Chondroblastic Osteosarcoma of the Mandible: Case Report and Treatment Considerations

SUMMARY

Background: Osteosarcomas (OS) are the most common primary malignant neoplasms of bone. OS of the head and neck are extremely rare.

Case Report: A male patient, age 33, presented to the Oral and Maxillofacial Surgery Clinic with severe swelling in the left mandibular region a month after initial resection of a chondroblastic OS of the left mandible. Hemimandibulectomy up to the region of the canine, supracyclic neck dissection and temporalis muscle reconstruction was performed. The patient was administered adjuvant chemotherapy and radiation therapy further to head and neck tumour board counselling.

Discussion: Negative surgical margins appear to be the only significant predictor of overall and disease-specific survival. Radiation therapy is more frequently employed in the OS of the head and neck when compared to OS of long bones, especially in patients with high grade tumour or in those where wide surgical margins cannot be obtained. In the latter patients neoadjuvant chemotherapy has been suggested to be beneficial. A multidisciplinary approach is justified, but the head and neck surgeon has the leading role. Review of the literature and case-wise counselling by the head and neck tumour board is recommended for every new case diagnosed.

Keywords: Osteosarcoma; Jaw; Surgery; Chemotherapy; Radiotherapy

Background

Osteosarcomas (OS) are the most common primary malignant neoplasms of bone. They are usually found in long bones, especially around the knee. Their incidence in the head and neck region is extremely rare and they are mainly located in the maxillofacial region. Local swelling with or without pain is the most frequent early clinical manifestation of the OS in the head and neck. The mean age of patients with OS of the jaw is between 30-40 years. OS may be described as central, periosteal, parosteal or extra skeletal, depending on their origin. According to their predominant histological differentiation, OS are classified as osteoblastic, chondroblastic or fibroblastic. Histologically OS are characterized by a malignant, undifferentiated stroma, which is producing neoplastic osteoid or bone. For the diagnosis of OS, the presence of osteoid formation is critical.

OS of the head and neck (OSHN) are rare tumours and have been reported to constitute <10% of all cases of OS. OSHN typically occur in the 3rd or 4th decade of life and with equal gender distribution, whereas OS of the long bones occur mostly in the 2nd decade of life and have a slight male preponderance.

The aim of this paper was to present a case of a large chondroblastic OS of the mandible, which was treated after local recurrence. Given the lack of a specific treatment protocol for the OS of the jaw, together with the large tumour size, the prognosis could not be certain, thus particular reference is given to the treatment followed.

Case Report

A 33-year-old male patient presented to the Oral and Maxillofacial Surgery Clinic with severe swelling...
in the left mandibular region. On clinical examination, the buccal mucosa of the region was found reddish, but its texture was normal and painless. His history revealed previous local surgical resection in the ENT department of a district general hospital, a month before referring to our clinic. Histology of the first operation reported chondroblastic OS of the left mandible resected in close surgical margins. On admission (same with referral day), a clinically evident recurrent lesion existed. Routine laboratory tests were normal with the exception of serum alkaline phosphatase, which was increased to 181 IU/L (35-145 nl).

MRI and CT scan demonstrated an osteolytic destructive process located at the left mandibular angle and body, extending to the left mandibular ramus, with presence of bone trabeculae, and an accompanying soft tissue mass that was extending into the subcutaneous tissue with abnormal enhancement, which was extending into the left medial and lateral pterygoid muscles (Fig. 1, a-c). Whole-body bone scintigraphy showed increased pathological osteoblastic activity at the entire left side of the mandible. No other pathological loci were found in any other site of the body (Fig. 1d). Thoracic x-ray and CT scan revealed no pathologic findings that would indicate distant metastasis of the tumour.

The tumour was resected with hemi-mandibulectomy up to the region of the canine (43), including intraoral preparation, dislocation of the left condyle, and en block removal of the tumour with the body of the mandible, and supra-omohyoid neck dissection. The temporalis muscle was prepared and sutured intra-orally via semicoronary incision (left side) at the site of the defect. The tumour measured 13 cm in its larger diameter. Routine laboratory tests performed the first day after surgery showed that the patient’s serum alkaline phosphatase levels declined to normal (109 IU/L).

