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Chondrosarcoma of the Mandible: Case Report and Review of Literature

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Abstract

Chondrosarcomas are the malignant cartilaginous neoplasms rarely seen in the head and neck regions, characterized by a painless swelling. Light microscopically it reveals malignant chondrocytes with cellular atypia and nuclear pleomorphism. The neoplasm is usually treated by wide surgical resection because it is traditionally radioresistant. The treatment and management are primarily guided by the histological grades of the neoplasm. Prognosis of jaw lesions is poor as compared to the lesions affecting the long bones of the body, and the cause of death is usually by direct extension in the base of the skull or due to distant metastasis to lungs and other bones. A clinical case report of Chondrosarcoma in the mandibular region of a 17year-old female patient, encompassing the entire gamut of clinicopathological, radiological and treatment modalities have been rendered.

Introduction

Chondrosarcomas are uncommon malignant tumours characterized by the formation of cartilage but not bone by the tumour cells. They are rarely found in the head and neck region accounting for 5.76% of all the cases. In contrast to osteosarcoma, chondrosarcomas usually occur in adulthood. In the head and neck region, the maxilla, nasal cavity, nasal septum, and mandible are commonly involved. (1)

Here, we present a case report of Chondrosarcoma in the mandibular region of a 17 year-old female patient which

was previously diagnosed as nodular fasciitis along with review of literature.

Case Report

A 17year-old female weighing 41kgs reported to the Department of Oral and Maxillofacial Surgery, Guru Nanak Institute of Dental sciences and Research, Kolkata with pain & swelling in the left side of the face since 4 months.

History revealed that patient was apparently alright 4months ago after which she noticed a small swelling in lower left backside teeth region. The swelling reduced after taking medications from a local dentist. 2months later, the swelling recurred and an incisional biopsy was performed followed by rapid increase in size. There was h/o trauma to the left side of the jaw 2months ago. She had difficulty in opening the mouth, pain in left side of the jaw and difficulty in mastication.

She was of ectomorph (lean & long) build and normal gait. All vital signs were normal. There was no abnormal breath sound and the chest x-ray appeared normal.

On extraoral examination, facial asymmetry was present on left side of the face. The swelling was extending superiorly up to zygomatic arch, medially 2cm from the nasolabial fold, laterally 1cm posterior to the mandible, inferiorly below the hyoid bone on left side. There was an exophytic growth protruding outwards from the mouth. Drooling of saliva from angle of the mouth on right side. Obliteration of nasolabial fold on left side. Cervical lymph node right level 1b palpable, <3cm , mobile, non tender, non matted, left level 1b palpable, <3cm, mobile, non tender, non matted. No other ipsilateral or contralateral lymph nodes were palpable. No such skin fixity present over and around the swelling. Slight local rise of temperature over the swelling near the angle of the mouth region on left side was present.

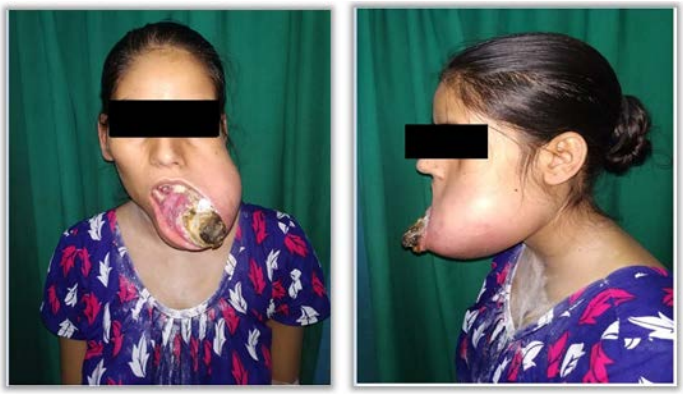


Fig 1: Extraoral Examination- Front and Side View

On intraoral examination, exophytic growth present extending from superiorly upper gingivobuccal sulcus crossing the occlusal plane to inferiorly lower gingivobuccal sulcus, medially from 43 laterally to pterygomandibular raphe in lower arch, in upper arch 12 to 28 region. Reduced mouth opening (1.5 finger). Tongue movement was normal except restricted lateral movement to the left side due to mechanical obstruction. Mallampatti score was 4. Floor of the mouth was involved from 42 to 47 region. Posterior part of the lesion was hard and anterior part was firm in consistency, and the lesion was tender in nature.

