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Case Report

Primary osteosarcoma of the thoracic spine: report of an unusual elderly patient with autopsy findings

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Study design: A case report of primary osteosarcoma of the spine in an elderly patient.
Objective: The histopathological features of osteosarcoma vary widely, often leading to diagnostic difficulties particularly when there is little evidence of osteoid formation. The report describes the difficulty in the diagnosis of osteosarcoma of the thoracic vertebra.
Setting: Department of Orthopaedics and Rehabilitation Medicine, Fukui University Faculty of Medicine, Fukui, Japan.
Method: A 78-year-old man presented with paraparesis and underwent urgent anterior excision of a primary spinal tumor emanating from the T10 vertebra followed by artificial vertebral replacement. The patient eventually died of disseminated disease of vertebral osteosarcoma.
Results: Samples from the T10 vertebral tumor showed neoplastic growth of atypical spindle-shaped cells, with foci of storiform-like proliferation. The tissue also demonstrated positive immunohistochemical staining for vimentin and α-smooth muscle actin and a tentative diagnosis of leiomyosarcoma was made. However, a metastatic nodule of the chest wall at autopsy showed focal osteoid formation, a finding not seen in the primary tumor.
Conclusion: Early detection and accurate diagnosis is important for improving not only patient prognosis but also the quality of life. We should always consider this rare entity, particularly in elderly patients who present with back pain and vertebral collapse.
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Keywords: spinal malignancy; leiomyosarcoma; osteosarcoma; autopsy

Introduction

Primary osteosarcoma of the spine is a rare condition accounting for 3.7–14.5% of primary spinal tumors[1,2] and 0.4–2.7% of all osteosarcomas.[3–6] Osteosarcoma is a malignant bone tumor that frequently affects patients in their second and third decades of life, however, it is reported there exists two peaks in the incidence of osteosarcoma, one is in the second decade and another in the seventh decade of life.[7] Huvos[8] reported three cases of osteosarcoma of the spine among 117 patients with osteosarcoma older than 60 years. Histopathologically, the diagnosis of osteosarcoma may be difficult especially when the tumor presents with an extensive fibrohistiocytic storiform pattern, infiltration of atypical spindle cells, and minimal or scarce osteoid formation.[9]

This short communication describes an elderly man with paraparesis caused by a solitary primary vertebral tumor at T10 vertebral level, which was finally diagnosed as osteosarcoma at autopsy. Histopathological examination of the tumor at surgery, 5 months prior to death showed histological features suggestive of leiomyosarcoma.

Case report

The patient, a 78-year-old previously healthy man, initially complained of intractable back pain following a minor fall 4 months prior to admission. The pain gradually worsened and the patient had difficulty in walking for 1 week prior to referral to our hospital.

On admission, the patient was noted to have paraparesis (Frankel-ASIA grade B scale) below the level of T9, with sensory deficit in the lower extremities and bladder dysfunction. Blood tests were normal. Radiographs demonstrated a collapsed T10 vertebra with evidence of decreased radiolucency, suggestive of a vertebral malignancy (Figure 1a). The lesion showed

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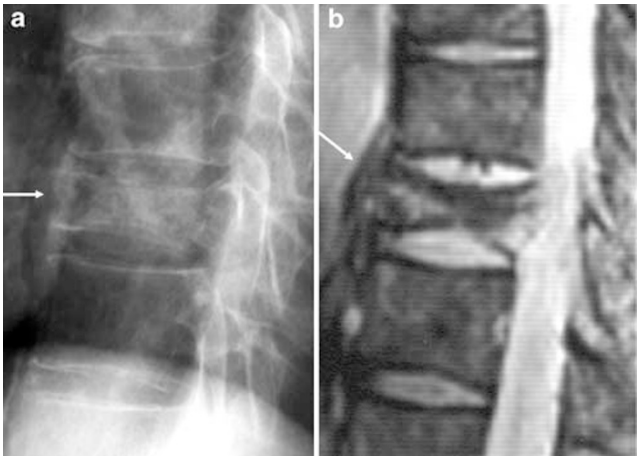

Figure 1 (**a**) Preoperative lateral plain X-ray of the thoracic spine showed T10 vertebral collapse (arrow). (**b**) Irregular high-intensity signal on T2-weighted magnetic resonance image (arrow)

a decreased intensity signal on a T1-weighted magnetic resonance image and an irregular high-intensity signal on a T2-weighted image (Figure 1b). Skeletal surveys, which included ^{99m}Tc bone scintigraphy, were normal apart from the T10 vertebral body lesion. Furthermore, regional surveys, including brain, chest, and abdominal CT and gastrointestinal endoscopy, were also normal.

The patient underwent an anterior resection of the T10 vertebra (through a left-sided transthoracic approach) with replacement by an artificial vertebra (LIFT vertebral body®; Sofamore-Danek, Paris, France) in conjunction with LD instrumentation® (Sofamore-Danek), consisting of screws and plate system for stabilizing the vertebrae after complete resection of the tumor as well as excellent spinal cord resection. At surgery, the tumor had a yellowish or gray-brown appearance. There was no evidence of excessive hemorrhage during resection of the tumor. Histopathological examination of a frozen section obtained intraoperatively from the resected tumor showed features suggestive of a high-grade sarcoma, probable leiomyosarcoma.

