

Case Report

Maxillofacial Bones Chondrosarcoma: Review of Literature with Case Report.

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Submitted on: 4-6-2023

Accepted: 15-9-2023

Abstract:

Introduction: Chondrosarcoma is a malignant cartilaginous tumor which occurs rarely in the head and neck. Chondrosarcoma may present with a wide variation of clinical manifestations, depending on its site. It harbors somatic mutations in the isocitrate dehydrogenase genes 1 and 2 (*IDH1*, *IDH2*). Microscopically it is formed of cellular nodules of malignant cartilage. Different treatment modalities applied according to many factors, but Surgical excision is the most common modality followed in head and neck region.

Case presentation: A 20-year-old male patient presented with an intraoral painful swelling on the upper anterior maxilla for one month before. Clinically, A large 3*3*2 cm circular swelling of normal gingival color causing displacement of right upper central incisor was seen. Radiographically, there is a periapical radiolucency around the central incisor. The histopathological examination revealed a lobulated tumor formed of hyaline cartilage with areas of myxoid matrix. The chondrocytes display nuclear atypia and irregular nuclear membrane. The diagnosis of Conventional Chondrosarcoma grade II was established. There was no recurrence after 6 months.

Conclusion: The distinguishing head and neck chondrosarcoma from other lesions which have similar histological picture, but different treatment modalities, clinical behavior and prognosis is highly important and need through search to reach the final diagnosis.

Key words: Chondrosarcoma, head and neck sarcomas, maxillofacial sarcomas, conventional chondrosarcoma, *IDH1* mutation and cartilaginous tumors.

Introduction:

Chondrosarcoma is a rare malignant cartilaginous tumor that most commonly occurs in the pelvis, extremities, and ribs. It accounts for 11 % of all primary malignant bone tumors. 1–12 % of all cases of chondrosarcoma occur in head and neck region (Coca-Pelaz *et al.*, 2014). According to the definition of the World Health Organization (WHO), head and

neck chondrosarcoma (HNCS) is a malignant tumor characterized by the formation of cartilage by tumor cells (Fletcher *et al.*, 2013). The most affected sites in head and neck are the sinonasal area, maxilla, nasal septum, and the mandible respectively, but it may occur in any maxillofacial bone. Chondrosarcoma is a slowly growing tumor with non-specific symptoms depending on location. These tumors usually cause symptoms by

compression or invasion of important structures. Nasal chondrosarcoma can result in nasal obstruction. Chondrosarcomas of the skull base can produce diplopia, proptosis, facial pain, headache, cranial nerve deficits (most commonly VI nerve palsy), visual loss and otalgia (Evans, Ayala and Romsdahl, 1977). HNCS located in the sinonasal tract can cause nasal obstruction, epistaxis, mass effect and pain Dysphonia is the most common initial symptom in the larynx; while dyspnea is the main complaint in subglottic area (Knott, Gannon and Thompson, 2003). At other sites asymptomatic or painful swelling (Coca-Pelaz *et al.*, 2014). Nodal and distant metastases are rare however, the most common distant metastases occur in the lungs. The principal diagnostic imaging modalities of chondrosarcoma are computed tomography (CT) and magnetic resonance imaging (MRI). The tumor ranges from well-defined to aggressive destruction with varying opacity producing stippled pattern or irregular masses best seen on CT. Dedifferentiation may produce a purely lytic area or soft tissue extension best localized on MRI. Chondrosarcoma has a high T2-weighted signal. Definite diagnosis can be established by incisional biopsy and histopathological examination (Pontes *et al.*, 2012).

There are many histological *subtypes of chondrosarcoma*:

- 1- Conventional chondrosarcoma which arises in the medullary cavity.
- 2- Periosteal chondrosarcoma that develops on the surface of bone.
- 3- Dedifferentiated chondrosarcoma which shows abrupt transition into a high-grade, non-cartilaginous sarcoma.
- 4- Clear cell chondrosarcoma is a low-grade malignancy of lobules of cells with

abundant clear cytoplasm (Almansoori *et al.*, 2019).

There are many theories about the origin of chondrosarcoma one of them refer the origin of skull base chondrosarcoma to the remnants of cartilage from failures of the ossification of chondrocranium that may persist at the skull base that later on give rise to chondrosarcoma (for example, at the temporo-occipital junction, and clivus) (Neff *et al.*, 2002). However, islands of hyaline cartilage that are often present in the nasopalatine duct in adults may account for chondrosarcomas in anterior maxilla, second theory referring the development of chondrosarcoma from ossified cartilage e.g Laryngeal chondrosarcomas usually arise in the cricoid and thyroid cartilages. However significant under-representation of chondrosarcomas in the mandibular condyle, a site where calcified cartilage is common in adults, argues against this being the only mechanism for development (Sciubba, 2001). The origin of periosteal chondrosarcoma below to periosteum concise with another theory in which the mesenchymal pluripotential cells undergo malignant transformation and differentiate towards a chondrocyte (Neff *et al.*, 2002). Additionally, chondrosarcomas can develop in non-hereditary skeletal disorders like Ollier disease, Maffucci syndrome and Paget's disease. (Helliwell, 1999).

