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CITATION:

Kusakabe, Morimi ...[et al]. Paraplegia Caused by Multifocal Osteosarcoma With Spinal Lesions. International Journal of Spine Surgery 2021, 15(6): 1234-1237

ISSUE DATE:

2021-12

URL:

<http://hdl.handle.net/2433/278948>

RIGHT:

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Paraplegia Caused by Multifocal Osteosarcoma With Spinal Lesions

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ABSTRACT

Background: Multifocal osteosarcoma is a rare condition that may be either synchronous or metachronous. Spine involvement of multifocal osteosarcoma is very rare. Synchronous multifocal osteosarcoma is typically described as the occurrence of tumors at two or more sites in the absence of pulmonary metastases.

Methods: A 55-year-old man initially presented with low back pain. Multiple osteosclerotic lesions were observed, primarily in the spine and pelvis, as well as in soft tissues. Lung lesions were observed, but they were relatively small at reference. Laboratory tests showed a markedly elevated alkaline phosphatase (ALP) level of 36,416 U/L (normal range, 115–359 U/L). Based upon a diagnosis of osteosarcoma on biopsy, chemotherapy was administered, resulting in a decrease in ALP to 17,833 U/L.

Results: Decompression of the symptomatic compressed spinal cord and posterior spinal stabilization of T8–12 were performed. However, progressive extensions of multiple lesions to the spinal canal led to paraplegia with urinary dysfunction. Eleven months after the first visit to our hospital, the patient died due to multiple organ failure.

Conclusions: Multifocal osteosarcoma accompanied by spinal lesions may lead to paraplegia, a clinical problem that negatively affects the quality of activities of daily living.

Level of Evidence: 4.

Clinical Relevance: Multifocal osteosarcoma accompanied by spinal lesions may lead to paraplegia, a clinical problem that negatively affects the quality of life and activities of daily living.

Tumor

Keywords: osteosarcoma, paraplegia, spinal canal, spinal cord, spine, multiple

INTRODUCTION

Osteosarcoma is a malignant bone-forming tumor¹ that is the most common type of bone tumor, followed by chondrosarcoma and Ewing sarcoma.² Multifocal osteosarcoma, or multicentric osteosarcoma, is a rare condition that was first described by Silverman.³ It is typically defined as the presence of two or more lesions in the absence of pulmonary metastases.⁴ Multifocal osteosarcoma can be divided into two categories: synchronous and metachronous. Synchronous multiple lesions develop within 6 months of each other, while metachronous lesions appear over a longer period.^{5,6} Synchronous multifocal osteosarcoma is predominantly observed in children and young adults, and it accounts for approximately 0.4% to 4.2% of all osteosarcomas.^{7,8} Because the incidence of osteosarcoma is relatively low, opportunities to see patients with multifocal osteosarcoma in the clinic are rare.

Spinal osteosarcoma tends to occur in older individuals compared to osteosarcoma of the extremities.⁹ The spine is a rare site for osteosarcoma, with spinal

osteosarcoma representing 0.85% to 3% of all osteosarcomas.^{9,10} For synchronous multifocal osteosarcoma, involvement of the spine is rather rare at 8%, with the most commonly involved anatomic sites being long bones, including the distal femur (17%), proximal tibia (16%), and proximal humerus (10%).¹¹

In the current case report, paraplegia was caused by synchronous multifocal osteosarcoma due to multisite compression of the spinal cord.

CASE PRESENTATION

A 55-year-old man initially presented to a nearby hospital with low back pain of more than 1 month duration. Multiple osteosclerotic lesions were observed in the spine and pelvis. Biopsy of the iliac lesion was performed, and he was diagnosed with osteosarcoma and referred to our institute. He reported no fever but complained of general fatigue. Laboratory test results were normal, except for a markedly elevated alkaline phosphatase (ALP) level of 36,416 U/L (normal range, 115–359 U/L). The inflammatory marker C-reactive



Figure 1. A 55-year-old man with multicentric osteosarcoma. Plain radiography shows multifocal osteosclerotic lesions in the pelvis and spine (A). Magnetic resonance imaging shows multiple vertebral and pelvic lesions with low-signal intensity on T2-weighted (B-top, middle) and T1-weighted (B-bottom) images. Whole-body bone imaging using technetium-99m shows uptake primarily in the bone of the trunk (C). A lesion is observed in the lung (yellow arrow), but it is relatively small in size (C-top). Extraosseous ossified lesions are observed in the mediastinum (top), retroperitoneum (middle), and mesentery (bottom) (D) (orange arrows).

protein value was negative (<0.1 mg/dL). His leukocyte count was normal at $4370/\text{mm}^3$ (neutrophils, 64.3%; lymphocytes, 22.4%; monocytes, 8.2%; eosinophils, 3.0%; and basophils, 2.1%).

