable primary undifferentiated pleomorphic sarcoma of the 11th thoracic spine: a case report

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Abstract

Objective: Primary undifferentiated pleomorphic sarcoma (UPS) of the bone is rare. However, the common sites are the knee and proximal femur and humerus, while spinal involvement is rare. We report a case of primary UPS of the 11th thoracic vertebra, where corpectomy would have been difficult and extensive, treated with carbon ion radiotherapy.

Case report: A 76-year-old man presented with an osteolytic tumor of the 11th thoracic vertebra on plain computed tomography (CT). The spinal cord was compressed and displaced posteriorly by the tumor on magnetic resonance imaging (MRI), and extraosseous extension was observed. An incisional biopsy was performed, and primary UPS of the 11th thoracic vertebra was diagnosed pathologically. Total *en bloc* spondylectomy was considered to be challenging because of the extraosseous extension and the patient's age; thus, carbon ion radiotherapy (70.4 GyE / 32 fraction) was performed. Denosumab (120 mg) was administered subcutaneously every four weeks. No adjuvant chemotherapy was administered. Four years post-treatment, imaging revealed a compression fracture of the 11th thoracic vertebra, but there was no recurrence.

Conclusion: Despite a poor prognosis and an aggressive course of UPS of the spine, the tumor continues to be controlled without local recurrence four years after carbon ion radiotherapy.

Key words: undifferentiated pleomorphic sarcoma, spine, carbon ion radiotherapy

(J Rural Med 2022; 17(3): 176–180)

Introduction

Undifferentiated pleomorphic sarcoma (UPS) is an aggressive type of mesenchymal malignancy previously known as malignant fibrous histiocytoma (MFH). The 2002 World Health Organization (WHO) Soft Tissue Tumor Classification included MFH in conjunction with UPS, but MFH was

subsequently removed in the 2013 WHO classification¹⁾. UPS rarely develops in the bones, accounting for less than 2% of primary malignant bone tumors¹⁾. Bone UPS usually occurs around the knee, proximal femur, and proximal humerus, whereas spinal development is extremely rare. Spinal UPS reportedly has a worse prognosis than UPS at other sites, with a 5-year survival rate of only 7%^{2,3)}. We report a case of primary UPS of the 11th thoracic vertebra, in which total *en bloc* spondylectomy would have been challenging and highly invasive and was thus treated with carbon ion radiotherapy.

Case report

A 76-year-old man with no medical history visited a local physician with a one-month history of low back pain without any trigger. Abdominal computed tomography (CT) revealed a hepatic mass and an osteolytic lesion in the 11th thoracic vertebra, and the patient was referred to the gastro-

Received: September 23, 2021

Accepted: February 9, 2022

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enterology department of our hospital. The hepatic lesion was diagnosed as a hemangioma. The patient subsequently visited our department with a thoracic spinal tumor. The patient was fully ambulatory, but pain was elicited upon percussion of his back. Plain CT at the initial examination demonstrated an osteolytic lesion with slight ballooning in the 11th thoracic vertebra that was partly lobulated and accompanied by marginal osteosclerosis. Thinning and partial disruption of the bone cortex were also observed (Figure 1). Magnetic resonance imaging (MRI) revealed a thoracic spinal tumor with a high signal intensity on the T1-weighted image and a slightly high signal intensity on the T2-weighted image. A peripheral, low-intensity margin suggested osteosclerosis. The tumor slightly displaced the spinal cord,

and extraosseous extension was observed. No abnormal findings were observed in other vertebral bodies (Figure 2).