Postoperatively, the patient became ambulatory with use of a single cane (Frankel-ASIA grade D scale), even though the spasticity of the legs did not show any improvement. The patient refused chemotherapy consisting of a high-dose methotrexate and *cis*-platinum as well as radiotherapy. The patient died 8 months after the surgery due to disseminated pulmonary disease.

Histopathological, immunohistochemical, and autopsy findings

Histological examination of the tumor samples obtained from both surgery and autopsy showed that they consisted of infiltrates of atypical pleomorphic spindle-shaped cells with eosinophilic cytoplasm. Foci of storiform-like cellular proliferation and abnormal mitoses were seen in the samples obtained at surgery (Figure 2a).

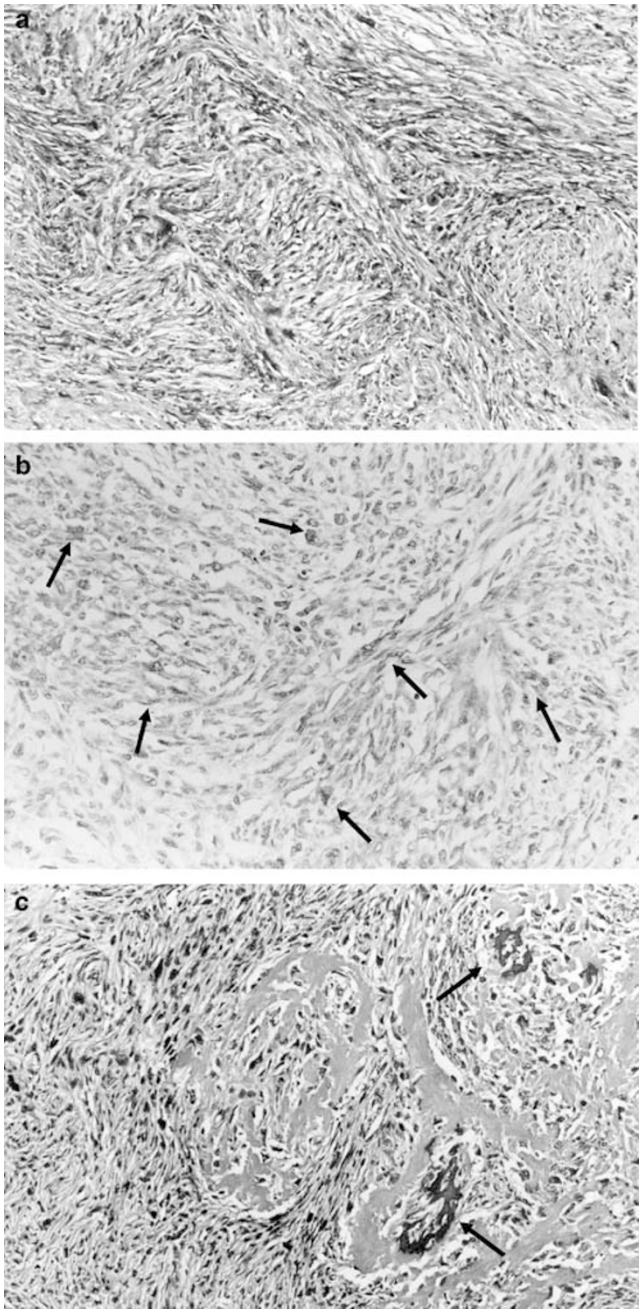

Figure 2 Histopathological and immunohistochemical examinations. (**a**) The primary tumor (T10 vertebral body) consists of spindle-shaped cells in a storiform pattern. No osteoid formation is seen. (**b**) Cells of the primary tumor stain diffusely positive for α-SMA (arrows). (**c**) Chest wall dissemination at autopsy. Osteoid formation is evident, with calcification of some areas (arrows) (Magnification × 120 (**a**, **c**), × 240 (**b**))

The majority of tumor cells stained positive for vimentin and α-smooth muscle actin (Figure 2b) by immunohistochemistry. Some tumor cells were immunohistochemically positive for HHF35 and desmin but all cells were negative for S-100 protein, keratin, epithelial membrane, and CD-34 antigens.

At autopsy, the tumor surrounded the seated artificial vertebra and involved the adjacent pleura. Multiple disseminated and/or metastatic lesions were observed in the left chest wall and in the vicinity of the descending aorta. Multiple metastatic masses were also present in the lung bilaterally and in the liver. There was no macroscopic evidence of tumor in the remaining viscera including the musculo-skeletal system.

Although osteoid formation was not evident in the vertebral tumor resected 5 months earlier, a nodule excised from the left chest wall at autopsy demonstrated areas of osteoid formation both with and without calcification (Figure 2c). Both the tumor cells surrounding and those within the osteoid areas stained positive for vimentin, α-smooth muscle actin, and HHF35, indicating that the tumor was an osteosarcoma, with fibroblastic features.