Plain radiographs showed diffuse osteosclerotic lesions in the spine and pelvis (Figure 1A). Magnetic resonance imaging (MRI) demonstrated vertebral and pelvic lesions with low-signal intensity on T1- and T2-weighted images (Figure 1B). Bone scintigraphy demonstrated systemic bone lesions, primarily in the trunk (Figure 1C). Extraosseous ossified lesions were also observed in soft tissue of the mediastinum, retroperitoneum, and mesentery on computed tomography (CT) (Figure 1D). The patient received chemotherapy for palliation. The chemotherapeutic regimen consisted of 1.5 g/m^2 ifosfamide per day for 3 days, carboplatin 300 mg/m^2 per day for 3 days, and 100 mg/m^2 etoposide per day for 3 days. Laboratory tests showed that his ALP level had decreased to 17,833 U/L after 6 treatment courses and that his ALP levels had been controlled at $<25,000$ U/L throughout the 6 months of chemotherapy. After 6 courses of chemotherapy, he began experiencing back pain and gait disturbance, and his knee gave way. Due to decreased daily activity and onset of general fatigue, chemotherapy was discontinued, and his ALP level increased to 49,943 U/L 1.5 months later.

On physical examination, his muscles had slightly weakened. However, deep patellar tendon reflexes and achilles tendon reflexes were elicited. CT and MRI showed an increase in size of the ossified lesion in the spine, as well as compression of the spinal cord at the level of T9-10 (Figure 2A,B), so (Figure 2)decompression and posterior spinal stabilization of T8-12 were performed (Figure 2C). The resected vertebral laminae were confirmed to harbor osteosarcoma (Figure 2D). After surgery, the patient experienced improvement in gait. One month after surgery, he noticed muscle weakness of the right upper extremity and right thigh pain. His right extremity weakness was judged to be fair and he was able to move the extremity against gravity (Manual Muscle Testing Grading System, grade 3). In contrast, no palpable contraction was observed in either of the lower extremities (Manual Muscle Testing Grading System, grade 0), indicating paraplegia. He developed bladder and rectal disturbances. CT showed narrowing of the spinal canal and spinal cord compression at T6 and T7, which were above the fixed vertebrae (Figure 2D). The weakness of the right upper extremity was diagnosed due to radiculopathy in the cervical spine. The paraplegia and right upper extremity caused a decreased performance state. Ossified lesions in the bone and soft tissue continued to increase in size