Histopathology reported a malignant neoplastic lesion of spindle-shaped neoplastic cells, with intermediate or severe nuclear atypia and increased mitotic activity (Figs. 2a and 2b). The cellular arrangement was diffused and in bundles, with focal formation of osteoid and osseous tissue (Fig. 2c). The cells also showed focal cartilage differentiation (Fig. 2d). Areas of coagulation necrosis were also found. These characteristics are compatible with those of a chondroblastic OS. At least 1.5 cm of tumour free margins were reported all around tumour periphery.

The head and neck tumour board counselled adjuvant chemotherapy and radiation therapy in order to prevent further relapse. 1 month after operation the patient underwent chemotherapy (6 cycles for a period of 4 months). The regimen included ifosfamide (5gr day1-day3) and epirubicin (130mg day1) for the first 3 cycles, and ifosfamide only (5gr day1-day3) for the remaining 3 cycles. Supportive regimen with antiemetics, antihistamines and Mesna (for the prevention of the ifosfamide toxic effect) was also administered. Concurrent radiation therapy was administered; the left mandibular
area was irradiated using a 6MV photon beam produced by a linear accelerator and an estimated total dose of 6400 Gy (200 Gy fractionation).

The patient was followed-up for 20 months postoperatively and did not develop any clinical signs of the disease. Upper abdominal CT scans exhibited no evidence of metastasis.

Figure 1c. Axial CT section from a 33-year-old male with recurrent OS of the mandible;

Figure 1d. Whole body scintigraphy shows no evidence of distant or regional metastasis, and a marked peri-tumoural inflammation.

Figure 2a and 2b. Presence of spindle-shaped neoplastic cells, with intermediate or severe nuclear atypia and increased mitotic activity;

Figure 2c. Diffused cellular arrangement with focal formation of osteoid and osseous tissue;
Discussion

OS, on the basis of the predominant matrix, are classified into osteoblastic, chondroblastic and fibroblastic\textsuperscript{13}. Osteoblastic OS shows the predominant bone and/or osteoid matrix\textsuperscript{13}. Fibroblastic OS shows a spindle-cell malignancy with only minimal amounts of osseous matrix\textsuperscript{13}. Chondroblastic OS contains chondroid matrix dominantly\textsuperscript{13}. There is disagreement in the literature with regard to the predominant histologic subtype of the OSHN. The chondroblastic has been described to be the predominant type in head and neck region\textsuperscript{2-5,10,14}. However other authors reported the osteoblastic type to be more frequent\textsuperscript{7-8,15}.

Concerning the radiographic appearance, the presence of a widening of the periodontal ligament space, with or without an irregular absence or attenuation of the lamina dura, is estimated based on the panoramic and intraoral radiographs, as noted by Garrington et.al\textsuperscript{8,16}. Another sign is the presence of the “classic” sunburst or sunray appearance caused by osteophytic bone production on the surface of the lesion\textsuperscript{2}. An additional significant sign analyzed on CT is the pattern of osteogenesis and bone destruction. However, in a recent studies, Nakayama et. al\textsuperscript{13,16} showed that there was no significant association between the histological subtype and these CT findings.

It has been reported that with OSHN, there is a predominance of high grade tumors\textsuperscript{5,7,14}. On the other hand, others reported that the majority of the cases belong to the intermediate grade of malignancy\textsuperscript{5,10}. In our case, the tumour was of intermediate grade. Distant metastasis of the OSHN is rare, compared with the OS of the long bones, and mainly occurs in the lungs as a late stage event\textsuperscript{6}. The main reason of failure in OSHN is local recurrence\textsuperscript{5}.

The majority of studies could not correlate the histological type with the prognosis of OSHN. Specifically Clark et. al. reported that patients with chondroblastic OSHN had a better overall survival rate when compared to patients with osteoblastic or fibroblastic tumours\textsuperscript{4}. Takahama et.al\textsuperscript{5} found similar results, whereas other authors consider the chondroblastic subtype of OSHN as an unfavourable prognostic factor\textsuperscript{16}. This could be clearer in the future with studies on larger groups of cases. Current studies report that factors influencing prognosis are the size of the tumour, the site and the incision margins.