Discussion

Immediate surgical decompression is a crucial therapy in acute paraplegia caused by tumor-related spinal cord compression, as it may restore or preserve gait function and improve the quality of life. During adulthood, neural tissue has less capacity for neuronal plasticity, although plastic changes may be found at any age,[10] in which spinal cord morphological plasticity correlates with neurological function.[11] In the presence of complete paralysis before the operation, surgical treatment does not produce any essential improvement apart from pain relief, however, neurological improvement tends to be provided by immediate decompression in case of paresis.[12,13] Accordingly, in our case, the patient showed improvement of neurological deficits, although he underwent operation 1 week after the onset of paresis. Thus, these results confirm that early diagnosis is important for better neurological improvement in patients with paresis caused by tumor-related spinal cord compression.

Local recurrence of the spinal tumor causes paralysis, and influences mortality. Talac *et al*[14] described in their study of spinal sarcomas that residual tumor at the surgical margin, and resection in a piecemeal fashion, resulted in a high recurrence rate that was associated with early mortality. Similarly, a recent review of 1702 patients with high-grade osteosarcoma[5] indicated that failure to achieve a surgical remission of osteosarcoma was associated with increased age, axial site, long history, delayed start of therapy, intralesional surgical resection, and poor response to chemotherapy. However, Gore *et al*[15] reported a case with long-term survival after intralesional resection of thoracic spine osteosarcoma with multidisciplinary, multimodal approach, using aggressive chemoradiotherapy with surgical resection. They applied chemotherapy preoperatively, which consisted of high-dose methotrexate, cisplatin, doxorubicine, ifosfamide, and muramyl tripeptide phosphatidyl ethanolamine. Subsequently, during the planned intralesional tumor resection, a total of 47 ^{125}I-impregnated seeds were placed along the area of residual tumor. Postoperatively, they performed external beam radiation and provided additional chemotherapy. The response rate of fibroblastic osteosarcoma to chemotherapy was reported to be more than 40%.[16,17] In addition, Ozaki *et al*[6] reported that postoperative radiotherapy improved the survival rate in patients with osteosarcoma. In our case with a final diagnosis of fibroblastic osteosarcoma, the prognosis might have improved had the patient agreed on chemotherapy and/or radiotherapy. In addition, there was a problem with respect to establishing a definitive postoperative diagnosis.

Histopathologically, osteosarcoma usually rests on the presence of malignant tumor; osteoid and/or bone production within the tumor. However, in elderly patients, the diagnosis of osteosarcoma may be difficult because of its histological features. Huvos[8] indicated that osteosarcoma of elderly patients may often present with fibrohistiocytic and fibrous variants. One variant may show little osteoid formation, as suggested by Campanacci and Enneking,[9] indicating that the tumor specimen should be carefully examined if this diagnosis is suspected. In such instances, they indicated that it might be difficult and subjective to decide whether the coarse pink-stained and homogenous intercellular matrix is actually hyaline collagen or osteoid tissue, and that special stains for osteonectine, alkaline phosphatase, and electron microscopy (matrix extracellular vesicles) might help to distinguish osteoid from collagen.[9] The diagnosis of fibrohistiocytic osteosarcoma has been made only by confirmation of direct tumor osteoid formation by the sarcoma growing in a storiform pattern, even if this only appeared in one microscopic field.[8,18] The histopathological features of the T10 vertebral tumor in our patient included atypical spindle cells arranged in a storiform pattern, immunoreactivity to vimentin α-smooth muscle actin, HHF35, and desmin, and absence of osteoid formation suggesting smooth muscle differentiation. The diagnosis therefore at the time of surgery was high-grade sarcoma, probable leiomyosarcoma. However, osteoid formation with calcification was subsequently observed in a chest wall nodule at autopsy, indicating that the correct diagnosis was in fact osteosarcoma. One cause of the inaccurate postoperative diagnosis might be related to the failure in examining the entire specimen, which was resected at surgery. However, osteoid formation was found only in the specimen of metastases at autopsy.[9]

Osteosarcoma may demonstrate immunoreactivity for α-smooth muscle actin. Devaney *et al*[19] reported that one of the 16 cases of small cell osteosarcomas were positive for anti-α-smooth muscle antibody. Hasegawa *et al*[20] found positive immunoreactivity for α-smooth muscle actin in 15 of 30 osteosarcomas, and proposed that tumor cell expression of α-smooth muscle actin be regarded as myofibroblastic differentiation. Povýšil *et al*,[21] however, proposed that the presence of these antigens is due to aberrant actin microfilament expression. It remains unclear whether the presence of muscle tissue antigens in the case presented here is indicative of

myofibroblastic differentiation of the tumor, or due to aberrant actin microfilament expression. Malignant bone tumors with features suggestive of myofibroblastic differentiation, however, require careful histopathological examination to distinguish them from the fibroblastic variant of osteosarcoma.

Based on the current case of T10 vertebral osteosarcoma, early detection and accurate diagnosis is important for improving not only patient prognosis but also the quality of life. We should always consider this rare entity, particularly in elderly patients presenting with back pain and vertebral collapse.

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