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Case Report

Pathology Section

Osteosarcoma of Jaw Masquerading as Calcifying Epithelial Odontogenic Tumour- A Diagnostic Dilemma

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ABSTRACT

Osteogenic osteosarcoma is the most widely recognised primary malignant bone tumour involving particularly the appendicular skeleton. Osteosarcoma of jaw including maxillary and mandibular osteosarcoma accounts for about 7% of cases. The variants of osteosarcoma involving jaw include- osteosarcoma, Not Otherwise Specified (NOS) Low grade central osteosarcoma; chondroblastic osteosarcoma; parosteal osteosarcoma; periosteal Osteosarcoma. The present case was a 27-year-old male who came to the dental Outpatient Department (OPD) with the complaints of swelling in the upper vestibule and loosening of upper alveolar teeth and was reported as Calcifying Epithelial Odontogenic Tumour (CEOT) on histopathological examination and excision of the lesion was done. After two months the patient again presented with a recurrent lytic and sclerotic lesion involving the left maxillary bone with soft tissue extension in the maxillary sinus. Provisional diagnosis was made as malignant transformation of CEOT and immunohistochemistry was performed for the confirmation of the diagnosis. This case represented the challenges in the diagnosis of osteosarcoma of jaw which can be due to difficult biopsy procedure; limited imaging and challenges in legitimate resection because of the proximity to essential structures and the challenges are being faced to get the optimal treatment of jaw osteosarcoma.

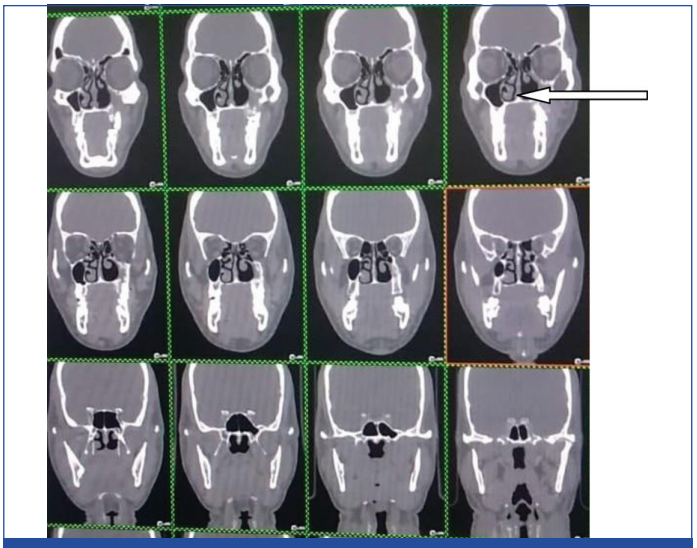
Keywords: Histopathological, Immunohistochemistry, Mandibular, Malignant, Pleomorphism

CASE REPORT

A 27-year-old male presented to the dental OPD of Mahatma Gandhi hospital, Jaipur, Rajasthan with swelling in the left upper vestibule (oral region) and loosening of left second molar for past six months. The patient underwent excision of the lesion and was diagnosed as CEOT on histopathological examination.

The patient again presented with lytic and sclerotic lesion of the left second molar region of left upper vestibule (oral region) after two months. On examination, the lesion was approximately 3 cm in size, oval in shape, hard in consistency and having soft and smooth texture. There was tenderness but no discharge. Contrast Enhanced Computed Tomography (CECT) scan of the neck revealed an ill-defined enhancing lesion in the left buccal mucosa and upper gingivobuccal sulcus with bony erosion involving the left maxilla with extension of the lesion in the maxillary sinus, suggestive of a malignant lesion [Table/Fig-1]. Also enlarged level II cervical lymph nodes were seen. Curettage biopsy was done in the left second molar region and buccal vestibule.

