

Maxillary Osteosarcoma: Two Case Reports and Literature Review

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Abstract

Osteosarcoma is a rare malignant tumor of the maxilla. Although clear surgical margin is the only predictor for the prognosis of the disease, neoadjuvant chemotherapy showed a reasonable effect on the tumor with variable degree of necrosis. In this article, we report two cases where neoadjuvant chemotherapy was used with review of the literature.

Key words: Osteosarcoma, Maxilla, Chondroblastic, Jaw osteosarcoma

Introduction

Osteosarcoma (OS) is the most common primary bone malignant tumor [1]. However, in the craniofacial skeleton it is considered very rare. Jaw Osteosarcoma (JOS) represent only 4% of all OSs reported [1,2]. It is characterized histologically by anaplastic stroma with direct osteoid production [3]. Although the JOS and OS of long bones have similar histological features, JOS has different biological behavior [1,2,4-6]. It occurs in a mean age of 10-20 years later than OS of long bones and it rarely metastasizes. This could influence better prognosis, however, the painless swelling presentation of JOS could hide the disease until an advanced stage [2,7]. The etiology of OS is not quite clear. Paget's disease, fibrous dysplasia and ionizing radiation are thought to be predisposing factors [2,4]. A high cellular activity may have a role in OS etiology as the most common site affected is the metaphyseal end-plate in growing bones [2].

Case Reports

Case 1

A 31-year-old gentleman presented to our clinic complaining of swelling in the left maxilla related to the area of extracted first and second premolar, which he noticed two months ago (*Figure 1*). He denied any medical illness or tobacco use. On examination there was a non-tender small elevation of the alveolar bone with normal covering mucosa and there were no palpable cervical lymph nodes. The radiograph showed ill-defined mixed radiolucent-radiopaque lesion (*Figure 2*). The



Figure 1. Patient with swelling in the left maxilla.

biopsy showed atypical mesenchymal cells with small foci of osteoid and prominent cartilage component consistent with high-grade chondroblastic osteosarcoma (*Figure 3*). Bone scan showed high uptake in left maxilla (*Figure 4*). The patient refused any surgery at that time and disappeared for a year then he came back with significant swelling in the same area. The swelling was involving the alveolus and the palate from the first molar almost to the midline. Incisional biopsy result was consistent with the previous diagnosis. Chest and brain radiographs were taken to rule out any metastasis. The patient underwent neoadjuvant chemotherapy four cycles of cisplatin

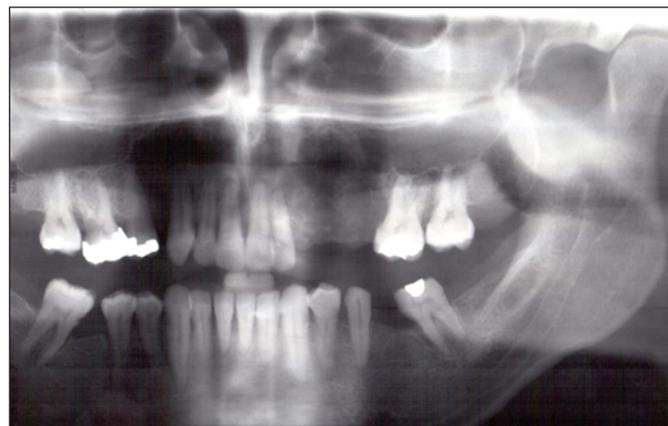


Figure 2. Panoramic radiograph of the patient showing ill-defined mixed radiolucent-radiopaque lesion.

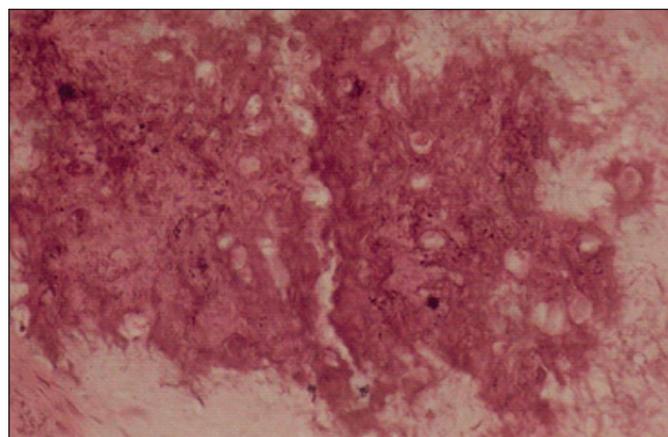


Figure 3. Histological analysis showing atypical mesenchymal cells with small foci of osteoid and prominent cartilage components.

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100 mg and Adriamycin 25 mg. Then subtotal maxillectomy was done. The tumor showed 15% necrosis and negative soft tissue and bony margins. The patient has been followed-up for four years without any sign of recurrence or metastasis (Figure 5).

