

Osteosarcoma presenting as an aggressive nodular mass in the region of the mandible

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Abstract: Osteosarcomas are highly malignant neoplasms of bone that are challenging to diagnose. These neoplasms often show atypical behavior. In the initial phase they may present as nondescript bony swellings with an indolent growth rate, only to become overtly aggressive and malignant towards the later phase of the disease. Similarly, the histological growth pattern of this neoplasm can be quite diverse, presenting with areas that mimic benign myofibroblastic tumors, giant cell granulomatous conditions and partial encapsulation. The final diagnosis of an osteosarcoma is often reached after thorough sampling and examination of multiple biopsy specimens. All these clinical features and histological diagnostic difficulties were encountered in a case of osteosarcoma affecting the right mandible of a 62-year-old Chinese woman described here. The diagnostic lessons accrued from this case are discussed. (*J. Oral Sci.* 46, 55-59, 2004)

Key words: osteosarcoma; jaw; myofibroblastic tumor; giant cell.

Introduction

Osteosarcoma represents the most common primary malignant tumor of bones, accounting for 40% to 60% of all malignant bone tumors (1). Approximately 10% of all osteosarcomas occur in the head and neck region, chiefly

in the mandible or maxilla. Osteosarcomas of the jaws tend to affect adults at a later age than those of long bones: i.e. 30 - 39 years (1-3). There is usually an equal gender distribution, unlike osteosarcomas of the long bones, which show a male predominance (1). Clinically, an osteosarcoma of the jaw presents as a swelling associated with pain and the loosening of adjacent teeth. Radiologically, it can appear as an osteolytic/osteocytic lesion or a mixture of both. The histologic criterion for the diagnosis of osteosarcoma is dependent upon the demonstration of sarcomatous stroma that directly elaborates malignant osteoid.

Myofibroblastic tumors are a group of lesions with malignant potential and are characterized by myofibroblastic proliferation (4-5). The etiology remains debatable, and they have been regarded as infection-associated lesions, pseudo- or true neoplasms (5). The myofibroblasts in these lesions have been viewed as reactive or proliferative cells which can show a range of atypical morphologies. Consequently they are sometimes classified as low-grade sarcomas.

Typical examples of osteosarcoma and myofibroblastic tumors present little difficulty in diagnosis. However, in practice, the clinical, radiological and histological features of these two entities may overlap and diagnosis becomes problematic. The case reported here highlights this diagnostic dilemma.

Case Report

A 62-year-old Chinese woman was referred for management of a painless right mandibular swelling that had recurred three months after conservative excision. According to the referral, she initially presented with a swelling that interfered with her lower denture, and

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numbness of her right lower lip. The accompanying radiograph showed slight erosion of the underlying bone (Fig. 1). She underwent excision of this lesion which included skimming of the underlying bone, but it recurred three months later.

The patient's medical history was otherwise unremarkable. She had tolerated the previous surgery well.

Extraoral examination disclosed a slight right mandibular swelling. The overlying skin was of normal color and texture. There was neither limitation of mouth opening, nor enlargement of the cervical lymph nodes. However, the paresthesia of the right lower lip noted previously was still present.

Intraoral examination showed a nodular non-ulcerated swelling involving the edentulous alveolus of the right lower premolars (Fig. 2). It measured approximately 3 cm by 2

cm by 1.5 cm. The overlying mucosa was inflamed and bled easily. However, the surrounding mucosa was normal. There was no tethering of the tongue to the floor of the mouth. The patient was totally edentulous, and there were no other abnormalities detected in other parts of the oral cavity.

A panoramic radiograph at this visit showed a crater-like defect in the right parasymphiseal region (Fig. 3). The lower border of the mandible was intact. This radiographic appearance corresponded in extent to the postoperative panoramic radiograph taken about three months previously by the referring clinician.

At this department, an incisional biopsy was performed, and the specimen obtained was submitted for histopathological examination. Following the report of a myofibroblastic tumor, the patient was scheduled for excision of the lesion under general anesthesia. However,

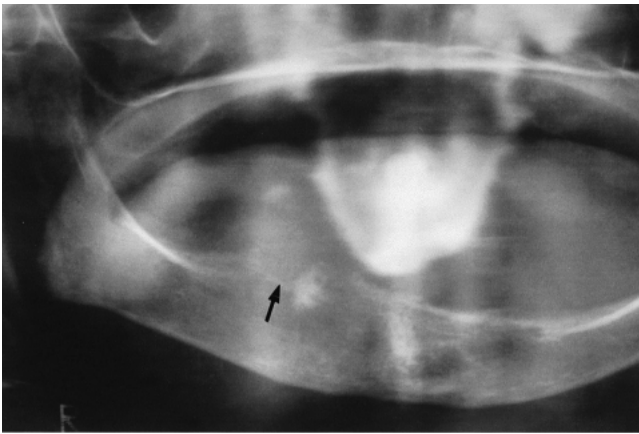


Fig. 1 Panoramic radiograph of the lesion at the very first presentation: i.e. prior to the first excisional biopsy. (Arrow shows the area of superficial bony erosion.)