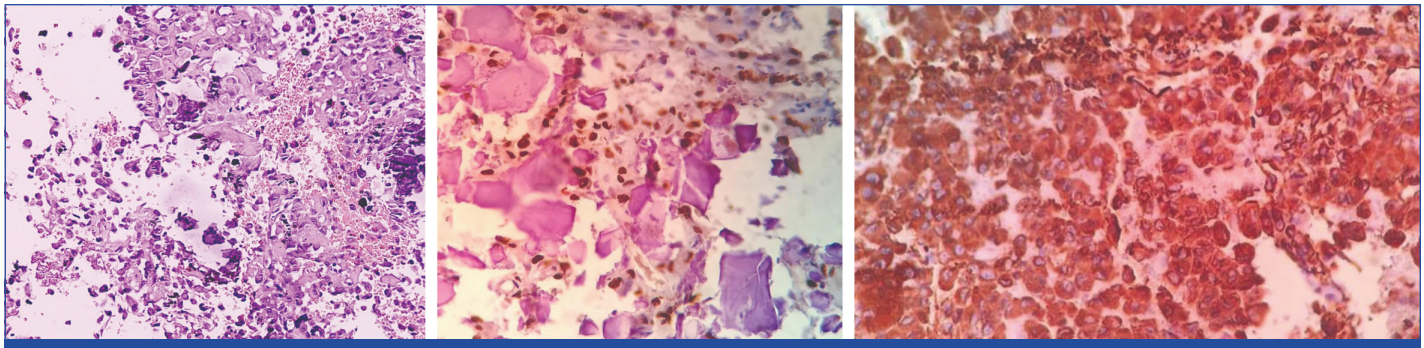
The biopsy was sent to the Department of Pathology. Microscopically, the Haematoxylin and Eosin (H&E) stained sections showed presence of atypical polygonal cells arranged in sheets showing high Nucleus Cytoplasmic ratio (N:C) nuclear pleomorphism and prominent nucleoli. The cells showed abundant eosinophilic cytoplasm and were plasmacytoid at places. Tumour cells were seen along with pink eosinophilic material deposition and with areas of calcification [Table/Fig-2]. Mitotic activity was noted to be 2-3/10 High Power Field (HPF) along with atypical mitosis. Provisional diagnosis was made as malignant transformation of CEOT and immunohistochemistry was performed for the confirmation of the diagnosis. Differential diagnosis includes Adenomatoid Odontogenic Tumour (AOT), Calcifying Odontogenic Cyst (COC), Ameloblastic Fibro Odontoma (AFO). However, on Immunohistochemistry (IHC) tumour cells were diffusely immunopositive for Special AT rich Sequence-Binding protein 2) (SATB2) nuclear positivity and vimentin, respectively [Table/Fig-3,4]. Pancytokeratin and p63 were found to be negative



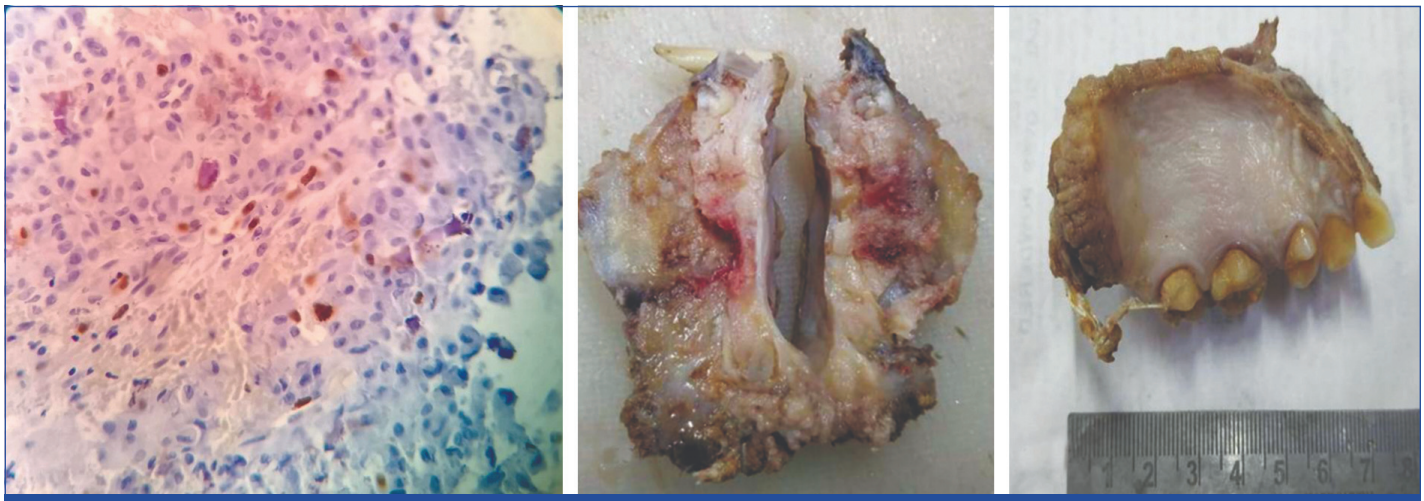
[Table/Fig-1]: CECT scan of the neck showing an ill-defined enhancing lesion the left buccal mucosa and upper gingivobuccal sulcus with bony erosion involving left maxilla with extension of the lesion in the maxillary sinus.