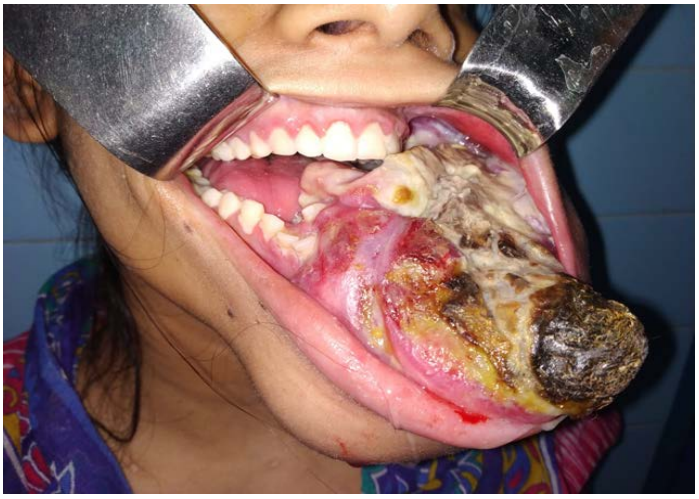


Fig 2: Intraoral examination showing the lesion on left side the mandible crossing the midline

On radiological evaluation, CECT of face and neck showed, a heterogenous space occupying lesion on left side extending superiorly from zygomatic arch inferiorly

to hyoid bone, anteriorly crossing the midline to the opposite site canine region. Absence of fat planes between medial and lateral pterygoid muscle was there. Involvement of infratemporal fossa, parotid, masseter was there. Within the lesion multiple radiopaque areas present having CT number range of 172- 379 HU which indicate areas of ossification. The overlying skin was free.

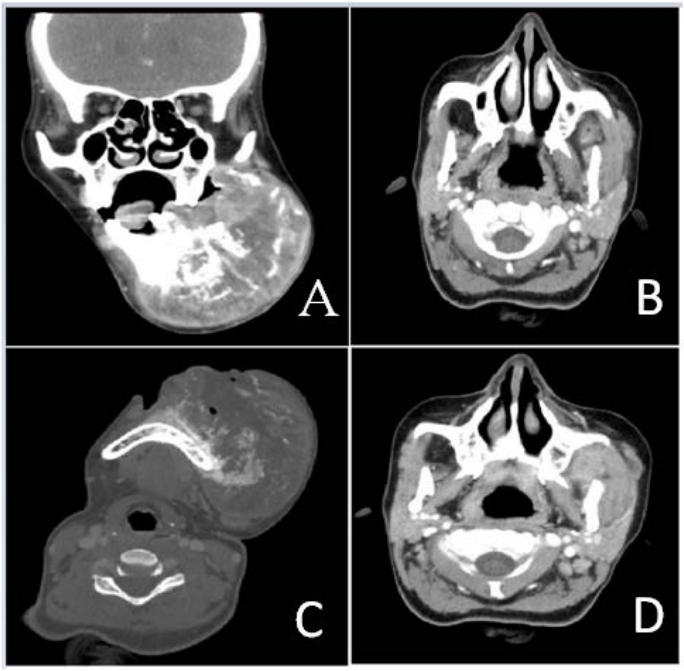


Fig 3: A=Contrast coronal soft tissue window showed the extend of the lesion, B= Contrast axial soft tissue window showed involvement of infratemporal fossa, C= Contrast axial bony window showed areas of ossification, D= Contrast axial soft tissue window showed involvement of parotid gland and masseter

An incisional biopsy was performed from the represented site under local anaesthesia and was submitted for histopathological evaluation. Sections stained with H&E revealed the presence of hypocellular and hypercellular areas; the hypocellular areas showing chondroid tissue which was pale basophilic and cells resembling chondrocytes and lacunae with prominent cellular atypia and nuclear pleomorphism. The hypercellular areas showed proliferation of ovoid to spindle cells having pronounced cellular and nuclear pleomorphism together with increased abnormal mitosis. Numerous foci of calcification and areas resembling endochondral ossification were noted too. There was also presence of necrotic areas and non specific inflammation. Light microscopic features were suggestive of " High-grade Chondrosarcoma"