Case 2

A 27-year-old female with unremarkable past medical history was presented with swelling and pain in right maxilla since 3 months. The swelling was apical to the first molar, hard with mild tenderness and normal mucosa. Radiographs showed well-circumscribed radiopacity giving the impression of a benign lesion (osteoma). A biopsy showed a malignant osteoid and cartilage producing cells consistency with

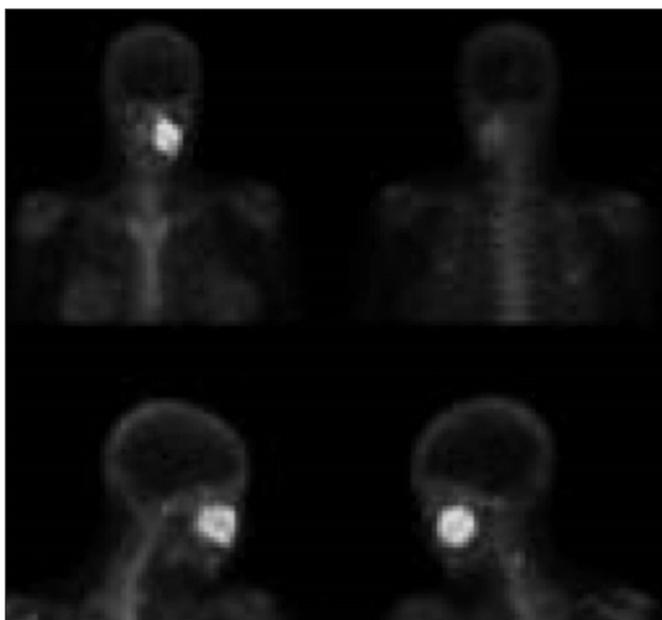


Figure 4. Bone scan of the patient showing high uptake in left maxilla.



Figure 5. Follow-up CT scan of the patient 1 (Case 1). There is no sign of recurrence.

chondroblastic osteosarcoma. The patient received five cycles of Cisplatin 100 mg and Adriamycin 25 mg followed by hemimaxillectomy with wide margins. Post resection biopsy showed negative soft tissue and bone margins and 30% necrosis. The patient has been on regular follow-up for 32 months without any sign of recurrence (Figure 6).

Discussion

While osteosarcoma of the jaw considered very rare tumor, maxilla is more frequently affected than the mandible. It accounts more than 47% of craniofacial osteosarcoma which by itself accounts between 4-10 % of all osteosarcomas [8]. It is becoming more believable that ionizing radiation is a risk factor for developing Maxillary Osteosarcoma (MOS) [9]. Previous radiotherapy for other head and neck malignancies was an interesting history of some cases presented with MOS [9]. Also finding a MOS in a patient who experienced malignancies in other areas gave the clue of genetic predisposition. MOS was reported to occur in patients with Li-Fraumeni syndrome which characterized by mutation in gene *p53* [8,10]. In heredity retinoblastoma the deletion of the long arm of chromosome 13 may have a role also in OS as it occurs in those patients independent to the radiation therapy [11]. Other diseases, Paget's disease and fibrous dysplasia, were also associated with OS [1,5,12,13].

MOS has almost 1:1 male to female ratio and occurs in a mean age of 35 years [14]. It usually present clinically as a painless swelling in its early stage. As the tumor advances the patient could complain of pain, ulceration of the mucosa, looseness of the teeth, paralysis of the infra orbital nerve,



Figure 6. Follow-up CT scan of the patient 2 (Case 2), without any signs of recurrence.

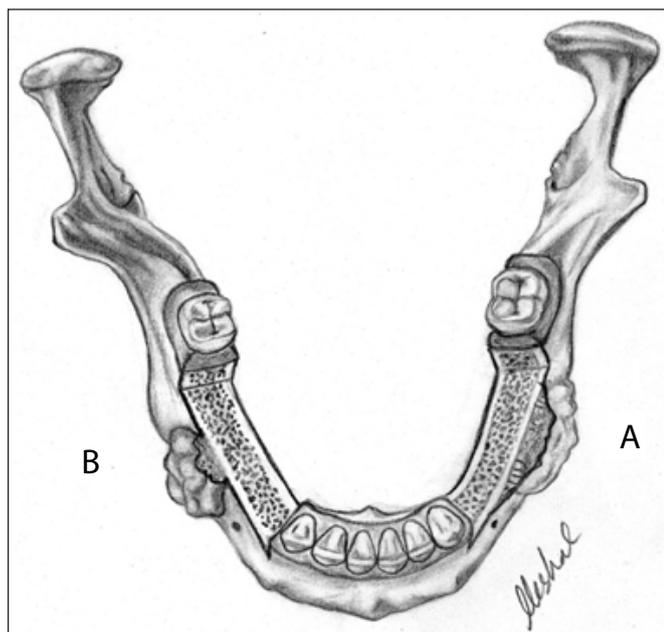


Figure 7. Juxtacortical "extrabony" osteosarcoma
A-Periosteal osteosarcoma, B-Parosteal osteosarcoma.

nasal obstruction and reduced visual acuity. JOS is unlikely to metastasize to the lymph node [15]. The radiographic appearance of the MOS varies depending on the degree of its calcification. It may show benign well-defined homogenous radiopacity mimicking osteoma [16], as in our second case, but it usually appears as an ill-defined mixed radiopaque-radiolucent lesion. It could invade the cortical bone and the adjacent soft tissue. The involvement of the periosteum may result in the described sun ray or sunburst appearance. When the tumor reaches the teeth, it proliferates in the periodontal ligament space (PDL) causing loss of the lamina dura and widening in the PDL. This was described by Garrington et al as a diagnostic feature of JOS [17]; and can be easily differentiated from scaloderma, which manifest in generalized widening of PDL, by its localized effect.

