Case Report
An extended resection of periosteal osteosarcoma combined with neoadjuvant chemotherapy: a case report and literature review

Yi Lin¹, Dan Yu¹, Xian Zhang²

Departments of ¹Oral and Maxillofacial Surgery, ²VIP, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, Zhejiang, China

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Abstract: This report describes a rare case of a periosteal osteosarcoma (PO) of the mandible in a 56-year-old Chinese man. The diagnosis was confirmed by a biopsy and a pathological examination. Furthermore, a unique treatment was performed in this case, including preoperative neoadjuvant chemotherapy, an extended resection of the tumor, and reconstruction of the mandibular defect with the fibular myocutaneous flap. Radiological and clinical evaluations were performed during follow-up. The patient was free of disease at the latest follow-up and was satisfied with the results of the treatment, including the improvement of his facial appearance. Herein, we summarize the epidemiology, diagnosis, treatment, and prognosis of the disease after conducting an extensive literature review. In conclusion, patients with PO can be treated by an extended resection of the mass with a simultaneous reconstruction. Neoadjuvant chemotherapy is greatly effective in inhibiting tumor growth and achieving valuable time for digital surgical design.

Keywords: Periosteal osteosarcoma, neoadjuvant chemotherapy, reconstruction

Introduction

Periosteal osteosarcoma (PO) was first recognized by Ewing in 1939 and further described by Lichtenstein in 1959 [1]. PO presents typical radiological features such as fusiform masses located in the periosteum that are accompanied by periosteal reactions and a soft tissue mass [2]. It is a rare tumor that is located most frequently on the diaphysis of the tibia and femur [3]. PO of the mandible is extremely rare, and only few cases have been reported; hence, the treatment of mandibular PO is controversial. At present, there is a widely accepted consensus that a wide surgical resection is the mainstay of treatment for PO [4], which often leads to large bone defect; however, controversy remains as to whether chemotherapy is necessary. We report a case of PO located at the mental region of the mandible, which was treated with preoperative neoadjuvant chemotherapy. Moreover, we reviewed the literature in order to discuss the diagnostic and therapeutic criteria of PO.

Case report

A 56-year-old man presented to our hospital with a 2-month history of a progressively enlarging mass in the floor of the mouth (Figure 1). An imaging examination, including computed tomography (CT), magnetic resonance imaging (MRI) (Figure 2A), and positron emission computed tomography (Figure 2B), revealed that an osseous fusiform mass covered the body of the mandible and the cortical bone was rough, and T1W1 showed low signal intensity and T2W1 showed high signal intensity with visible enhancement in contrast imaging. Fluorodeoxyglucose metabolism increased in the mass, which had the standardized uptake value of 5.8. Thereafter, a biopsy of the lesion confirmed a diagnosis of PO. The hematoxylin and eosin-stained slides showed that tumor cells were heterosexual and had flaky distribution, and an eosinophilic bone matrix was located in the tumor (Figure 3). The results of immunohistochemistry were as follows: S100 (+), CK (+), CD117 (+), CD34 (+), Ki67 (+), and calponin (-).
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The patient started on one 3-week cycle of neoadjuvant chemotherapy (18 mg/m\(^2\) of epirubicin and 2.4 mg/m\(^2\) of ifosfamide) to inhibit the rapid growth of PO and to achieve valuable preoperative preparation time. After 3 weeks of chemotherapy, there was no significant change in tumor size. Furthermore, an extended resection and reconstruction were performed according to a computer-aided design and a digital surgical guide plate. We repaired the soft tissue and bone defects with the fibular myocutaneous flap (Figure 4), and a postoperative examination revealed that the operation was successful, and the patient's appearance was improved (Figure 5).

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with the approval of the Ethics Com-

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**Figure 1.** Mass located in the floor of the mouth.

**Figure 2.** A: An MRI showed a soft tissue mass in the body of mandible, markedly enhanced. B: PET-CT showed an irregular thickening of the soft tissue and increased FDG metabolism in the right-median floor of mouth, considered malignant lesions.

**Figure 3.** A: Tumor cells are patchy, heterogeneous, and eosinophilic bone-like matrix. (hematoxylin and eosin stain; original magnification ×100). B: The nuclei are hyperchromatic and irregular in shape, and the giant cells of the tumors can be seen. (hematoxylin and eosin stain; original magnification ×400).
PO, a very rare disease, is an intermediate-grade osteosarcoma, accounts for less than 2% of all osteosarcomas [5], and is less commonly located in the oral and maxillofacial region. PO occurs most often in adolescents and has a predilection for the diaphysis of the tibia or the femur [6]. We have searched the case reports of this disease from the past 30 years and found a total of seven papers reporting eight case reports (3 case reports for females and 5 case reports for males), of which six cases occurred in the mandible and two in the maxilla. Together with our case, there were nine cases with an average age of 41.6 years. The median age of PO in the jaws is about 15 years later than it is in the long bone counterparts [5]. On radiological examination, PO presents as fusiform masses located in the periosseum that are accompanied by periosteal reactions. In general pathology, the tumor is soft and lobulated, and its microscopic characteristics are moderately differentiated, which are mainly composed of chondroblasts, cartilage, and bone-like and fibrous (spindle cell) components [7]. In the long-bone sites, the prognosis for PO is thought to be considerably better than for conventional osteosarcoma [8]. Similarly, PO has an approximately 15% rate of distant metastases, while in about 50% of osteosarcoma in the jaws, metastases are present [9]. PO often needs to be differentiated from parosteal osteosarcoma. PO is predominantly a cartilaginous neoplasm, but parosteal osteosarcoma is characterized by a spindle cell stroma with mild to moderate atypia and rare mitotic figures dispersed between the irregular osseous trabeculae [10].