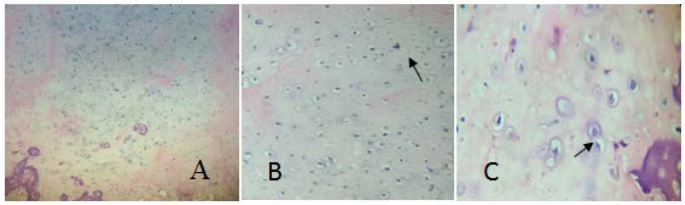


Fig 4: A- low power view, H&E stained section showing both hypo and hypercellular areas showing pale basophilic chondroid tissue with pleomorphic chondrocytes. Areas of endochondral ossification are also noted; B-High power view shows increased proliferation of chondrocytes revealing cellular atypia and nuclear pleomorphism along with mitotic figures. [black arrow]; C-High power view reveals the presence of chondrocytes showing prominent cellular atypia and nuclear pleomorphism in the basophilic chondroid background. Rare binucleate form can also be observed. [black arrow]

Surgical treatment: Prior to intubation central line was placed according to Seldinger technique. Awake fibreoptic intubation was done. An extraoral incision (apron) was given after palpating the posterior and inferior limit of the lesion, from left mastoid tip to the lower lip on right side corresponding to 44 regions. Then hydro-dissection using 0.9% NaCl done. Segmental mandibulectomy from 43 region with disarticulation of left condyle done. Elective tracheostomy was done and a 7mm cuffed tracheostomy tube was placed.

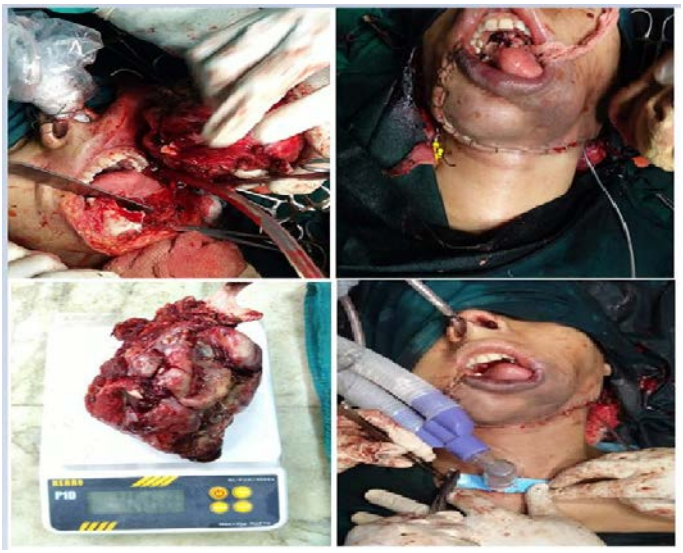


Fig 5: [A] Segmental resection from 43 region with disarticulation of left condyle, [B] After wide local excision of the lesion and segmental mandibulectomy, [C] surgical specimen, weighing around 466mg, [D] Tracheostomy tube in position

Postoperative period was uneventful with regular irrigation, dressing and tracheostomy care. The tracheostomy dependence was weaned off sequentially and de-cannulation was done by the end of one week postoperatively. No hindrance of tongue movement persisted. The patient was referred for subsequent chemoradiotherapy.

After surgery, the sample was sent for histopathological evaluation. The light microscopic features were corroborative to the pre-operative biopsy findings. The tissue was sent for immunohistochemical analysis and positivity with markers such as S100 and Ki-67 was noted.