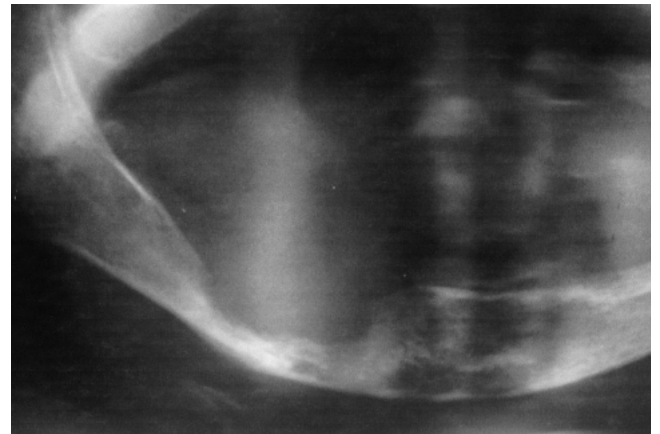


Fig. 3 Panoramic radiograph of the lesion in Fig. 2. This radiograph was taken approximately six months after Fig. 1.



Fig. 2 Nodular appearance of the lesion (arrow) at first presentation to this clinic: i.e. prior to the incisional biopsy.

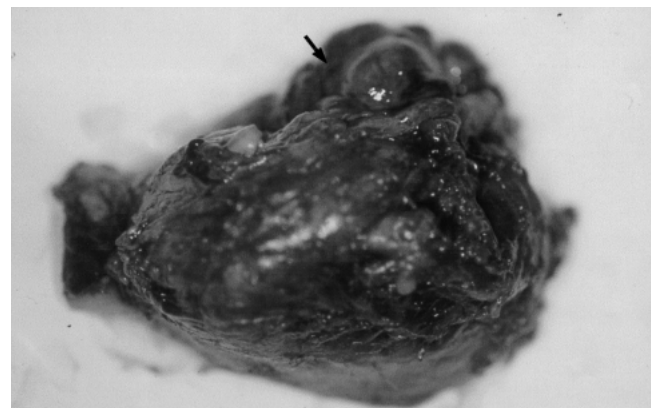


Fig. 4 Excised specimen. Arrow shows the granular appearance of the lesion grossly resembling a bunch of grapes, as noted in the clinical assessment of the lesion.

when the patient returned four weeks later, the swelling had increased in size to about 4 cm by 3 cm by 2 cm. It extended from the lower right molar region to the symphysis. The mucosa overlying the swelling was granular and grossly resembled a bunch of grapes (Fig. 4). The right submandibular lymph node was enlarged and palpable. Panoramic radiographs (Fig. 5) showed destruction of the lower border of the mandible. Computer tomography showed a similar extent of the lesion, which was confined to the mandible, with no other involvement of the skull.

Diagnosis and Management

A provisional diagnosis of a benign odontogenic tumor was considered in the very first instance and an excisional biopsy was planned. The referring clinician enucleated the lesion (specimen A) under general anesthesia and skimmed the underlying bone. Microscopic examination of the

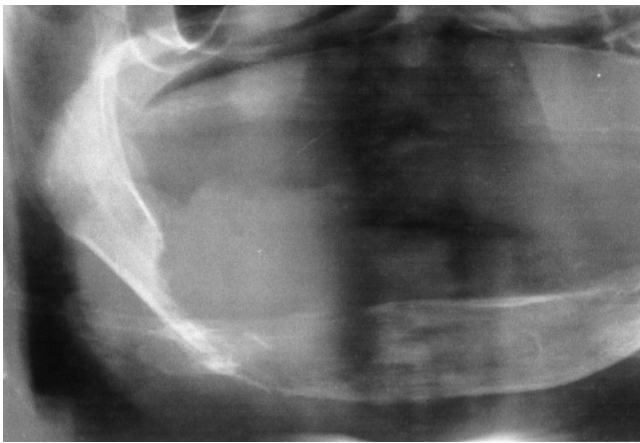


Fig. 5 Panoramic radiograph of the lesion prior to resection. This radiograph was taken approximately six weeks after that of Fig. 3.