The ideal treatment of PO in the maxillofacial region is unclear due to the limited cases reported to date. Referring to the treatment of
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PO in the long bones, the most effective therapy for PO of the jaws is wide surgical resection of either the mandible or the maxilla [5]. PO has been reported to metastasize further than could be imaged using CT or MRI [2], and clinical studies have demonstrated that local recurrence is an important prognostic factor for survival in PO [11]. Therefore, an extended resection is considered mandatory to achieve the complete resection of PO. We referred to the clinical summaries of the eight patients in the case reports (Table 1) and decided to perform an extended resection of the mandible. Simultaneously, we repaired soft and hard tissue defects, which are caused by the extended resection with a fibular myocutaneous flap.

Table 1. Clinical summary of the eight patients in the case reports

<table>
<thead>
<tr>
<th>Authors</th>
<th>Tumor size</th>
<th>Tumor site</th>
<th>Surgical procedure</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zarbo RJ</td>
<td>3.5×3.5 cm</td>
<td>Mandible</td>
<td>Radical resection</td>
<td>No recurrence</td>
</tr>
<tr>
<td>Yoon JH</td>
<td>2.0×1.5 cm</td>
<td>Mandible</td>
<td>Marginal mandibulectomy</td>
<td>No recurrence</td>
</tr>
<tr>
<td>Wang GD</td>
<td>4.0×5.0 cm</td>
<td>Mandible</td>
<td>Partial mandibulectomy</td>
<td>Recurrence</td>
</tr>
<tr>
<td>Piattelli A</td>
<td>Undescribed</td>
<td>Maxilla</td>
<td>Marginal resection</td>
<td>Recurrence and lung metastases</td>
</tr>
<tr>
<td>Piattelli A</td>
<td>Undescribed</td>
<td>Mandible</td>
<td>Radical resection</td>
<td>No recurrence</td>
</tr>
<tr>
<td>Douglas M</td>
<td>4.5×3.0 cm</td>
<td>Mandible</td>
<td>Partial mandibulectomy</td>
<td>Undescribed</td>
</tr>
<tr>
<td>Patterson A</td>
<td>2.5×2.7 cm</td>
<td>Maxilla</td>
<td>Hemimaxillectomy</td>
<td>No recurrence</td>
</tr>
<tr>
<td>Roman G</td>
<td>1.5×1.0 cm</td>
<td>Mandible</td>
<td>Segmental mandibulectomy</td>
<td>No recurrence</td>
</tr>
</tbody>
</table>

It is not clear whether chemotherapy as a treatment for PO is effective. However, a report of two cases with a mean follow-up time of 72 months showed good effects from neoadjuvant chemotherapy (8-12 g/m² of methotrexate, 30

Figure 5. A: Postoperative frontal photography. B: Postoperative intraoral photography. C: Postoperative CT review.
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mg/m² of doxorubicin, and 2 g/m² of ifosfamide), and the postoperative histological findings indicated a good response to the neoadjuvant chemotherapy (necrosis percentage, ≥ 90%) and a negative resection margin [12]. However, controversy remains as to whether chemotherapy is necessary in the management of PO. Grimer and his colleagues reported that the use of chemotherapy was not shown to be a prognostic factor in a study of 80 patients [13]. Additionally, a retrospective study of 33 patients with PO found that the patients who received chemotherapy had a 10-year overall survival rate of 86%, and those who received only local treatment had an overall survival rate of 83% (P=0.73) [2]. The retrospective study indicated that survival was not influenced by the performance of chemotherapy. It is certain that the prognosis of PO is determined by several factors, including the anatomical location of the tumors, the degree of invasion into the medulla, and the histological grade of the malignancy [14]. In the present case, there was no significant change in the size of the tumor before and after chemotherapy. Although the tumor was not sensitive to chemotherapy, its rapid growth was inhibited. Hence, we considered that neoadjuvant chemotherapy was significant. The rarity of PO suggests that a multicenter prospective study is necessary to evaluate the role of neoadjuvant chemotherapy.

In a recent report by Maheshwari et al. [15], bilateral synchronous tibial PO was described. Two patients belonging to the same family had a TP53 mutation, and direct sequencing of exons 5 to 8 demonstrated a missense mutation in at least one allele of the TP53 gene. With additional studies in the future, gene therapy may be another feasible treatment for PO.

Conclusion

At present, there are no ideal treatments or guidelines for PO. We describe some valuable therapeutic options in this case report. We suggest that the prognosis of PO undergoing an extended resection is good, and immediate reconstruction can be considered. If the tumor is large and growing rapidly, preoperative neoadjuvant chemotherapy can be performed.

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Disclosure of conflict of interest

None.

Address correspondence to: Xian Zhang, Department of VIP, The First Affiliated Hospital, College of Medicine, Zhejiang University, 79 Qingchun Road, Hangzhou 310003, Zhejiang, China. Tel: +86-571-87236893; Fax: +86-571-87236395; E-mail: docxianzhang@126.com

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