Periosteal osteosarcoma of the jaw bones: a clinicopathological review

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Abstract: Periosteal osteosarcoma (PO) is a rare variant of osteosarcoma that arises on the surface of bones from the deep layer of the periosteum. It most commonly affects the long bones of the extremities, and its involvement in jaw bones is extremely rare. PO is an intermediate-grade tumor, and its prognosis is usually better than that of conventional intramedullary osteosarcoma (CIO). However, care should be taken to differentiate PO from other surface bony tumors that could simulate its clinical, radiographic or histopathological features. This report reviews current knowledge of this particular tumor that has profound significance to specialists in oral and maxillofacial surgery, radiology, and pathology as well as oral medicine. [Oral Med Pathol 2007; 12: 3-10]

Key words: periosteal osteosarcoma, jaw bones, intramedullary involvement.

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Introduction

Periosteal osteosarcoma (PO) was first recognized by Ewing in 1939 (1) and was further described by Lichtenstein (2) as a periosteal counterpart of conventional intramedullary osteosarcoma (CIO). However, due to its particular behaviors distinct from those of CIO, the term PO as a distinct clinicopathologic entity was first used by Unni et al. in 1976 (3). The tumor is thought to arise from undifferentiated cells of the inner layer of the periosteum (4). POs are rare; they account for 1-2% of all osteosarcomas (5). The tumors occur most often in adolescence and have a predilection for the diaphyses of the femur and tibia. Histopathologically, the tumor is characterized by formation of poorly-differentiated cartilaginous lobules and scattered areas of delicate, lace-like osteoid associated with entrapped malignant osteoblasts (6). While suspected risk factors for CIO include rapid bone growth, environmental factors such as ionizing radiation, genetic predisposition and preexisting benign bone lesions (7), the exact cause of PO or its predisposing factors are unknown. The biological behavior of this tumor is basically regarded as an intermediate-grade malignant tumor (8).

PO of the jaw bones is extremely rare. To date, only nine cases have been reported in the English literature (9-16) (Table 1). Intramedullary involvement (IMI) was reported in only one of these nine cases (9). In this article, we review the literature and detail pathological features of periosteal osteosarcoma based on a case which we experienced, to understand more accurately this unique tumor for better clinical intervention.

Gender and age

Gender and age were documented in all cases as shown in Table 1. There was no marked gender predilection, with a male-to-female ratio of 5:4. This was similar to PO affecting the other bones of the whole body (BPO) (3-5) and to CIO affecting jaw bones (17). The mean age of the patients was 36 years (range 15-65 years) with no significant difference between males and females. In contrast, an analysis of 188 patients in four different studies (3-6) with BPOs showed an average age of 22 years. This tendency of jaw bone PO to affect older patients was also recognized in the case of CIO. The mean age of patients with CIO of the jaws was found by Nissanka et al. (18) to be 34 years compared to the second decade peak incidence of CIO of other body bones.
Primary site

Six patients (67%) had tumors in the mandible and 3 (33%) had tumors in the maxilla. In contrast, jaw distribution for CIO is a controversial issue, although a slight mandibular predilection has been reported (19-21). The mean age of presentation of mandibular lesions was 31 years, and in maxillary lesions it was 47 years. Interestingly, seven (78%) of the jaw bone POs affected the right side of the mandible and maxilla. The right side was also affected more commonly in BPO. Around 60% of 69 cases reported in three studies of BPOs (3, 4, 6) affected the right side.

Clinical presentation

The clinical presentation of jaw bone POs is similar in all reported cases. Patients complained of slowly enlarging tumors, and the duration of symptoms varied from one month to one year. Six patients presented with PO within the first six months (9, 11, 13-16). The patients were otherwise asymptomatic; however, some reported hypoesthesia of the inferior alveolar nerve (16), trismus (14) and mild pain (9, 12). In contrast, pain was reported in more than 55% of BPOs (3, 4, 6). When compared with CIO between jaws and long bones, a similar trend was found; pain is less frequently reported in CIO of jaw bones (21). However, features like rapid growth, paraesthesia, displacement and loosening of teeth that accompany CIO of the jaws have not been reported in jaw bone POs. At presentation, jaw bone POs were usually around 3 cm in their largest diameters and were covered by normal oral mucosa. However, some clinicians reported increased vascularity of the overlying mucosa (12, 15) but no ulceration. The tumors were usually hard, sessile, and nodular, although some were lobular (11-12) and rubbery (11). One patient had a history of trauma (14) and one tooth extraction (9) before the appearances of the lesions (Fig. 1).