in tumour cells because of the presence of atypical hyperchromatic cells and atypical mitotic figures; possibility of malignancy was considered which was proven by IHC [Table/Fig-5]. Hence on the basis of radiological, histomorphological and immunohistochemical methods, the challenging diagnosis of osteosarcoma, conventional type was made. Patient then underwent left maxillectomy, with level IA (submental lymph nodes) and IB (submandibular lymph nodes) lymph node dissection.

The gross examination showed a greyish white hard tumour measuring 4.5×2.5×1.6 cm, microscopically involving the whole of maxilla with unremarkable overlying mucosa [Table/Fig-6,7]. Overall histomorphology favoured osteogenic osteosarcoma and Tumour, Nodes, Metastases (TNM) staging was pT1N0. Patient received free flap reconstruction at the operative site and his postoperative period and six month follow-up period was uneventful.



[Table/Fig-2]: Focal pink eosinophilic material seen in between malignant cells (H&E 200X). **[Table/Fig-3]:** IHC showing SATB2 nuclear positivity in tumour cells (400X). **[Table/Fig-4]:** IHC showing vimentin positivity in tumour cells (400X). (Images from left to right)



[Table/Fig-5]: IHC showing pan CK negativity in tumour cells (400X). **[Table/Fig-6]:** Gross photo showing variegated cut surface of tumour involving maxilla. **[Table/Fig-7]:** Gross photo showing unremarkable stretched mucosa. (Images from left to right)

DISCUSSION

Mandibular and maxillary osteosarcomas account for about 7% of all the osteosarcomas. The mean age for diagnosis is between 20-40 years with heterogeneous sex distribution. The signs and symptoms include regional swelling, low intensity pain, paresthesia, changes in tooth position, and loose teeth. The radiographic appearance may be purely osteolytic, mixed or osteogenic (sun-ray appearance) [1]. Chaudhary M and Chaudhary S, reported that the widening of periodontal ligament space and inferior dental canal, together with sunburst effect are almost pathognomonic of osteosarcoma of jaw bone, radiologically [2]. Also the presence of destructive unicentric lesion with poorly defined margins and a predominantly sclerotic, lytic or mixed radiographic pattern should lead one to suspect an osteogenic sarcoma. The significance of special investigations such as Computerised Tomography (CT) and Magnetic Resonance Imaging (MRI) lies in evaluating the size of the lesion for staging, intramedullary and extramedullary involvement, tumour calcification and invasion into adjacent tissues [2].

