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Case Report

Giant cell rich osteosarcoma of the mandible with abundant spindle cells and osteoclast-like giant cells mimicking malignancy in giant cell tumor

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Abstract: Giant cell rich osteosarcoma is a relatively unusual histological form of osteosarcoma, common lesion usually presenting in the long bones of the appendicular skeleton. The occurrence in the mandible is exceptional rare. Histologically, this tumor tends to be a highly anaplastic, pleomorphic tumor in which the tumor cells may be: plasmacytoid, fusiform, ovoid, small round cells, clear cells, mono-or multinucleated giant cells, or, spindle cells. Herein, we present a case with the sternum and first thoracic vertebra metastasis from primary giant cell rich osteosarcoma of the mandible in a 28 year-old Chinese female. The tumor was predominantly composed of abundant spindle cells with marked atypia and numerous osteoclast-like giant cells reminiscent of malignancy in giant cell tumor. The unusual histological appearance can pose a great diagnostic challenge. It may be easily misdiagnosed, especially if the specimen is limited or from fine-needle aspiration.

Keywords: Giant cell rich osteosarcoma, mandible, osteoclast-like giant cells, malignancy in giant cell tumor

Background

Giant cell rich osteosarcoma, first described by Bathurst and Sanekin [1], is a rare variant of osteosarcoma that account for 1-3% of all cases of conventional osteosarcomas. Conventional osteosarcoma is largely a disease of the young. It most frequently occurs in the second decade with some 60% of patients under the age of 25 years [2]. Conventional osteosarcoma shows a profound propensity for involvement of the long bones of the appendicular skeleton; in particular, the distal femur, proximal tibia, and proximal humerus. On review of world literature, most of cases giant cell rich osteosarcoma has been reported in the extremities [3, 4]. To the best our knowledge giant cell rich osteosarcoma of the mandible has only one case been reported in the world literature [5]. Histologically, giant cell rich osteosarcoma is an undifferentiated sarcoma with scanty osteoid formation. The microscopic appearance of giant cell rich osteosarcoma is characterized by numerous osteoclast-like giant cells dominating the picture, however the presence of osteoid formation by the tumor cells gives a clue regarding the diagnosis [6]. Herein, we present a case with the sternum and first thoracic vertebra metastasis from primary giant cell rich osteosarcoma of the mandible in a 28 year-old Chinese female. Histologically, the tumor was predominately composed of sheets of atypical spindle cells and numerous osteoclast-like giant cells reminiscent of malignancy in giant cell tumor. The unusual histological appearance may pose a great diagnostic challenge. It may be easily misdiagnosed, especially if the specimen is limited or from fine-needle aspiration.

Case presentation

Clinical history

A 28-year-old female referred to our hospital for complaining of fatigue and chest distressed. Blood examinations were in normal levels. Computed tomographic scan of the chest revealed her mandible missed and the lytic lesion of her sternum and first thoracic vertebra

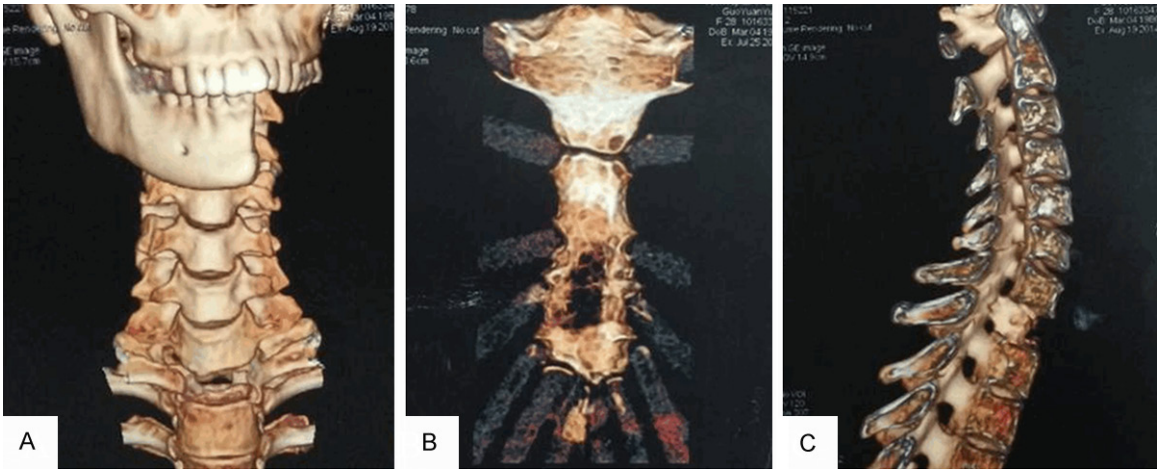

Figure 1. Computed tomographic scan of the chest. A. The left mandible missed. B. The lytic lesion of the sternum. C. The lytic lesion of the first thoracic vertebra.

