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High-Grade Chondrosarcoma of Mandibular Molar Region- A Case Report and Review of Literature

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ABSTRACT

Chondrosarcomas are malignant tumors of cartilaginous origin with only 5-10% reported in the head and neck region. Intraorally it has higher incidence of occurrence in anterior maxilla followed by posterior mandible. The 5-year survival and metastases rates are adversely affected by the grade of tumor, which necessitates its early diagnosis. Histopathology and immunohistochemistry are vital for its accurate diagnosis. Chondrosarcomas being radio-and chemo-resistant are treated surgically although adjuvant radiotherapy helps in prevention of local recurrences. A case of high-grade chondrosarcoma of the mandibular molar region is presented, along with pertinent review of literature.

INTRODUCTION

Chondrosarcomas are malignant tumors of cartilaginous origin characterised by cartilage deposition by the tumor cells and is said to be uncommon and aggressive in behaviour in the head and neck region. Chondrosarcoma affecting the craniofacial bone amounts to 2% to 3% of all, out of which the jaw illustrates 10% cases. Majority of head and neck chondrosarcomas affect the vestigial rests of jaw bones and base of skull.[1] Kragh et al, in 1960 were the first to report a series of head and neck chondrosarcoma. In the jaws, they tend to occur frequently in anterior maxilla followed by the mandibular posterior region although prognosis is grave in both the instances.[2] The tumor mostly presents as a painless swelling or mass causing displacement of affected teeth.[3]

Chondrosarcomas present with a variety of histological variants namely, conventional, juxtacortical, dedifferentiated, myxoid and mesenchymal and clear cell type depending on predominant histological features evident, and may be central or peripheral depending upon location.[2] The overall 5 year survival rate of chondrosarcoma is 77% which tends to decrease substantially with the increasing grade.[4] A case of Grade III chondrosarcoma of the mandibular molar region with prudent diagnosis based on complete clinical, radiographic, histopathological and immunohistochemical evaluation is reported along with relevant review of literature.

CASE REPORT

A 36-year-old Indian male with no systemic debilitation reported with the chief complaint of swelling in the lower left back teeth region which gradually increased in size over a period of 4 months. He had a dental

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history of extraction of carious second molar in the same region one year back, was an avid smoker with no relevant past medical history.

Clinically, a firm non-mobile facial swelling was present extra orally which resulted in mild facial asymmetry. Intraorally, a solitary, well defined, oval swelling of size 3 x 2.5 cm was present over the gingiva which extended from left mandibular first to third molar anteroposteriorly and involved buccal and lingual vestibule mediolaterally (Figure 1a). An ulcer with pus discharge was present on the 37 alveolar region with respect to the swelling. It was non tender, soft to firm and compressible on palpation. Enlarged and tender ipsilateral submandibular lymph node and paraesthesia of lower lip were the adjuvant sign and symptoms noted at the time of initial assessment. The surrounding soft and hard tissue were apparently normal.

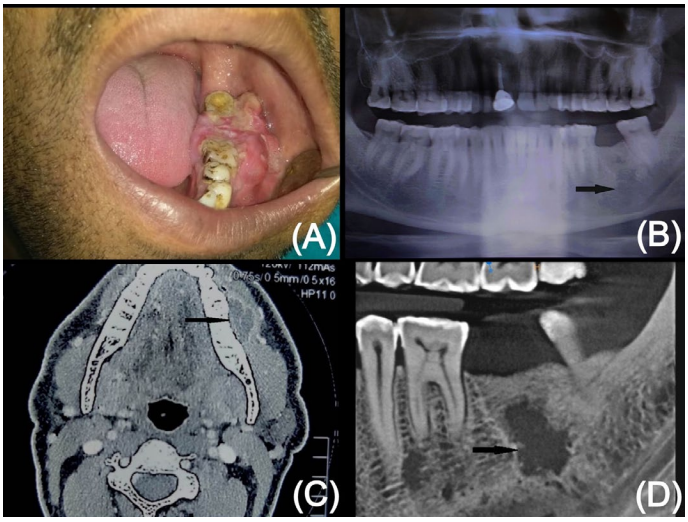

Fig 1: (a) Intraoral picture of patient showing ulcerated swelling present over gingiva in relation to 36-38 region (b) Orthopantomogram showing mild radiolucency (arrow) present in relation to 37 region (c) Contrast enhanced computed tomography image showing a soft tissue lesion present in left gingivobuccal sulcus (arrow) abutting the alveolar process in 36-38 region (d) Cone beam computed tomography image showing bone involvement (arrow)

Orthopantomogram was performed to see hard tissue implications which showed radiolucency present in relation to 37 region indicating cortical bone involvement (Figure 1b). Contrast enhanced computed tomography of the region showed a heterogeneously enhancing solid soft tissue lesion, with few cystic/necrotic areas, of size 2.8 x 2.5 x 2.5 cm present in the left gingivobuccal sulcus abutting the alveolar process in relation to 36, 37, 38 causing erosion of cortex and rarefaction of the medullary bone (Figure 1c). Cone beam computed tomography revealed significant cortical plate erosion both on the medial and distal aspect of alveolus (Figure 1d).