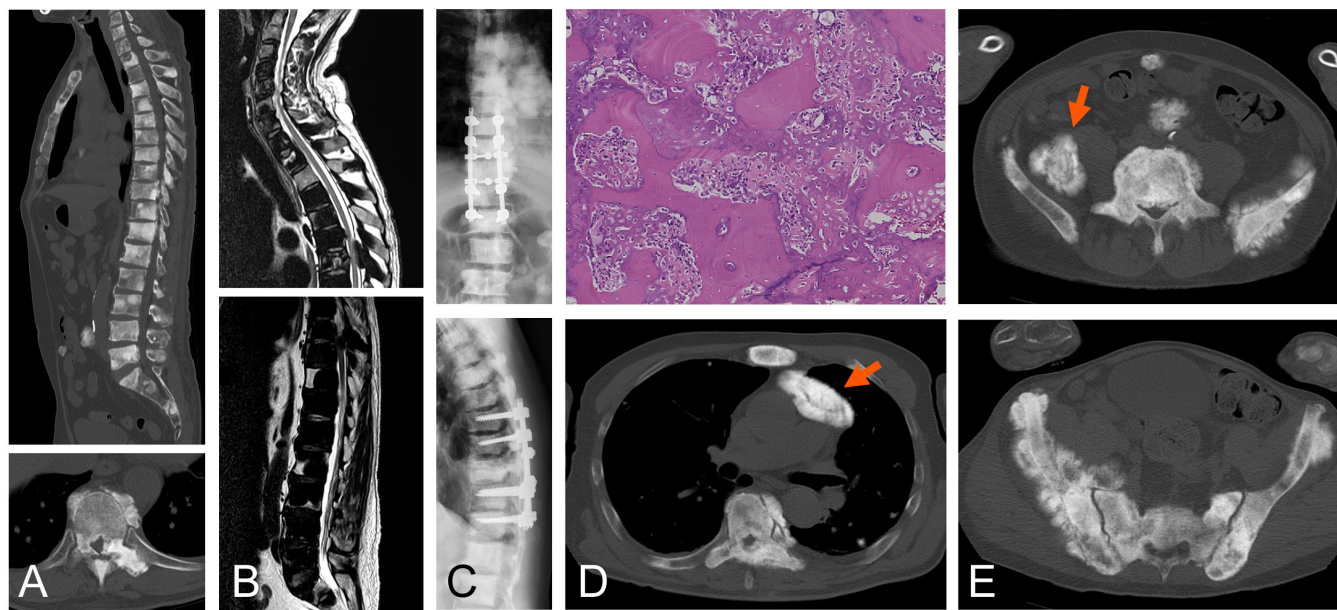


Figure 2. A 55-year-old man with multicentric osteosarcoma. In the osteosclerotic spine, the spinal canal is narrowed at T10-11. An axial view at T10 shows that this narrowing is due to an ossified lesion (A). Magnetic resonance imaging shows compression of the spinal cord (yellow arrow) on a T2-weighted image (B). Fixation and decompression of T8–12 was performed (C). Histologic analysis of the resected laminae shows an osteoid tumor with atypical cells among trabecular bone (D-top). Two months after surgery, the spinal canal is narrowed at T7 (D-bottom). Extraosseous lesions are indicated with orange arrows (D and E). The ossified lesion in the pelvis is increased in size (E).

(Figure 2D,E). Eleven months after the first visit to our hospital, the patient died of multiple organ failure.

DISCUSSION

Whether synchronous multifocal osteosarcoma is a true multicentric tumor or an aggressive tumor with early systemic dissemination remains controversial.^{7–9,11} Synchronous multifocal osteosarcoma is thought to possibly represent extreme systemic osseous metastasis of osteosarcoma^{12,13} because a large dominant tumor is observed on primary assessment in most cases.¹ In the current case, while the right pelvic lesion was larger than the other lesions, the distribution of lesions was nearly symmetrical, including a lesion on the other side of the pelvis, at initial assessment. Lung metastases were present but relatively small. Furthermore, during the disease course, multiple osseous and soft-tissue lesions increased in size almost simultaneously. The current case can be classified as multifocal osteosarcoma rather than ordinary solitary osteosarcoma. Although multifocal osteosarcoma is generally characterized by vast metastatic lesions, in consideration of the fact that the predominant site of osteosarcoma metastasis is the lungs, multifocal osteosarcoma may alternatively be characterized by bone- and soft-tissue-predominant metastasis. Genetic analysis might allow “multifocal osteosarcoma” to be distinguished from ordinary osteosarcoma using precision genomic

medicine.¹⁴ Therefore, we believe that proper clinical classification of multifocal osteosarcoma remains important.

The prognosis of multifocal osteosarcoma is reportedly poor, and the prognosis of metachronous osteosarcomas is poorer than that of synchronous osteosarcoma.¹¹ For ordinary osteosarcoma, the prognosis of spinal osteosarcoma is much lower than that for extremity osteosarcoma.¹⁰ The patient in the current case also had a poor prognosis and died almost 1 year after the appearance of symptoms. No reports about the prognosis of associated affected bones in multiple osteosarcoma have been published.¹ In the present case, the patient suffered from paraplegia that impaired daily activity. Involvement of the spine in multiple osteosarcoma is rather rare.¹ The complications experienced by the present patient may be specific to multifocal osteosarcoma affecting the spine.

For osteosarcoma of the extremities, adjuvant and neoadjuvant chemotherapy combined with surgery dramatically improves the prognosis of patients without metastasis.^{15,16} In contrast, in multifocal osteosarcoma, roles for chemotherapy and resection have not been investigated.⁵ In the current case, multidrug chemotherapy consisting of ifosfamide, carboplatin, and etoposide was administered, and during the chemotherapy course, ALP values decreased; ALP levels reflect activity of bone-forming sarcoma. However, it remains inconclusive

whether the efficacy of chemotherapy contributes to prolongation of survival, including with respect to the current case.