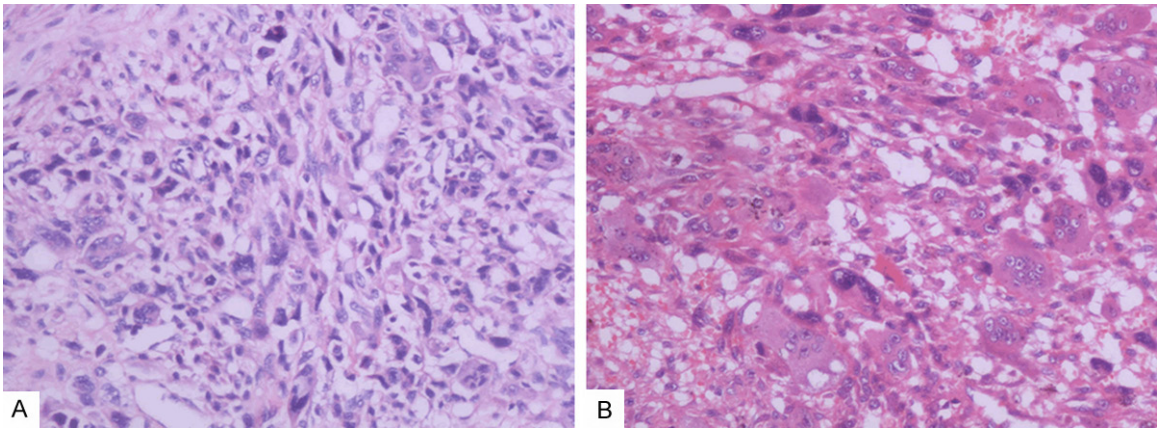

Figure 2. Morphological change of the tumor. A. Numerous spindle cells were arranged into sheets or swirling patterns. B. The spindle cells had marked cellular atypia, scattered multinucleated osteoclast-like giant cells were present amidst the spindle cells.

(**Figure 1**). Biopsy of the sternum rendered the diagnosis of a giant cell rich osteosarcoma. She had a history of left maxillofacial swelling four years ago: CT images presented the mandible lytic lesion. The tumor was clinically diagnosed as a malignant tumor, and then an excision was performed in our hospital. At surgery, the mass was removed, and underwent diagnostic examination. After histopathologic and immunohistochemical analysis the diagnosis was of a malignancy in giant cell tumor. Then the patient underwent adjuvant radiotherapy and chemotherapy. Lesion recurred in the original site and was diagnosed as a malignancy in giant cell tumor three years ago. Reviewing all information, it was concluded that the mandible tumor was the primary giant cell rich osteosarcoma misdiagnosed as a malignancy giant cell tumor. This case emphasizes the importance of the general clinicians' multidisciplinary approach and association of information to arrive at the proper diagnosis, particularly in rare and difficult situations. He was alive with recurrence three years ago and metastasis two months ago within 45 months of follow-up.

Materials and methods

The resected specimens were fixed with 10% neutral-buffered formalin and embedded in paraffin blocks. Tissue blocks were cut into 4-μm slides, deparaffinized in xylene, rehydrated with graded alcohols, and immunostained with the following antibodies: cytokeratin (CK)

(1:200; Mouse mAb (AE1+AE3), Merck), CD68 (KP-1, MaiXin, China, Ready to use), Vimentin (1:200; Mouse mAb (V-9), Merck), CD31 (SP38, MaiXin, China, Ready to use), CD34 (QBEnd/10, MaiXin, China, Ready to use), Desmin (1:200; Mouse mAb (DE-B-5), Merck), Actin (SM) (EPR16769, MaiXin, China, Ready to use), CD56 (MEM-188, MaiXin, China, Ready to use), CD99 (1:200; Mouse mAb (WLM04), Merck), S-100 (4C4.9, MaiXin, China, Ready to use) and Ki67 (1:200; MIB1, Dako). Sections were stained with a streptavidin-peroxidase system (KIT-9720, Ultrasensitive TM S-P, MaiXin, China). The chromogen used was diaminobenzidine tetrahydrochloride substrate (DAB kit, MaiXin, China), slightly counterstained with hematoxylin, dehydrated and mounted. For the negative controls, the primary antibody was replaced with PBS.

Results

Gross features

Grossly, the mass was approximately 4.2 × 4.1 × 1.5 cm, and was poor circumscribed. The cut face of the tumor was firm and grey-white or grey-red in colour.