Radiographic findings

Characteristically, BPO appears radiographically as a broad-based soft tissue mass attached to the cortex (6). The radiological characteristics of BPO were defined by de Santos et al. (22) and include the following parameters: (1) inhomogeneous tumor matrix with calcified spiculation interspersed with areas of uncalcified radiolucent matrix; (2) occasional periosteal reaction in the form of Codman’s triangle; (3) thickening of the periosteal surface of the cortex at the base of the lesion with sparing of the endosteal surface; and (4) extension of the tumor into the surrounding soft tissue. The underlying cortex, in the majority of BPO cases,
appears thick with surface scalloping and “hair-on-end” appearance (6).

Computed tomography (CT) is valuable in the preoperative assessment of PO to exclude macroscopic IMI, delineate extents of the bone cortex and soft tissue involvements and to detect skip lesions (23-24). CT can be useful in detecting cortical thickening or periosteal reaction perpendicular to the bone surface (Fig. 2A). Magnetic resonance imaging (MRI) has several advantages over CT in the evaluation of PO (Fig. 2B). These include better assessment of tumor sizes and depiction of IMI using axial and coronal gadolinium-enhanced fat-saturated T₁-weighted images, respectively. MRI also shows better definition of tumoral margins in relation to neighboring muscle on T₂-weighted images (6, 25).

Reviewing radiological features of all cases of jaw bone POs, similar to BPOs, they were always located superficially on the bone cortex with expansions into the adjacent soft tissues. They appear most commonly as ill-defined radiolucencies or slightly radiopaque shadows overlying intact cortices (12, 16). The presence of fine, focal calcified spicules or trabeculae are observed within the tumor. The cortical surface of the mandibular bone appears intact, and there are hyperdense areas with irregular margins within the bone marrow at the first molar region, suggesting medullary invasion by the tumor. (B) Post-contrast T₁-weighted MR image showing an intensely enhanced tumor mass on the mandibular buccal cortex with diffuse involvement of the medullary space.

Gross pathology

Easy separation of the mucoperiosteum from the tumor has been reported (12). The tumor is closely apposed to the cortical surface of the mandible or maxilla without gross involvement of the medullary cavity (16). Taking an incisional biopsy is not a difficult procedure, because the lesion is soft, fleshy and easily sectioned with a blade, although it is gritty (12, 16). Jaw bone POs are usually well-circumscribed and do not seem to infiltrate into surrounding tissues (16). The cut sections of resected jaw bone POs show lobulated, glistening, and grayish-white tissues (Fig. 3) (11-12, 15-16).

Histopathology

Unni et al. (3), who first described PO as a separate entity, stated the following as characteristic microscopic features of this tumor. PO develops peripheral to the cortical bone with a fairly distinct outer margin and has little tendency to infiltrate adjacent soft tissues. The tumor mass is composed of lobules of poorly-differentiated chondroid tissues and malignant osteoid islands. The amount of cartilage in POs is variable. In the first pattern, POs may show predominant malignant chondroid tissues isolating small islands of anaplastic spindle cells that contain fine, lace-like osteoid with or without mineralization (pattern I). On the other hand, some POs are composed of small islands of cartilage surrounded by large sheets of anaplastic spindle cells that produce osteoid (pattern II). In the third variant, PO is composed of lobulated malignant cartilage forming a cap overlying thin interlacing bands of heavily calcified osteoid surrounded by anaplastic spindle cells (pattern III). The malignant cartilage in PO may undergo calcification or endochondral ossification. According to an ultrastructural study of PO (26), the tumor is mostly comprised of round or
polyhedral chondroblast-like cells with round nuclei, prominent nucleoli, and nuclear envelopes showing discrete indentations. The tumor cell cytoplasm contains conspicuous rough endoplasmic reticulum, lakes of glycogen, and lipid vacuoles, and the cytoplasmic membrane shows scanty and thin projections. The cells are surrounded by an abundant intercellular matrix of low electron density with thin fibrils and granules.

Malignant chondroid, anaplastic spindle cells and osteoid with or without calcification were the histological features stated in all of the reported cases of jaw bone PO. However, the pattern or the histological variant was not stated in any of the previous reports of jaw bone POs, although we could presume that some cases (12, 15-16) represented the first variant depending on the histological features written in these reports. In some cases of jaw bone PO (11-12, 15), mitotic figures were reported to be common along both the chondrocytic and osteocytic cells. Fine bony trabeculae, radiating a short distance from the cortex corresponding to radiographically-seen spicules, were reported in other cases (16).