The current report describes multifocal osteosarcoma paraplegia due to multisite compressions of the spinal cord. Awareness of spinal involvement in patients with multifocal osteosarcoma is important for supporting the activities of daily living for such patients.

REFERENCES

1. Cho H, Park BJ, Park YK. Multifocal osteosarcoma of the skull: multiple primary or metastatic? A case report. *Korean J Pathol*. 2014;48(2):146–150. doi:10.4132/KoreanJPathol.2014.48.2.146.
2. Ottaviani G, Jaffe N. The epidemiology of osteosarcoma. *Cancer Treat Res*. 2009;152:3–13. doi:10.1007/978-1-4419-0284-9_1.
3. Silverman G. Multiple osteogenic sarcoma. *Arch Pathol*. 1936;21:88–95.
4. Currall VA, Dixon JH. Synchronous multifocal osteosarcoma: case report and literature review. *Sarcoma*. 2006;2006:53901. doi:10.1155/SRCM/2006/53901.
5. Qin L-F, Fang H, Qin L-H, Guo X, Peng D. Synchronous multifocal osteosarcoma with hypocalcemia. *Libyan J Med*. 2013;8. doi:10.3402/ljm.v8i0.20359.
6. Hameed S, Vijayan S, Naik M, Rao S. Multicentric osteosarcoma. *Singapore Med J*. 2012;53(10):e214–e217.
7. Bacci G, Fabbri N, Balladelli A, Forni C, Palmerini E, Picci P. Treatment and prognosis for synchronous multifocal osteosarcoma in 42 patients. *J Bone Joint Surg Br*. 2006;88(8):1071–1075. doi:10.1302/0301-620X.88B8.17809.
8. Jones RD, Reid R, Balakrishnan G, Barrett A. Multifocal synchronous osteosarcoma: the Scottish bone tumour registry experience. *Med Pediatr Oncol*. 1993;21(2):111–116. doi:10.1002/mpo.2950210206.
9. Katonis P, Datsis G, Karantanas A, et al. Spinal osteosarcoma. *Clin Med Insights Oncol*. 2013;7:199–208. doi:10.4137/CMO.S10099.
10. Ozaki T, Flege S, Liljenqvist U, et al. Osteosarcoma of the spine: experience of the Cooperative Osteosarcoma Study Group. *Cancer*. 2002;94(4):1069–1077.
11. Corradi D, Wenger DE, Bertoni F, et al. Multicentric osteosarcoma: clinicopathologic and radiographic study of 56 cases. *Am J Clin Pathol*. 2011;136(5):799–807. doi:10.1309/AJCP0V0OATK-CNAZP.
12. Daffner RH, Kennedy SL, Fox KR, Crowley JJ, Sauser DD, Cooperstein LA. Synchronous multicentric osteosarcoma: the case for metastases. *Skeletal Radiol*. 1997;26(10):569–578. doi:10.1007/s002560050289.
13. Shinozaki T, Chigira M, Watanabe H, Kaneko K. Osteosarcoma with multiple skeletal metastases. A case of “nonstochastic” metastasis. *Arch Orthop Trauma Surg*. 1993;112(6):292–295. doi:10.1007/BF00452968.
14. Zhang HQ, Li MH, Gao P, et al. Preliminary application of precision genomic medicine detecting gene variation in patients with multifocal osteosarcoma. *Orthop Surg*. 2016;8(2):129–138. doi:10.1111/os.12249.
15. Bacci G, Briccoli A, Rocca M, et al. Neoadjuvant chemotherapy for osteosarcoma of the extremities with metastases at presentation: recent experience at the Rizzoli Institute in 57 patients treated with cisplatin, doxorubicin, and a high dose of methotrexate and ifosfamide. *Ann Oncol*. 2003;14(7):1126–1134. doi:10.1093/annonc/mdg286.
16. Thompson RC, Cheng EY, Clohisy DR, Perentes J, Manivel C, Le CT. Results of treatment for metastatic osteosarcoma with neoadjuvant chemotherapy and surgery. *Clin Orthop Relat Res*. 2002;(397):240–247. doi:10.1097/00003086-200204000-00028.

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of Conflicting Interests: The authors report no conflicts of interest.

Patient Consent for Publication: The patient represented herein was informed that his data would be deidentified and published in a journal and provided his consent.

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Published 21 December 2021

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