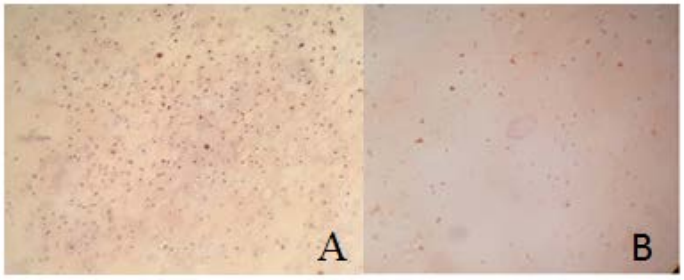


Fig 6: A= Low-power photomicrograph showing positive immunostaining of chondrocytes with S100; B=Low-power photomicrograph showing positive immunostaining of chondrocytes with Ki-67

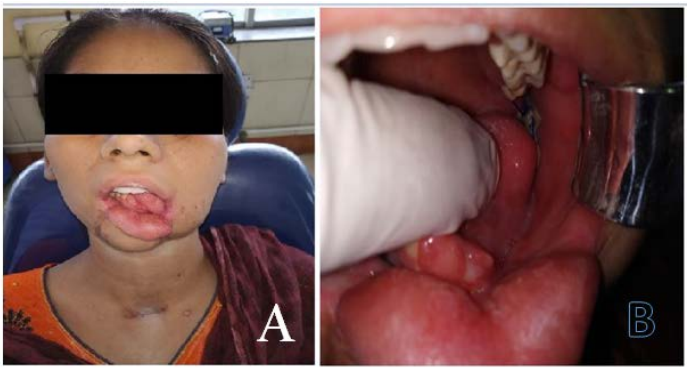


Fig 7: Post op appearance of the patient, B= Post op healed intraoral resected site

Discussion

Chondrosarcomas are a heterogeneous group of malignant bone tumours with diverse histopathology and clinical behaviour, which are characterized by the production of cartilage matrix. [(2)] Chondrosarcoma is the third most common primary malignancy of bone after myeloma and osteosarcoma. [(3)] The chondrosarcomas of the maxillofacial region account for 1-3% of chondrosarcomas of the entire body [(4)]

Types of chondrosarcoma- These malignant cartilaginous tumours may either arise *de novo* or develop from pre-existing benign lesion (e.g., enchondromas and osteochondromas), termed primary (or conventional), and secondary chondrosarcomas, respectively. Tumours can arise in both skeletal (central) and extra-skeletal (peripheral) locations. The majority of cases are primary central chondrosarcomas; together, primary central and secondary peripheral chondrosarcomas constitute approximately 85% of all chondrosarcomas. Other specialized types of chondrosarcoma, such as dedifferentiated, clear cell, and mesenchymal chondrosarcomas, account for the remaining 10%–15% of cases [(2)]

Clinically this neoplasm usually grows within a bone or on its surface. It may occur at any age; however, most frequently is found between the 3rd and 6th decades of life. Males are more commonly affected than females. The usual clinical finding is a painless swelling leading to the expansion of the buccal and lingual cortical plates with occasional premature exfoliation of teeth. Pain may be a late stage feature, and regional lymphadenopathy is very rare. [5] They arise predominately in the maxilla with a predilection for the anterior maxillary region and occur at a lower incidence in the mandible. The preferred site in the mandible is the molar region, and they infrequently occur in the ramus, condyle, coronoid process, or symphysis [4] Chondrosarcoma of the mandible mostly present as a painless swelling or may appear as mass of long duration with pain, paraesthesia, trismus, and loosening of the teeth, which points toward the progression of the disease [4]

Histologically, Conventional chondrosarcomas are characterized by varied light microscopic features and are divided into following three histologic grades primarily depending on cellularity, nuclear staining (hyperchromasia) of the tumour cells and size of the nuclei: -

• Grade I (or Low grade) – These tumours are characterized by the presence of benign cartilage, have a relatively uniform and lobular histologic appearance. Presence of atypical cells including binucleate forms may also be recorded.

• Grade II (or Intermediate grade) – These tumours are characterized by a higher cellularity with a greater degree of nuclear atypia, hyperchromasia with often having myxoid stroma and enlarged chondrocyte nuclei.