A slow-growing tumor with hematoma was considered based on the imaging findings. Because there was no past history of malignancy and no primary malignancy was detected on positron emission tomography CT (PET-CT), a CT-guided core needle biopsy was performed. Pathological findings revealed proliferation of atypical cells. Immunohistochemical staining for cytokeratin AE1/AE3 was negative, and bone metastasis from carcinoma was ruled out. Since core needle biopsy did not yield a diagnosis, an incisional biopsy was performed under general anesthesia. Pathological examination of the biopsy specimen revealed multiple multinucleated giant cells with diffuse histiocyte-like mono-

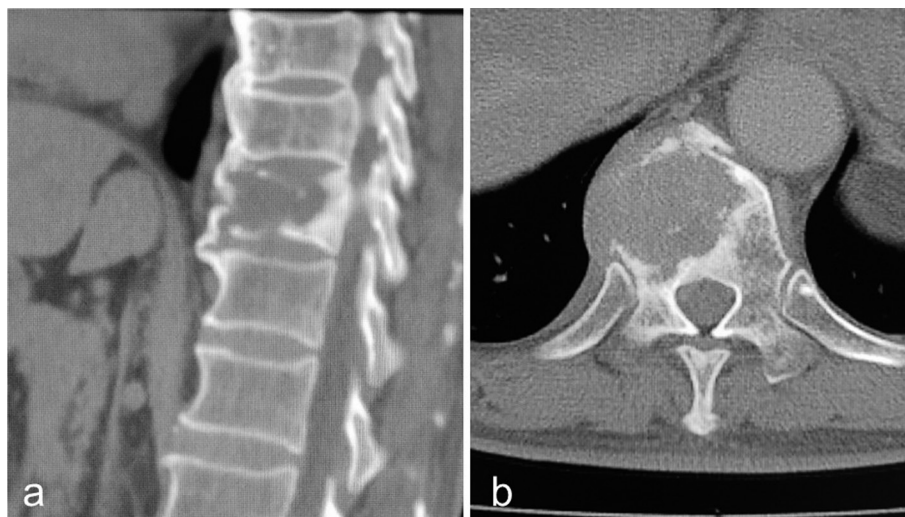


Figure 1 Plain CT of the thoracic spine at the first visit. Plain CT showing an osteolytic lesion with slight ballooning in the 11th thoracic vertebra, some of which were lobulated and accompanied by marginal osteosclerosis, thinning, and partial disruption of the bone cortex. a. Sagittal view b. Axial view.

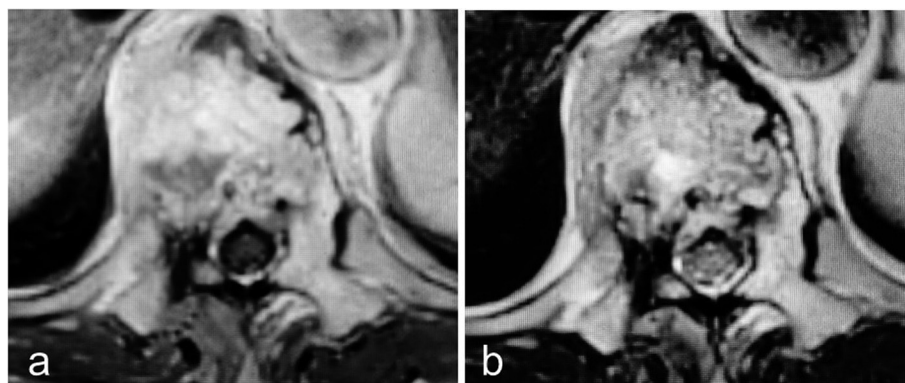


Figure 2 MRI of the thoracic spine at the first visit. MRI showing a tumor with high signal intensity on a T1-weighted image (a) and slightly high signal intensity on a T2-weighted image (b) slightly displacing the spinal cord, with extraosseous extension.

nuclear cells. Despite the general appearance of a giant cell tumor, mononuclear cells showed strong atypia. Immunohistochemistry was negative for cytokeratin, thyroid transcription factor-1(TTF-1), prostate-specific antigen (PSA), cluster of differentiation 31(CD31), and CD34, but positive for CD68 with an MIB-1 labeling index of 20% (Figure 3). A primary UPS of the 11th thoracic vertebra was diagnosed based on pathological findings. Although there were no distant metastases, total *en bloc* spondylectomy was con-

sidered to be challenging because of the extrasosseous extension and high invasiveness for his age; thus, carbon ion radiotherapy (CIRT; 70.4 GyE/32 fraction) was performed (Figure 4). After the CIRT, the patient wore a rigid thoracolumbar brace for two years. Subcutaneous denosumab (120 mg) was administered every four weeks. Denosumab was discontinued after two years. Single-agent adjuvant chemotherapy with doxorubicin was advised; however, the patient refused treatment. At one year follow-up, imaging revealed