Fine needle aspiration cytology revealed abundant binucleated as well as multinucleated giant cells with bubbly cytoplasm along with macrophages and plasma cells (Figure 2). Biopsied tissue obtained was grossed, processed and sectioned after formalin fixation into 4-µm sections. Hematoxylin and eosin-stained sections when viewed under microscope revealed abundant round to polygonal pleomorphic tumor cells with hyperchromatic bizarre nuclei, abnormal mitotic figures (8/10 HPF). The pleomorphic cells were mostly binucleated which were present along with multinucleated tumor giant cells. Few cells with small centric or eccentric nuclei and bubbly cytoplasm (appeared to be 'physaliferous-like' cells) were also evident, in a chondroid appearing background with no associated osteoid elements evident (Figure 3a, b, c, d). Immunohistochemistry (IHC) panel involving S100, CK8, EMA, NSE, HMB45, vimentin, and Ki67 was applied for confirmatory diagnosis which showed positivity for all (Figure 4 a, b, c, d, e) except HMB45 and NSE, thus ruling out melanoma and neural origin. Histopathology combined with IHC narrowed the differentials to chondroid chordoma and chondrosarcoma. Brachyury, an important marker for notochordal origin was further applied which came out be negative (Figure 4f) hence ruling out chordoma. Based on all significant findings a final diagnosis of high-grade chondrosarcoma was made [5]. Positron Emission Tomography scan (Figure 5) was further advised which did not reveal any other hypermetabolic lymph node/ tissue except the parent lesional tissue.

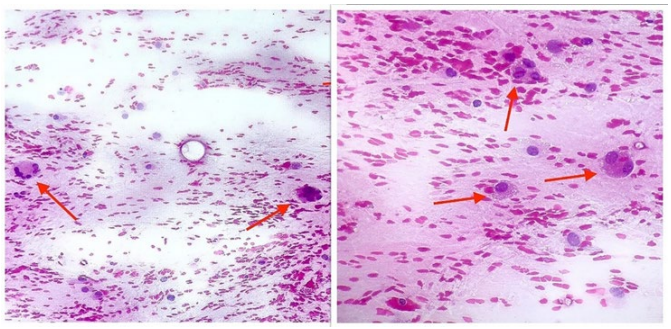

Fig 2: Photomicrographs of smear depicting (a) Giant cells (b) Abundant mono, bi and tri- nucleated cells with bubbly basophilic cytoplasm (red arrows) (H&E, 40X)

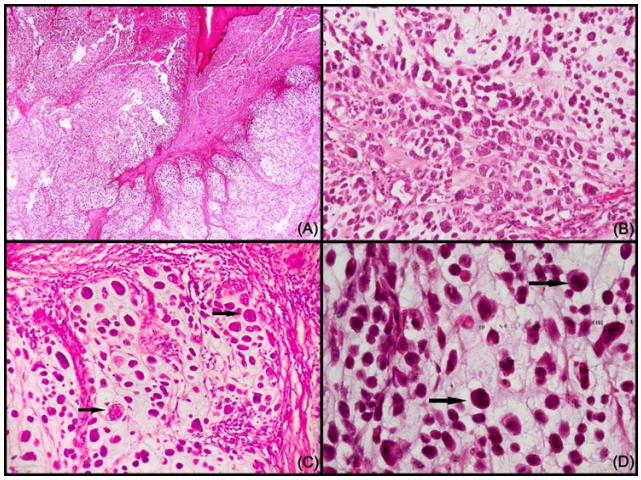

Fig 3: Photomicrographs of sections showing (a) Fibrous septa dividing the connective tissue stroma into lobules in a chondroid background (H&E, 2X) (b) Abundant cellularity with pleomorphic hyperchromatic cells (H&E, 10X) (c) Abundant physaliferous- like cells having bubbly cytoplasm (arrows) along with giant cells in the chondroid background (H&E, 20X) (d) Abundant binucleated cells (arrows) of variable sizes (H&E, 40X)