• Grade III (or High grade) - These tumours are characterized by a higher cellularity, marked cellular and nuclear pleomorphism, nuclear hyperchromasia and increased mitosis with occasional presence of giant cells. [5]

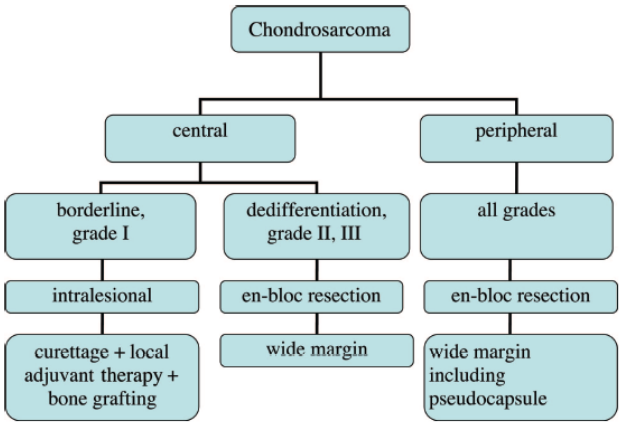
The hypercellularity, pronounced cellular and nuclear pleomorphism together with increased abnormal mitosis noted in the present case were suggestive of high-grade variety.

The conventional radiological findings usually include irregular intramedullary radiolucencies interspersed with punctuate radiopacities, expansion and destruction of the cortical plates, widening of the PDL spaces or even sunburst appearance at the periphery. CT scan is superior in defining the peripheral extent of the neoplasm compared to panoramic or flat-plate radiographs. [6] Radiographically, the appearance of the lesion varies from ill-defined radiolucent to obvious radio-opaque shadow. However, contemporary imaging techniques like computed tomography (CT) scan, magnetic resonance imaging (MRI) and fluorine-18 fluorodeoxyglucose positron emission tomography (FDG PET) are useful to diagnose chondrosarcoma and to differentiate this malignancy from its benign counterpart. However, these findings are not pathognomonic. Conventional radiograph, Computed tomography scan and magnetic resonance imaging are quite valuable in determining the nature and extent of the lesion, but a definitive diagnosis should be made histologically which states significantly that chondrosarcomas are composed purely of hyaline cartilage and fulfil cytologic malignant criteria [4]

IHC: As diagnosis is challenging when limited tissue is available for analysis, it may be assisted by ancillary pathologic techniques such as immunohistochemistry (IHC). S100 positivity is varied with loss of expression in the round cell component unlike the conventional CS which is strongly positive. The round cell component is strongly positive for CD99. Ki- 67 is used as a proliferative marker in chondrosarcoma. Type II collagen

is a selective marker for chondrogenic neoplasms which is specific for MC (mesenchymal chondrosarcomas) as it is not expressed in other small cell sarcomas. [4] Commonly used markersare bcl-2, cox-2, D2-40 (podoplanin), mdm-2, and YKL-40, osteonectin. [6] GAL-1 (Galectin-1) mainly expressed in high-grade chondrosarcomas (grade III) [7] The present case also showed strong positivity with S100 and Ki-67.

Treatment: Grade I and Grade II chondrosarcomas of the jaws and facial skeleton are best treated with local resection using 1.5 cm margins of bone and soft tissue. Neither chemotherapy nor radiotherapy is indicated as the primary treatment. However, the Grade III chondrosarcomas are treated with an initial aggressive resection of 3 cm in bone and 2 cm in soft tissue followed by chemotherapy [5] Radical resection is the most effective primary modality for the treatment of chondrosarcoma, as this is considered to be radioresistant. However, chemoradiation is usually advised for locally recurrent or residual tumour. [4]



Flowchart of the surgical management of central and peripheral chondrosarcoma [3]

Role of chemotherapy in chondrosarcoma:

As chondrosarcomas grow slowly, with a relatively low fraction of dividing cells, and radiotherapy (RT) acts at dividing cells, chondrogenic tumours are considered relatively RT resistant. RT can be considered in two situations: after incomplete resection, aiming at maximal local control (curative), and in situations where resection is not feasible or would cause unacceptable morbidity (palliative). For curative intentions, doses >60 Gy are required to achieve local control. However, application of this dose with conventional high-energy photon RT is often impossible in the vicinity of critical (neurological) structures, especially in chondrosarcomas arising in the skull base and axial skeleton.

Unfortunately, in this situation, postoperative RT is often indicated because these tumours are less accessible for radical resection than lesions in the appendicular skeleton.