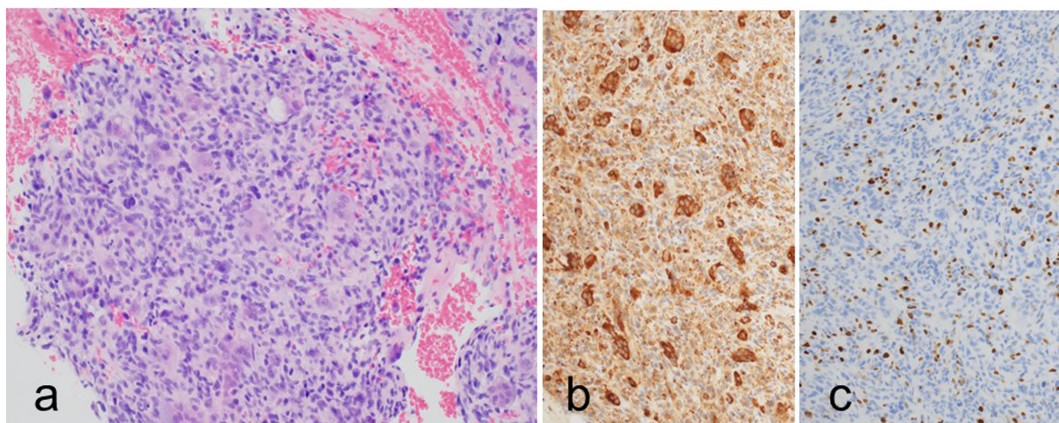


Figure 3 Histopathological findings and immunohistochemistry stain of incisional biopsy specimen. $\times 200$ magnification. Pathological findings of the incisional biopsy specimen demonstrating multiple multinucleated giant cells with diffuse presence of the surrounding histiocytoid mononuclear cells. Despite appearing similar to a giant cell tumor, mononuclear cells show strong atypia (a: hematoxylin and eosin stain). Immunohistochemical staining shows positive CD68 (b) with MIB-1 labelling index of 20% (c).