As per World Health Organisation (WHO), the variants of osteosarcoma involving jaw include- osteosarcoma NOS; low grade central osteosarcoma which arises in the medullary cavity of the bone; chondroblastic osteosarcoma has chondroblastic matrix; parosteal osteosarcoma arises on the cortical surface of the bone; Periosteal sarcoma is an intermediate grade malignant bone and cartilage forming neoplasm arising on the cortical surface of the bone. The low grade central type is the most common among them [3]. Elkordy MA et al., and Anil S et al., in their articles talked about the lesser incidence of distant metastasis of jaw osteosarcomas owing to their better prognosis as compared to that of long bone osteosarcomas [4,5]. Stewart BD et al., discussed about the differential diagnosis of jaw osteosarcomas [6]. Osteosarcomas can be difficult to distinguish when they have cartilaginous component as in chondrosarcomas. Another entity, fibrous dysplasia is a benign fibro-osseous lesion although malignant transformation rarely occurs but can be a secondary osteosarcoma. Ossifying fibroma, a benign fibro-osseous lesion has osteoblasts which are not atypical like the sarcomatous cells of osteosarcoma that produce osteoid. Lastly, osteoblastoma may mimic osteosarcoma radiographically but atypical mitosis is not seen as in osteosarcoma [6].

The WHO has mentioned that histopathologically osteosarcomas are composed of sarcomatous tumour cells that produce malignant bone or osteoid. The tumour cells may have densely eosinophilic cytoplasm resembling osteoblasts which are variable in size with nuclear atypia. The osteoid may be thin, lace like and variable in amount [3].

The CEOT is a benign odontogenic tumour of gingival sulcus called pindborg tumour which are locally aggressive tumour consisting of polyhedral squamous cells with amyloid bodies deposition. They are positive for pan cytokeratin on IHC [7]. Normally, IHC has a limited value in diagnosing osteosarcoma, but in difficult cases like the present case, markers denoting osteoblastic lineage can be helpful like osteocalcin, osteopontin, and SATB2. SATB2 is used for mainly pathological purposes it gives nuclear positivity [8]. In present case, because of vimentin and SATB2 positivity, mesenchymal and osteoblastic origin was established. Machado I et al., also established its role in differentiating osteosarcoma from their malignant bone mimickers like chondrosarcoma and ewings sarcoma [8]. Dev DA et al., also reported an unusual case of mandibular CEOT having aggressive presentation but histopathologically found to be CEOT [9]. Carvalho DL et al., in 2016 also reported a case of CEOT mimicking gingival inflammation [10]. Hada MS et al., in 2014 also reported a difficult case of CEOT mimicking sarcoma but the histopathology and IHC was helpful in ruling out the diagnosis [11]. Mouse Double Minute 2 Homolog (MDM2) and Cyclin-Dependent Kinase 4 (MDM2 and CDK4) immunostains reliably distinguish low-grade osteosarcoma from benign lesions, and their combination may serve as a useful tool in the differential diagnosis [12].

Wide radical excision is the treatment of choice for jaw osteosarcoma. In view of complex anatomy of head and neck region getting negative

margins in surgical resection as well as reconstruction is quite difficult. The use of chemotherapy before surgery can facilitate the surgical resection and improves the quality and adequacy of the surgical margin without compromising the functional and aesthetic aspects [13]. Early diagnosis and complete tumour resection are important in improving survival of the patient [5].

CONCLUSION(S)

This case was a perfect example to know the importance of the clinical, radiological and histopathological correlation and the role of a pathologist to reach to a final diagnosis in dilemmas. Most important prognostic factor is complete resection of the tumour with wide margins, other poor prognostic factor include metastasis. Use of radiotherapy along with surgery has favourable prognostic impact in terms of osteosarcoma. Osteosarcoma of the jaw is challenging in both diagnosis and management due to high incidence of faulty biopsy results, rare specific radiological features and difficulty in proper resection due to proximity to the vital structures. Histopathological diagnosis and immunohistochemistry can be of utmost importance in diagnosis of these cases. Early diagnosis of osteosarcoma facilitates the treatment procedure, reduces associated morbidity, significantly improves prognosis and ultimately leads to successful treatment outcome.

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