The median of the tumour size in OSHN is 4-6cm in greatest dimension\textsuperscript{5-6}. It has been reported that tumours bigger than 4cm in size are associated with negative prognosis since they showed significantly increased risk of local recurrence, which is the main reason of treatment failure\textsuperscript{5-6}. Compared with other reports\textsuperscript{2,3,6,7}, in our case the tumour was unusually large (13cm).

Negative surgical margins appear to be the only significant predictor of overall and disease-specific survival. For this reason complete surgical excision of the tumour is the mainstay of the treatment in patients with OSHN\textsuperscript{2,3,5,6}. However, only a few studies included information regarding surgical margins clearance. Specifically, van Es et al\textsuperscript{18} reported that 40% of their patients had positive surgical margins and their rates of local recurrence and distant metastases where 33% and 21%, respectively. These results are in accordance with other publications\textsuperscript{6}. An important factor in the surgical treatment alone protocol is the amenability to radical resection with clear margins\textsuperscript{2}. Clear margins may be difficult to achieve, particularly in the maxilla and skull base, where frequent positive margin rates of 31% to 54% have been reported, a condition that is associated with worse prognosis in the maxilla\textsuperscript{2,6}. Nakayama et. al\textsuperscript{13,16} report that patients with OS of the maxilla had a good outcome, in contrast to that of the mandible, which had a poor outcome, and the difference was significant. On the other hand there are few studies regarding the differences of the prognosis between the mandible and the maxilla, and therefore, further studies are needed. In the present case, given the previous excision in close surgical margins, extended effort has been put to ensure the widest possible clear free margins.

All these factors associated with negative prognosis, in addition to the lack of specific treatment protocol in OSHN, make choosing the optimal treatment not easy. The benefits of the use of multimodality treatment are not yet scientifically established in OSHN, in contrast to the OS of the long bones. However, an increasing number of studies report improved results with adjuvant chemotherapy and radiation therapy, as well as neo-adjuvant chemotherapy, although the results were not statistically significant\textsuperscript{2,3,6,7,19}.

Figure 2d. focal cartilage differentiation
Radiation therapy is more frequently employed in the OSHN than in those of the long bones, especially for patients with high grade tumour or in cases where wide surgical margins cannot be obtained. OS are relatively radio-resistant, requiring more than 6000 cGy to be effective in an area of several vital structures. However, many researchers have incorporated the use of radiation therapy in the multimodality treatment of OS, taking advantage of the modern radiation techniques (3D conformal radiation therapy, intensity-modulated radiation therapy).

Regarding the use of chemotherapy, Smeele et al. reported the improved survival in OSHN patients treated with adjuvant chemotherapy irrespective of the completeness of surgical resection, which was statistically significant. Another meta-analysis by Kassir et al. found no benefit for chemotherapy in the treatment of OSHN and actually reported a worse outcome for patients treated with adjuvant chemotherapy, while other researchers reported better survival with chemotherapy. Many authors have suggested that neo-adjuvant chemotherapy may offer benefit via a decrease in cellular viability at the tumour periphery, whereby better surgical margins can be obtained. Salvati et al. speculate that application of neo-adjuvant chemotherapy in OSHN may decrease the risk of local relapse, decrease the number of eventual pulmonary metastases, and increase the time interval from surgery to the appearance of pulmonary metastases. However, larger numbers of patients will be required to answer the question of whether neo-adjuvant chemotherapy favourably impacts the disease-free or overall survival of patients with OSHN or not. Randomized clinical trials reported improved disease-free survival using neo-adjuvant chemotherapy protocols indicating, however, the difficulty in assessing this response clinically or radiologically. Specifically, they report that despite the lack of demonstrable overall benefit of neo-adjuvant chemotherapy, a favourable histological response to neo-adjuvant chemotherapy is an important prognostic variable and predictor of long-term treatment outcome. Recent studies support this view without being powered enough to report a statistically significant difference.

Conclusively, OSHN is not as rare as one would anticipate. There is a considerable number of patients suffering from the malady. Choosing the optimal treatment for each one of them can be a tricky task. A multidisciplinary head and neck tumour board approach is justified, while the maxillofacial surgeon has the leading role. Ample knowledge of the craniofacial surgical complexities is a requisite to obtain negative surgical margins, which are the single predictor of survival. Review of the literature and case-wise counselling by the head and neck tumour board is recommended for every new case diagnosed.

References


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