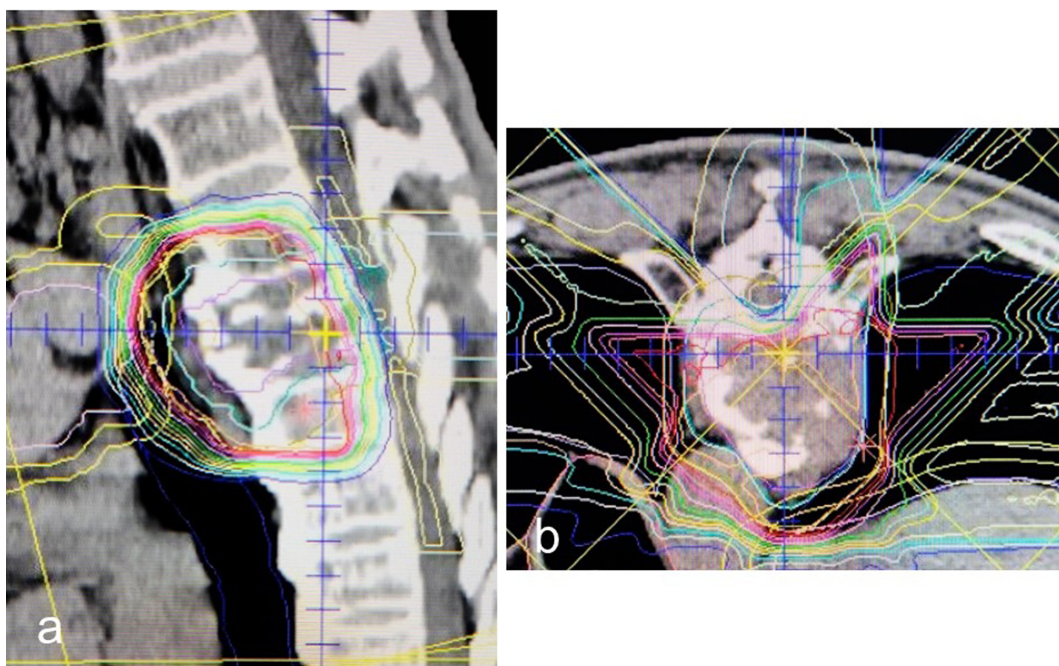


Figure 4 The dose distribution of carbon ion therapy is illustrated for UPS of the 11th thoracic spine (the pink line indicates 95% isodose of the prescribed dose). The spinal cord is in a donut-shaped low-dose irradiation area.

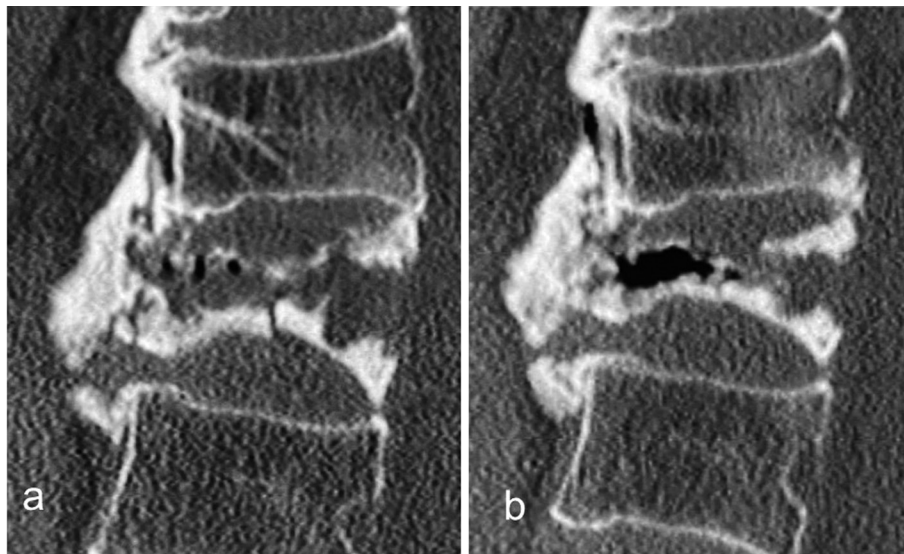


Figure 5 Plain CT after carbon ion radiotherapy. Plain CT after carbon ion radiotherapy showed collapse due to a compression fracture of the 11th thoracic vertebra and intravertebral cleft, and no recurrence of the tumor. a. 1 year after treatment; b. 4 years after treatment.

a compression fracture of the 11th thoracic vertebra and intravertebral cleft; however, the patient was asymptomatic. Subsequent follow-up imaging showed that the extraosseous tumor had decreased in size and osteosclerosis was noted in the vertebral body. At present, four years after CIRT, the patient has no evidence of recurrence, is pain-free, and can walk long distances (Figure 5).

This study was approved by the Institutional Review Board of our hospital. Consent for publication was obtained from the patient.

Discussion

Primary spinal UPS is very rare, many of which develop in the thoracolumbar spine followed by the sacrum. Lesions may involve multiple vertebrae, resulting in osteolytic bone destruction of vertebral bodies, radiculopathy, and myelopathy^{2, 3}.

Spinal UPS is often slow-growing and appears as a complete osteolytic lesion with clear margins, destruction of the bone cortex, and extension into the surrounding soft tissue. Bone destruction is characterized by the absence of a periosteal reaction or new bone²⁻⁵. Similar findings were observed in this case.

We initially suspected that the lesion was a spinal metastasis. However, no primary lesion was detected even on systemic imaging studies, including PET-CT. Histopathological findings were similar to those of giant cell tumors of the bone. However, the mononuclear cells were strongly atypical, and we diagnosed the lesion as a primary thoracic

spinal UPS. As in this case, it can be challenging to distinguish spinal UPS from giant cell tumors of the bone, and there are reports of sacral UPS diagnosed after surgery with extended curettage based on the preoperative diagnosis of giant cell tumor of the bone⁶.