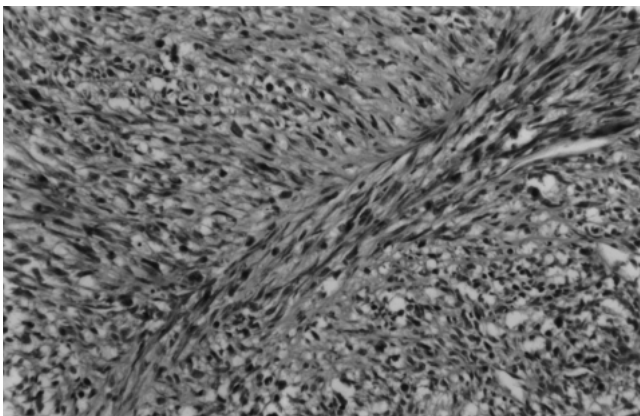


Fig. 6 Photomicrographic appearance of the tumor following primary enucleation. The tumor consists of neoplastic proliferations of pleomorphic spindle-shaped cells in a whorled and fascicular pattern. (HE, $\times 132$)

excised specimen showed lesional tissue composed of neoplastic proliferations of whorls and fascicles of pleomorphic spindle or strap-like cells intermingling with histiocytoid cells (Fig. 6). Scattered multinucleated tumor giant cells were present. There were fairly frequent mitoses, with six mitoses per 10 high-power fields. Occasional abnormal mitoses were present. The tumor cells showed some positivity for cytokeratin, epithelial membrane antigen, S 100 protein, vimentin and HMB 45. However, smooth muscle actin showed variable positivity. Focal areas of the intervening hyalinized stroma were seen. At parts of the periphery, the tumor appeared circumscribed, with a suggestion of “encapsulation”. Based on all these findings, a diagnosis of myofibroblastic tumor was made.

At this center, an incisional biopsy was performed and subsequent microscopic examination revealed a very similar histological appearance to that of specimen A: i.e. lesional tissue consisting primarily of spindle-shaped cells proliferating in an intertwining fascicular fashion; the presence of areas with a compact arrangement of multinucleated giant cells (Fig. 7); and an inflammatory cell infiltrate. In addition, hyalinized material resembling osteoid was observed. Again, a diagnosis of myofibroblastic tumor with an aggressive behavior was made.

Although the second biopsy did not confirm a diagnosis of a truly malignant tumor, the aggressive behavior of this lesion was evident. A segmental resection of the

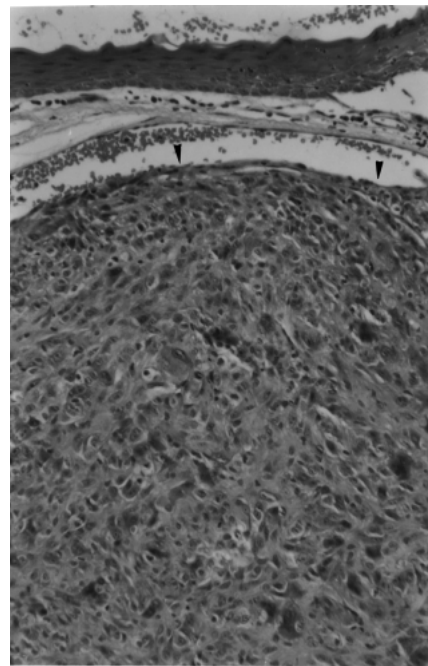


Fig. 7 Photomicrograph of the incisional biopsy specimen showing a compact arrangement of multinucleated tumor giant cells. Note the circumscribed periphery (arrowheads) of the tumor. (HE, $\times 132$)

lesional bone was performed, and the defect temporarily reconstructed with a titanium reconstruction plate, in view of the clinically destructive nature of the tumor at this stage. The enlarged right submandibular lymph nodes were also excised. A frozen section of a lymph node sample showed it to be reactive. The excised lymph nodes together with the resected specimen were submitted for histological examination. The excised bony lesion showed a malignant mesenchymal neoplasm with multiple growth patterns and a pleomorphic cellular population make-up. The lesion exhibited bland-looking hypocellular myofibroblastic areas and circumscribed peripheries with fibrous encapsulation. In other parts of the tumor, hypercellular areas of fascicular fibrohistiocytic proliferations associated with prominent cellular pleomorphism, frequent mitoses and sheets of multinucleated giant cells were observed. There was lace-like malignant osteoid formation (Fig. 8). Given this finding, a diagnosis of osteosarcoma was made. Decalcified sections showed adequate clearance of the anterior and posterior margins. The lymph nodes were reported to be those of reactive lymphadenopathy.

Following the histological report of an osteosarcoma, the patient was given a systemic check-up to rule out the possibility of a metastatic tumor from another part of the body. There were no other symptoms such as bone pain or swelling. The screening examination included a chest radiograph, computed tomography of the head and neck, and hematological tests for, among other things, liver function. No radiograph was taken of her long bones.