In the case our hospital reported before (9), the tumor was surrounded by thin fibrous tissue capsule in most parts of the outer surface; however, its capsulation towards the oral mucosa was not clearly seen (Fig. 4). The base of the tumor was directly attached to the surface of the cortical bone. And, at the lower end, the periosteum was lifted by the tumor and continued as the tumor’s outer capsule (Fig. 5). Pattern I of PO was noticed; the tumor was composed of...
lobular masses of poorly-differentiated chondroid stroma containing polyhedral-shaped cells with bizarre nuclei (Fig. 6). In addition, there were myxoid areas containing stellate-shaped cells, islands of osteoid tissue, and fine bony spicules (Fig. 7). No obvious mitotic figures were observed.

**Intramedullary involvement**

For the designation as PO, Unni et al. (3) emphasized that normal endosteal surface of the cortex and no involvement of the medullary portion of bone were required in tumors. If these two criteria were not met, they argued that the tumor could not be differentiated from the CIO. However, Hall et al. (4) suggested that an area of medullary extension of the tumor should not be counted to exclude the diagnosis of PO. Out of the six cases of BPO they had reported, they noticed IMI in three and cortical extension without IMI in one additional case. They argued that PO may or may not penetrate the underlying cortex depending on the nature of the individual tumor, the ability of the cortex to act as a barrier, and the time before treatment. As mentioned by them, PO has a pushing border and not an infiltrating one, and therefore IMI did not change the biological aggressiveness of PO or its prognosis. In a study of 40 cases of BPO, Murphy et al. (6) reviewed the radiological and pathological features and concluded that ultimate penetration of this malignancy should have not been surprising although PO was slow growing and the cortex acted as a neoplastic barrier. Of their 40 cases reported, IMI was noticed in only one case. Bone marrow involvements were reported in two cases of BPOs (27-28), which results in a total of 6 cases (27-28), indicating that IMI is not a usual event of POs.

Among jaw bone POs, tumors spreading through the cortex into the bone marrow spaces have not been reported before. In our case (9), the tumor extended from the right mandibular canine to the right first molar. The surgical specimen was cut into 3-7 mm-thick frontal slices. In the mandibular premolar region, the tumor infiltrated minimally into the cortical bone and showed a worm-eaten appearance (Fig. 8). Near the crest of the alveolar bone, the tumor had no surface capsule (Fig. 4). Although most of the thickness of the cortical bone was preserved in all tissue slices, tumor cell nests were observed within the bone marrow at the molar region. The periodontal ligament showed noticeable thickening from the premolar (Fig. 8) to the molar region, and at the distal side of the first molar it was replaced with tumor tissues (Fig. 9). Since there was no entry of the tumor tissue into the bone marrow through the cortex as far as our careful examination showed, and the mental foramen was out of the tumor extension, it was obvious that the spreading into the bone marrow was through the periodontal ligament space of the first molar tooth. This spreading tendency of jaw bone PO through the periodontal ligament space has been referred to in one of the PO cases involving the mandible (15). The tumor destroyed the crest of the alveolar bone of the first molar tooth and extended minimally into the periodontal ligament space. However, there was no IMI in that case, although it would have been possible if the tumor had been left without treatment for a longer period of time. It should be emphasized that the spread of jaw bone PO to bone marrow, when compared with BPO, is easier due to the presence of the periodontal ligament around teeth.

**Differential diagnosis**

Since jaw bone PO is an extremely rare lesion, clinicians may find it difficult to diagnose. As the tumor is sometimes painful, general dental practitioners may misdiagnose it as a dental abscess (9). Definitive diagnosis of jaw bone PO usually follows radiological and histopathological examinations. Surface osteosarcomas represent approximately 4% of all osteosarcomas and are classified into three types: PO, parosteal osteosarcoma, and high-grade surface osteosarcomas (HGSO) based on their clinical, radiographic, and histological presentation (29).
Parosteal osteosarcomas are the most common of these three categories (30) and are mostly seen exclusively around the knee in older persons in comparison to the clinical features of CIO (31). Radiographically, parosteal osteosarcoma is characteristically a radiodense and lobulated mass attached by a broad base to the underlying bone. Sometimes, a radiolucent clear space appears between the tumor and the normal bone cortex, and the tumor shows no obvious signs of periosteal elevation or bone formation (22, 32). Additionally, PO is dominated by malignant chondroid with lesser amounts of osteoid, whereas parosteal osteosarcoma is characterized by fibroblastic differentiation and well-developed bony trabeculae (33-34). High-grade surface osteosarcoma, a rapidly growing sarcoma, is the least common and has the worst prognosis of the surface osteosarcomas. The tumors are highly aggressive and approximately one-third may demonstrate IMI. Therefore, high-grade surface osteosarcomas require more extensive surgical resection when compared with PO (35). It is histologically composed of sheets of pleomorphic spindle cells that produce osteoid matrix, and it lacks the cartilaginous lobules seen in PO (7, 36).