Given the limitations of conventional RT with photons, alternative radiation modalities have been tested. Particle therapy with protons has the advantage of a minimal exit dose after energy deposition in the target volume, and hence better sparing of critical structures close to the tumour. Proton RT has been found to be beneficial in incompletely resected chondrogenic tumours of the skull base and axial skeleton. Local control rates of 85%–100% with mixed photon–proton or proton-only protocols (doses up to 79 cobalt Gray equivalents) have been reported by several authors, with limited severe late effects. RT with carbon ions or other charged particles represents another attractive radiation modality, which combines the physical advantages of protons with a higher radiobiological activity.

Chondrosarcomas that are not resectable and cause complaints might be considered for palliative RT, especially mesenchymal chondrosarcomas, because these tumours are more radiosensitive. Limited evidence from older series suggests benefit from conventional RT for chondrosarcomas that cannot be resected [3]

Systemic treatment in chondrosarcoma: Chemotherapy is generally not effective in chondrosarcoma, especially in

the most frequently observed conventional type and the rare (low-grade) clear cell variant. An additional explanation for this chemotherapy resistance may be expression of the multidrug-resistance 1 gene, P-glycoprotein, resulting in resistance to doxorubicin in vitro. Moreover, the access of anticancer agents may be hampered by the large amount of extracellular matrix and the poor vascularity, implying that the agents have to diffuse over a relatively long distance in order to reach the tumour cells. Moreover, chondrosarcoma grows relatively slowly, while most conventional chemotherapeutic agents act at actively dividing cells. The effect of chemotherapy on grade II and III chondrosarcoma is difficult to assess because the number of reported cases is too low and reported series are mostly retrospective, which may lead to selection bias.

Because of a lack of clear evidence, the role of adjuvant chemotherapy in dedifferentiated chondrosarcoma remains unclear, and the standard use of adjuvant chemotherapy outside a clinical protocol should be reconsidered.

Tumours with a high percentage of small cells and limited cartilage content are thought to be most sensitive to chemotherapy and RT, as with other small cell sarcomas. Although prospective studies are lacking, mesenchymal chondrosarcomas are considered sensitive to doxorubicin-based combination chemotherapy as used in other bone tumours. Thus, patients with mesenchymal chondrosarcoma should be considered for adjuvant chemotherapy, and in the case of metastatic disease, palliative chemotherapy.

More recently, the antitumor effects of histone deacetylase and aromatase inhibitors were described in chondrosarcoma cell lines, and angiogenesis inhibitors were described in an in vivo model. Several studies have reported incidental responses of chondrosarcomas to newer targeted agents, such as vascular endothelial growth factor antisense and recombinant human Apo2L/tumour necrosis factor receptor apoptosis-inducing ligand (TRAIL). [3]

Prognosis, the 5-year survival rate for chondrosarcomas of the jaws and facial bones has been reported to be 67.6%. The prognosis of chondrosarcomas depends on the size, location, grade, and surgical respectability of the tumours as chondrosarcomas show a wide variation in time of recurrence and metastasis. [14] Approximately 90% of conventional chondrosarcomas are grade 1 or 2, which have an indolent clinical course, low metastatic potential, and good prognosis; the remaining 5–10% are grade 3 tumours, which have high metastatic potential and are associated with poor outcomes. [2]

Conclusion

The exact aetiology of chondrosarcoma of the jaws is not known. The presence of a mass is the most common presenting symptom. Sometimes patients present with dental symptoms such as loose teeth. Paraesthesia may be a presenting symptom of mandibular chondrosarcoma. High-grade chondrosarcomas commonly do metastasize to regional lymph nodes and to long bones more than do other sarcomas. Survival rate of chondrosarcomas of the jaws in general appear to be poorer than that of chondrosarcomas in other parts of body. Chondrosarcomas are generally radioresistant. Moreover, the response of chondrosarcoma to chemotherapy is much poorer than that of osteosarcoma. Role of IHC is gaining importance as it can aid in selection of treatment methods as well as serve as a prognostic indicator.

These clinicobiologic characteristics of chondrosarcomas, specially the high-grade ones have rendered them to have a protracted clinical course and high recurrence rates, which in turn stresses on the importance of a proper pre-operative clinicopathological evaluation and a regular periodic post-operative screening

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