The results of this investigation did not suggest any other distant tumor with metastasis to the oral cavity or metastasis to other parts of the body. Based on this, we concluded that the tumor was a primary one with no distant metastasis.

The patient was reviewed every month for three months, and then every three months thereafter. A year after the

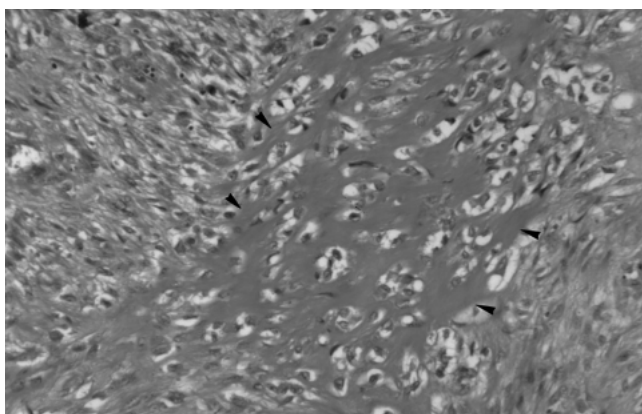


Fig. 8 Malignant osteoid formation (arrowheads) was found in the resected specimen. (HE, $\times 132$)

surgery the reconstruction plate was observed to have perforated through the mucosa into the oral cavity. Other than that, the oral mucosa had healed well, the patient remains symptom-free and there is no evidence of tumor recurrence. The routine chest radiograph taken prior to general anesthesia did not show metastasis. Her blood test results were all within normal limits. At this stage, the reconstruction plate was removed through an extra-oral approach, and this time the discontinuity was bridged with an iliac crest bone graft. It was found that the patient's bone was extremely soft; the screws to hold the plates to the graft and its recipient site did not catch very well. The surgeon who harvested the iliac crest also found the bone to be extremely soft at the donor site.

The graft took and the patient again made an uneventful recovery. She is still on regular follow-up visits to this center. Three years after the first surgery, she remains tumor-free.

Discussion

At initial presentation, the lesion occurred as a non-ulcerated swelling covered by an inflamed oral mucosa, and clinically resembled a benign intrabony tumor. However, the clinical course of this lesion changed rapidly following the second biopsy. Due to the speed at which the tumor destroyed the bone, myofibroblastic tumors and malignant neoplasms were considered in the differential diagnosis. A primary intraosseous neoplasm and a lesion from the soft tissues extending intraosseously were major considerations. In this respect, the principal diagnostic possibility considered was osteosarcoma as the primary bone neoplasm, or squamous cell carcinoma of the oral mucosa exhibiting local extension into bone. A malignant tumor of odontogenic origin: i.e. malignant ameloblastoma arising either *de novo* or from a pre-existing benign odontogenic precursor lesion, was also considered a diagnostic possibility (6). Another consideration was a tumor of peripheral neural tissue origin because of the proximity of nerve tissues in this region: i.e. the mental nerve. Finally, a neoplasm representing metastasis from distant sites was also included in the differential diagnosis of this lesion.

The tumor presented here exhibited atypical behavior. As mentioned earlier, it initially behaved like a locally invasive benign lesion but, following the second biopsy, its growth rate accelerated, whereupon it destroyed a considerable part of the mandible in a period of less than a month. In such a case, the tumor would almost certainly recur after limited excision, thus necessitating another operation. The literature also states that the treatment for osteosarcoma of the jaws is radical resection of that part

of the jaw (7-9).

Osteosarcomas, in particular the parosteal variant, often present with indolent behavior and a bland-looking microscopic appearance in the early stages of the disease, only to become aggressive later, and the final diagnosis is often only reached after repeated biopsies or treatment. The case discussed here illustrates such diagnostic difficulties and also how a tumor becomes more aggressive after a biopsy or incomplete treatment. When the very first surgery (enucleation) was performed, the entire tumor mass was sent for histopathological examination. The second incisional biopsy also involved a large portion of the tumor tissue and yet it was not possible to make a firm diagnosis of a malignant tumor.

The fact that during the surgeries the patient's bone was found to be soft could indicate a generalized bone disorder that predisposed the patient to the tumor. There have been cases of osteosarcoma of the jaws associated with bone diseases like Paget's and fibrous dysplasia, and with previous radiation therapy to the jaw area (10,11). However, this patient has no history of previous radiation or any other underlying bony disorders.

The patient is still on regular review at this center. Osteosarcoma of the jaw shows late metastasis to the lymph nodes in 18% of cases. It usually metastasizes about 1.5-2 years after initial diagnosis (12).

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