PO should also be differentiated from CIO with periosteal extension. In addition to its different radiological features and prognosis, CIO is of higher histological grade and shows extensive IMI in all cases. Careful attention should be paid to differentiate PO from periosteal chondrosarcoma. Microscopically, the presence of osteoid material is important to differentiate PO from this well-differentiated, low-grade chondrogenic tumor (37-38).

**Treatment and prognosis**

While the treatment of PO is by wide surgical excision, the role of chemotherapy remains unclear. The prognosis in BPO is much better than that of CIO (39). The overall survival rate is approximately 80% (5, 40-41) and a metastatic rate of 15%, mostly common to the lung, has been reported with local therapy alone (3, 8, 37). PO has a pushing border rather than an invading one and consequently has a low local recurrence rate (13%) (4). Therefore, some studies have recommended wide surgical excision without any adjuvant chemotherapy as the treatment of choice for PO (3-4, 37, 41). In support of that, some studies have reported no association of chemotherapy with local recurrences or overall survival (5, 42). Some patients with BPO who received chemotherapy developed other malignancies like leukemia (5). In contrast, some authors have reported 100% survival in patients who have been treated by surgery and chemotherapy (43). In addition, although local recurrence in PO is relatively rare, it has been associated with a very high incidence of death and metastases (5). Due to this and to the higher-grade nature of some of the tumors, systemic chemotherapy has been widely used in the treatment of PO. Of 119 patients reviewed by Grimer et al., 81 (68%) received postoperative chemotherapy (5). Another group of authors has suggested reserving chemotherapy for recurrent cases in combination with further surgery (10). As shown in Table 1, all cases of jaw bone POs were treated by wide surgical excision (9-16), including ours. Follow-up data were not available for one patient (14). Six of these patients were treated by surgery alone and none developed local recurrence or distant metastasis. These six patients had an average follow-up of 3 years, ranging from one to six years. Only two patients (22%) received postoperative chemotherapy (9, 13). One of these two patients is the case we reported before (9) and has been followed up regularly for 7 years until now with no evidence of local recurrences or metastases. The other patient (13) had a gingival mass which was initially diagnosed as osteoblastoma and was treated by local excision. The patient had a local recurrence 18 months later that was diagnosed as PO and was treated by wide surgical excision and chemotherapy. However, the patient developed lung metastases and died 5 years following the first diagnosis. Therefore, it is difficult to estimate local recurrence and metastasis rates in jaw bone POs due to the small number of documented cases, the short follow-up of some cases, and the inappropriate initial treatment in one case. However, what was apparent from these reports is that the usefulness of postoperative chemotherapy is doubtful; none of the six patients who were treated by wide surgical excision alone developed local recurrence or metastasis. This speculative better prognosis for jaw bone POs compared to BPOs is comparable to the better prognosis of CIO of the jaws compared with that affecting other bones (17).

Intramedullary extension appears to have no correlation on outcome. Neither the patients who had BPO (4, 14, 27) with IMI (main follow-up 3.5 years, ranging from one to seven years) nor the patient who had jaw bone PO (9) with IMI (follow-up 7 years) developed local recurrences or metastases. In addition, it is difficult to determine the best treatment patients should receive because the documented case numbers were small, and the vast majority of the patients were treated by surgery and postoperative chemotherapy. Therefore, it is difficult at present to determine the value of the added chemotherapy.

In conclusion, PO is a rare tumor that may affect the mandible or the maxilla with no specific gender or age predilections. It is important to determine its clinical, radiographic and histological features to be able to differentiate the lesion from other bone-surface tumors. PO is intermediate in its prognosis, and wide surgical excision is the best means of treatment. The value of the use of adjuvant chemotherapy is unclear, and whether it should be used for cases showing bone marrow spread remains unknown.

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