The distinguished histological feature of OS is the direct osteoid production by anaplastic stroma. It ranges between low-grade anaplasia, which may mimic a benign lesion, and high-grade poorly differentiated stroma. It is classified according to the predominant cell type, derived from the original malignant mesenchymal cell, into: chondroblastic, osteoblastic and fibroblastic osteosarcoma. In the JOS, chondroblastic type occurs more frequently than the two others [8]. Other rare variants of OS such as epithelioid osteosarcoma were also reported [18,19]. There was no association between the histological type and the prognosis of the disease; however, Jenior et al. found that osteoblastic osteosarcoma has the worst prognosis among the other types [20].

The few mitotic figures and minimal cytological atypia of low-grade osteosarcoma could be missed easily and be diagnosed as a fibro-osseous lesion [21,22]. It was reported in more than one case a recurrent fibrous dysplasia which was finally diagnosed as an OS [1,13]. Undiagnosed low-grade OS have the potential to transform to high-grade with the time [22]. Definitive diagnosis of low-grade OS therefore relies

mainly on the clinical behavior of the disease. Unexpected aggressive behavior of fibrous dysplasia, invasion of the periosteum and soft tissue, cortical destruction and poorly defined margin would not make the surgeon close an eye on fibrous dysplasia diagnosis.

Juxtacortical "extrabony" osteosarcoma is considered low-grade osteosarcoma. It is very rare tumor and it may occur subperiosteal "periosteal osteosarcoma" or attached to the periosteum "parosteal osteosarcoma" (Figure 7). Both have better prognosis than the central osteosarcoma [22-24].

Negative-margin surgery is the only promising treatment modality to increase the survival rate of osteosarcoma patients [25,26]. While it is recommended to sacrifice one uninvolved soft tissue barrier and have 3cm bony margin in sarcomas [8], it is very difficult to achieve that in maxillary tumor due to proximity of eyes, brain and other vital structures. With multimodality treatment, Fernandes et al reported seven cases of MOS which have been resected with single close or even positive margin and had only one case of recurrence over a mean follow-up of 46 months [8]. Neoadjuvant (preoperative) and adjuvant (post-operative) chemotherapy both were used beside surgery and their effect in increasing the survival rate of JOS is still controversy. Many cases have not shown any improvement in the survival rate of JOS with adjuvant chemotherapy as observed in OS of the long bones [27]. In contrast, Smeele et al. found a significant effect of adjuvant chemotherapy on the survival rate of JOS as Thiele et al reported [15,28]. The limited effect of chemotherapy in the survival rate of JOS compared with OS of the long bones could be explained by: low metastatic rate (18%) compared with 80% of the long bones, lower grade of malignancy and minimal response to the neoadjuvant chemotherapy [8]. In fact, the rarity of the disease and the difference in the chemotherapy protocols used in the reported cases may fail to show its effect clearly. Neoadjuvant chemotherapy is becoming common practice for the treatment of OS of the long bones as it showed significant improvement of the survival rate [29]. In addition, delivery of chemotherapy to an intact blood supply would have more effect on the tumor. It would allow us to assess the effect of chemotherapy agent on the resected tumor and modify the adjuvant chemotherapy doses [29]. In our cases we used neoadjuvant chemotherapy and found it to be effective as the tumor exhibited more than 30% necrosis.

OS is believed to be resistant to radiation therapy [8]. In one case series, radiation therapy have been used with no improvement in the survival rate [30]. Moreover, the side effects of the radiation therapy compromised the quality of life of the surviving patients. It also does not seem wise to use a risk factor to treat the same disease.

The survival rate of MOS found not to be different than the mandibular ones [8,27]. However, the complex anatomy and proximity of vital structures compromise the respectability of the tumor with negative margin: the only predictor of curability of the disease. In addition, the delayed detection of this asymptomatic expanding tumor increases the chance of adjacent structure invasion and the transformation to a higher grade OS. The mean time between the initial symptom and the diagnosis of MOS ranges from 3 to 5 months [24,25]. The

dentist usually is the first one whom the patient would go for. Many cases reported in the literature were referred from a dentist [7,23,31-33]. Because OS is a very rare disease and could mimic a localized periodontal disease, the patient may be referred to oral and maxillofacial surgeon and diagnosed at a late stage.

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