Microscopic features

Histologically, the tumor was relatively well defined. The tumor was predominantly composed of abundant plump spindle cells. The cells were diffusely arranged into solid sheets or whirling patterns with little stroma. The cells had moderate to marked cellular atypia, with pale chromatin and conspicuous nucleoli. There was approximately 2 mitosis/10 high power in spindle cells. In addition, numerous multinucleated osteoclast-like giant cells containing large pleomorphic nuclei with irregular nuclear membrane and few showing prominent nucleoli were present within the background of the diffuse spindle cells (**Figure 2**). In focal area of the tumor, the classic histologic structure, the scanty osteoid formation could be seen.

Immunohistochemistry

Immunohistochemical staining showed that the spindle cells and osteoclast-like giant cells were diffusely positive for CD56, CD68 and Vimentin, weakly positive for CK, negative for CK, CD31, CD34, Desmin, Actin (SM), CD99 and S-100. Ki67 index was approximately 15%. According to the morphological and immunohistochemical findings, the tumor was diagnosed as a giant cell rich osteosarcoma.

Discussion

Giant cell rich osteosarcoma, typically occurring in the extremities, in the head and neck region is extremely rare in the literature. On searching the world literature, we could find only one case report of giant cell rich osteosarcoma of the mandible [5]. Most of Osteosarcomas, highly malignant bone tumor, in the head and neck arise from the mandible and maxilla. Jaw lesions tend to occur at an older mean age [7]. Some series in literature also suggests the female predominance [8]. Present case is also a female but younger age group. However giant cell rich osteosarcomas of the jaws are very rare in literature. As the most common primary neoplasm in the mandible was ameloblastoma, the correct diagnosis of giant cell rich osteosarcoma may be a hard work.

Histologically, giant cell rich osteosarcoma is an undifferentiated sarcoma with scanty osteoid formation. The microscopic appearance of giant cell rich osteosarcoma is characterized by numerous osteoclast-like giant cells dominating the picture; however the presence of osteoid formation by the tumor cells gives a clue regarding the diagnosis [6]. In the present case, the histology showed extensive spindle cells change with numerous osteoclast-like giant cells. Areas of lace like osteoid formation by the tumor cells were also seen. Histologically, the tumor was predominately composed of sheets of atypical spindle cells and numerous osteoclast-like giant cells. So, we firstly thought it might be a tumor complicated with multinucleated giant cells such as malignancy in giant cell tumor. The presence of classic osteoid formation can usually favor the correct diagnosis and rule out malignancy in giant cell tumor. However, if the specimen is limited or from fine-needle aspiration, and histologically lacks the classic osteoid formation, the correct diagnosis may be a great challenge, as it is usually difficult for pathologists to think about the possibility of osteosarcoma.

In addition, the differential diagnosis also includes some other tumors which can possess osteoclast-like giant cells, such as: giant cell

tumor of bone or soft tissue, chondroblastoma, chondrosarcoma and dedifferentiated liposarcoma. Based on the classic histologic structure and immunostaining, the correct diagnosis can be made. Moreover, some sarcomatoid carcinomas can present as extensive spindle cells with osteoclast-like giant cells. Thus, sarcomatoid carcinoma is also an important differential diagnosis. Especially, in addition to the mesenchymal tissue markers such as Vimentin, giant cell rich osteosarcoma is also immunopositive for epithelial marker CK, which may be a potential diagnostic pitfall. It is essential for using a panel of antibodies to make the correct diagnosis.

To date, the reported case with osteoclast-like giant cells is exceptional rare [3-6, 9-13]. So the significance of osteoclast-like giant cells is still unclear. The osteoclast-like giant cells were simply immunopositive for CD68, indicating these cells may be only reactive cells. And, further follow up should be made to investigate its significance.

According to Zarbo RJ [14], the majority of osteosarcomas, in the head and neck, have a relatively better clinical course than highly aggressive osteosarcoma. They usually exhibit lower aggressive potential than their long bone counterparts and have excellent prognosis if completely resected. However, if the tumor shows marked cellular atypia, mitotic activity (> 1 mitosis per 10 HPF), necrosis and extensive spindling, it may have a more aggressive course. Giant cell rich osteosarcoma is considered high-grade conventional osteosarcoma, hence its importance of reporting this variant as it has therapeutic and prognostic significance [9]. But, it is still unclear whether the presence of osteoclast-like giant cells is associated with prognosis. Present case is alive within 45 months of follow-up.

Conclusion

Because of the exceptional rarity, the significance of giant cell rich osteosarcoma with osteoclast-like giant cells is still unclear. Our reported case was predominantly made up of abundant spindle cells, numerous osteoclast-like giant cells and the scanty osteoid formation. The unusual histological appearance may pose a great diagnostic challenge, especially if the specimen is limited or from fine- needle aspiration.

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Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in Chief of this Journal.

Disclosure of conflict of interest

None.

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