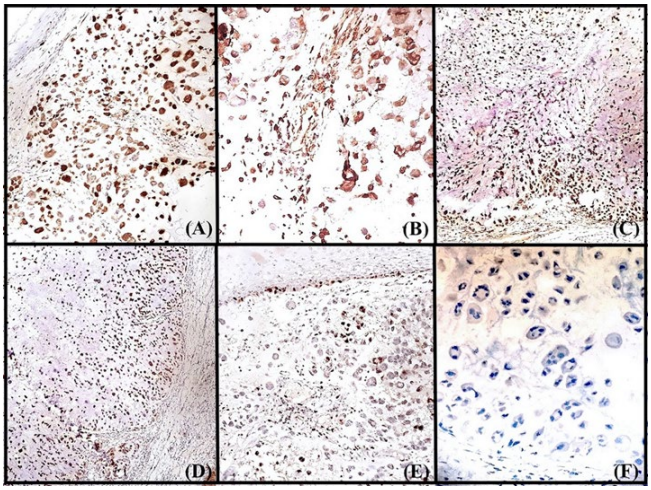

Fig 4: Photomicrographs of immunostained sections showing strong positivity for Cytokeratin 8 (a, 20X), Vimentin (b, 20X), S 100 (c, 10X), Epithelial membrane antigen (d, 10X), high immunostaining for Ki67-10 to 12% (e, 10X) and negative immunostaining for Brachyury (f, 40X)

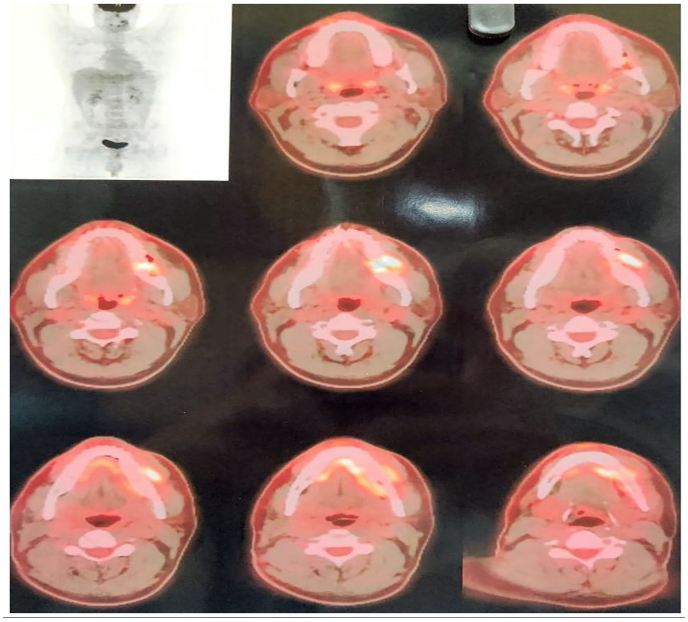

Fig 5: Positron emission tomography scan showing hypermetabolic ill-defined mass involving left buccal mucosa with no other hypermetabolic lesion/ lymph node detected.

The patient underwent segmental mandibulectomy followed by multiple sessions of radiotherapy to prevent any chances of local recurrence. Postoperative report confirmed the diagnosis of Grade III/high grade chondrosarcoma. The patient is on regular follow-up and is asymptomatic six months post-surgery.

DISCUSSION

Chondrosarcomas are slow growing, malignant mesenchymal cartilaginous tumors which could be primary if arising de novo or originate from pre-existing osteo or enchondroma termed as secondary chondrosarcomas. Chondrosarcoma should always be kept in mind as benign chondrogenic neoplasms are extremely rare to occur in the jaws.[3] Systemically, they commonly affect the pelvic bones, proximal and distal femur, proximal humerus, and the ribs; mere 512% arise in the head and neck region. The prevalent sites for head and neck chondrosarcomas are paranasal sinuses, nasal cavity, maxilla and vertebrae; mandibular ones are rare. The mandibular chondrosarcoma manifests as a swelling or mass with or without pain, causing loosening and/or displacement of involved teeth, and widening of the periodontium. Features like loss of nerve sensation and dysesthesia, could discern a malignancy from osteomyelitis.[5]

Radiographic features are not specific for chondrosarcoma, albeit single or multiple radiolucent

areas with ill-defined borders could be evident. Lesions could be lytic or cystic or necrotic in appearance.[3,5] Role of dentists could be pivotal in early recognition of symptoms thus avoiding misdiagnosis as well as effective management of complicated jaw lesions.[3] Thus as evident, the final diagnosis relies on histological and immunohistochemical examination of the lesion.

Histopathologically chondrosarcomas could be conventional, myxoid, mesenchymal, juxtacortical, dedifferentiated or clear cell type. Another classification proposed by Evans et al graded chondrosarcomas into grade I, II and III based on intercellular background of chondroid or myxoid, nuclear size and mitotic rates.[4]

Grade I present as benign cartilage with predominant cells with small densely stained nuclei cells in chondroid to myxoid background and frequent multiple nuclei within one lacuna. Moderate sized pale stained nuclei, <2 mitotic figures/10HPF, increased cellularity in myxoid background are features of Grade II and highest cellularity with even larger nuclei, no defined chondroid or myxoid stroma and >2 mitotic figures/ 10 HPF defines grade III chondrosarcoma.[4] Prevalence and survival rates vary significantly with tumor grade, low grade is more common with high survival rate than high grade and vice versa.[2] Our case fell in the Grade III or high grade category of chondrosarcoma.