Liu *et al.* conducted a clinical review of 318 patients with bone UPS and noted that the median survival of patients who underwent surgery was 56 months and that of patients who did not undergo surgery was only seven months. They found that surgery alone was a favorable prognostic factor in a multivariate analysis⁷. Özkurt *et al.* also investigated the surgical treatment of 14 patients with UPS in extremity bones and found that the 5-year survival rate for patients who underwent resection with a wide margin was 81.9%. However, the 5-year survival rate of patients who underwent marginal resection was 33.3%⁸. A few reports of a relatively large series of spinal UPS exist, and Teng *et al.* reported a case series of 13 patients with spinal UPS, with a median survival of 18 months. The median survival was 25 months in patients who underwent *en bloc* resection and 14 months after intra-lesional excision⁹. Lou *et al.* examined prognostic factors for survival in 44 patients with spinal UPS who underwent surgery and adjuvant therapy. They reported that subtotal or segmental resection was an independent poor prognostic factor³. In addition, the authors reported that *en bloc* resection at wide margins significantly improved prognosis³. Therefore, *en bloc* resection with negative surgical margins is recommended for spinal UPS^{2, 3, 5}. However, resection with a wide margin was considered impossible because of the extravertebral extension of the tumor in our

case; hence, carbon ion radiotherapy was chosen.

In a report by Matsumoto *et al.* of 47 patients with unresectable spinal sarcoma (excluding the sacrum) treated with carbon ion radiotherapy, the median survival was 44 months, with a 5-year local control rate of 79% and a 5-year survival of 52%⁹.

In cases of dural sac compression, the distance between the spinal cord and tumor cannot be secured, and recurrence at the margin of the irradiation field near the spinal cord becomes a problem⁹. However, four years after the CIRT, no local recurrence or distant metastasis was observed. Therefore, long-term survival is possible in this patient.

The use of chemotherapy for spinal UPS remains controversial. Lehnhardt *et al.* analyzed 140 cases of UPS in the extremities and noted that adjuvant chemotherapy had no prognostic impact¹⁰. Özkurt *et al.* reported that all 14 patients with bone UPS of the limbs were treated with wide resection and adjuvant chemotherapy using doxorubicin, ifosfamide, methotrexate, and cisplatin, which potentially showed efficacy and improved survival⁸. The authors concluded that it was appropriate to administer chemotherapy in addition to wide resection of the lesion to improve survival⁸. Liu *et al.* analyzed 318 patients with bone UPS in the extremities and reported that chemotherapy significantly prolonged survival in univariate analysis but was not significantly different in multivariate analysis⁷. All previous reports are based on the UPS of the extremity bone, and the effect of chemotherapy with spinal UPS is unclear.

High-dose radiotherapy, such as stereotactic radiother-

apy, can cause tumor shrinkage but may also cause osteonecrosis, leading to spinal compression fractures and spinal deformities¹¹. A retrospective analysis of spinal compression fractures after stereotactic radiotherapy by Sahgal *et al.*¹² revealed that the risk of fractures was 14% in 57 lesions. Therefore, the incidence of spinal compression fractures with stereotactic radiotherapy is higher than that with conventional radiotherapy (incidence rate, 3–5%), and 65% of these fractures occur within four months of stereotactic radiotherapy¹².

Matsumoto *et al.* reported that the incidence of spinal compression fractures after CIRT was as high as 23% at a median follow-up of seven months¹¹. In our case, spinal compression fracture occurred approximately one year after CIRT. The bone lesion was osteolytic, and more than half of the vertebral body was replaced by the tumor, which may have led to a post-irradiation fracture¹². Although CT revealed an intravertebral cleft, suggesting non-union, the patient did not complain of pain, and ambulation with long-distance walking was achieved.

Conflict of interest: The authors declare that they have no conflict of interest.

Acknowledgement

We would like to thank Editage (www.editage.com) for English language editing.

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