Mandible though reports few but harbors more deadly chondrosarcoma than maxilla, yet higher 5-year survival rate is witnessed in cases of mandible than maxilla.[6] The 5 years survival rate decreased from 81% in grade II to 43% in grade III whereas metastasis rate varied from 10% for grade II to 71% for those in grade III.[2] The reported cases of high-grade chondrosarcoma of the mandibular molar region have been summarised for ready reference (Table 1).

Table 1: Comparison of previous cases of High grade Chondrosarcoma in Mandibular Molar region based on Evan's grading criteria with the present case

Author	Country	Age (years)	Sex	Site	Extent	Histo-path-ological Grade	Treatment	Follow up
Kundu et al, 2011	India	36	M	Right Premo-lar- molar	-	High Grade	Wide field radical neck (segmental mandibulectomy with supra-omohyoid block dissection of neck) surgery	6 months, uneventful
Pontes et al, 2012	Brazil	26	F	Left retromo-lar region	9.3X3.7cm	Grade III	En-bloc tumor exci-sion	2 years, dead
Augustine et al, 2014	India	51	F	31-36	-	Grade III	Total mandibulec-tomy	12 months, disease free
Devine et al, 2017	UK	25	M	44-48	>3cm	High Grade	Segmental mandib-ulectomy, radiother-apy	12 months, dead
Sarin et al, 2021	India	37	F	Right preau-ricular to left preauricular region	16x14 cm	Grade III	Mandibulectomy with wide margins of the lesion leaving bilateral condyloid processes of the mandible	Receiving further treatment when she met with a road acci-dent and died.
Ismail et al, 2022	Moroc-co	70	M	46-48	4.5×2.8×2 cm	Grade III	Right segmental mandibulectomy	Follow-up without any recurrence
Present case, 2023	India	36	M	35-38	3X2.5cm	Grade III	Segmental man-dibulectomy followed by radio-therapy	3 months, disease free

The important histopathological differentials in our case were chordoma and chondroblastic osteosarcoma. Chordomas are notochordal tumors which are uncommon in head and neck region, occur predominantly in young adult males and classified into classical or chondroid type.[7] Binucleated or multinucleated 'physaliferous cells' with eosinophilic cytoplasmic inclusions pushing without distorting the nucleus towards one end is seen on FNAC.[8] Histopathologically, chordoma presents with three cell populations: large, 'physaliferous cells' with a vacuolated or bubbly cytoplasm, small, epithelial-like cells and stellate or spindle-shaped tumor cells in the background of basophilic matrix.[9] Particle ion radiotherapy following surgical resection is the treatment of choice for chordoma.[10]

Chondroblastic osteosarcoma (COS) on the other hand is the commonest subtype of conventional osteosarcomas, with predilection for mandible in the head and neck region. FNAC picture reveals discohesive plasmacytoid cells with vacuolated basophilic cytoplasm which may be bi or multinucleated in the background of chondroid/ osteoid matrix.[8] Histologically it exhibits high degree of hyaline cartilage closely associated with non-chondroid element.[11] Treatment involves resection with tumor-free margins and the use of systemic chemotherapy or radiotherapy.[12]

Review of immunohistochemical marker studies reveal that chordomas are positive for CK, EMA, HMFG and brachyury while CEA, S100 and vimentin have variable positivity. Chondrosarcomas are positive for S100 and vimentin and also show variable positivity for NSE but are mostly negative for EMA, CK and CEA.[12] S100 and SOX9 are markers for chondrogenic differentiation. COS shows positive IHC expression for vimentin, EMA, S100 but is rarely positive for cytokeratin.[8] In chondroid variant of chordoma CK expression may be negative which is not usually the case with classical type.[10] EMA, NSE are also negative in chondroid variant.[9]

The common and most successful way to treat a chondrosarcoma is by wide surgical resection and effective preservation of functions as far as possible. They tend to occur locally rather than metastasizing to distant sites; although cases of metastasis to lungs, sternum and vertebrae have been documented. Grading of tumor and resectability are directly proportional with the prognosis of chondrosarcoma. Thus, timely diagnosis of this tumor is of paramount importance. Adjuvant radiotherapy is generally accepted in cases of residual disease, positive margins or unresectable tumors rather than as the initial treatment.[3,5]

Owing to the rarity of occurrence of chondrosarcoma in the jaws, plus its similarity to other tumors, an early and accurate diagnosis is always a challenge. Thus, extensive clinical history, prognostic and diagnostic radiographic findings, cellular pathology report assisting the histopathology and immunohistochemistry altogether aid in its timely diagnosis.

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