Histologically, conventional chondrosarcoma has three grades. The high-grade conventional central chondrosarcoma has the classical appearance cellular nodules of malignant cartilage. The nodules consist of pleomorphic and mitotically active chondrocytes (chondroblasts) and basophilic "cartilaginous" matrix, surrounded by layers of spindled cells. The

atypical chondrocytes may contain one, two or multiple nuclei and are variably sized. Distinguishing between grade II and III tumors could be done by the degrees of cellularity, atypia, mitotic activity and decrease of matrix. Formation of metaplastic bone on the cartilaginous nodules can be seen. (Almansoori *et al.*, 2019)

The important challenges in the diagnosis of Head and neck chondrosarcoma are the recognition of grade I tumors that are only locally invasive, and distinction of it and chondroma. It has been established that many previously reported chondromas in head and neck would now be interpreted as low-grade chondrosarcomas. In fact, these grade I lesions have emerged as the most common subtype of central chondrosarcoma (Fletcher *et al.*, 2013). The criteria for the distinction have been reported in the 4th edition of WHO classification include assessment of nuclear size and hyperchromasia, cellularity and mitoses however, the application of these criteria in clinical practice has proved to be challenging (Fletcher *et al.*, 2013). Because of that, the WHO classification (2022) considering the rarity of chondromas in the maxillofacial bones, and referring the tumors with pure cartilaginous differentiation should always be considered to be chondrosarcoma until proven otherwise (Soluk-Tekkesin and Wright, 2022).

Chondroblastic osteosarcoma also is one of the most important diagnostic issues specifically in the jawbones where is Chondroblastic osteosarcoma is far more common than chondrosarcoma, requiring an accurate examination to exclude small foci of neoplastic osteoid formation. Therefore a diagnosis of maxillofacial chondrosarcoma could not

be made depending only on the core biopsy (Coca-Pelaz *et al.*, 2014).

The dedifferentiated chondrosarcoma is composed of high-grade component which resembles undifferentiated pleomorphic sarcoma. Regarding Clear cell chondrosarcoma it shows lobules of cells with abundant pale or slightly eosinophilic cytoplasm (glycogenated) and frequently includes woven bone formation. The clear cell chondrosarcoma lack to *IDH1* and *IDH2* mutations (Soluk-Tekkesin and Wright, 2022).

For staging purposes, the staging system endorsed by the American Joint Committee on Cancer (AJCC) can be used. Detection of *IDH1/2* mutations can be helpful in distinguishing conventional, periosteal and dedifferentiated chondrosarcoma from chondroblastic osteosarcoma in selected cases but is generally not required. Detection of *IDH1/2* mutation may be less likely in chondrosarcomas of facial skeleton, whilst the skull base tumours reportedly have a higher detection rate (Greene, 2002).

Surgical resection is standard for initial therapy of head and neck chondrosarcoma. The type of surgery depends on histologic grade, tumor extension and location (Greene, 2002). The key point for local control is to achieve adequate surgical margins (Greene, 2002).

A conservative wait-and-see policy implementing CT scanning at regular time intervals can be considered in case of an asymptomatic low-grade lesion in a surgically difficult to access location. adjuvant radiotherapy and chemotherapy are indicated in cases of high-grade chondrosarcoma with more aggressive clinical behavior, rapid local recurrence and high probability of metastasis (Khan *et al.*, 2013).

The factors influencing prognosis are the complete resection of lesion, the stage at diagnosis, histopathological grade of the lesion (poor prognosis for high-grade tumors) and location. In general, lymph node metastases are unusual (5 %) and distant metastases occur only in 7–18 %. However, high-grade chondrosarcomas may present with distant metastases in up to 71 % of cases (Coca-Pelaz *et al.*, 2014; Khan *et al.*, 2013).

Case presentation:

A 20-year-old male patient presented to the surgery department with a chief complaint of an intraoral swelling on the upper anterior maxilla for one month before. The swelling started to be painful for a few days. Clinical examination revealed a large 3*3*2 cm circular swelling of normal gingival color that caused displacement of right upper central incisor (Fig. 1).

Radiographically there is a slight periapical radiolucency around central incisor and saucerization of labial bone (Fig. 2). The patient was medically free. Excisional biopsy was done and the histopathological examination of H&E-stained sections revealed a lobulated tumor formed of hyaline cartilage, with areas of myxoid matrix (Fig. 3).

The malignant chondrocytes display nuclear atypia and irregular nuclear membrane (Fig. 4). Binucleation and spindling of chondrocytes is distinctive (Fig 3,4). The tumor is highly cellular, showing central relative maturation with endochondral calcification (Fig. 3). Thus, a diagnosis of Conventional Chondrosarcoma grade II is established. Follow up after 3 months was done, additionally after 6 months there was no recurrence.



Fig. (1) showing intraoral swelling on the upper anterior maxilla that caused displacement of right upper central incisor.



Fig. 2 showing slight periapical radiolucency around central incisor and saucerization of labial bone on the central incisors.

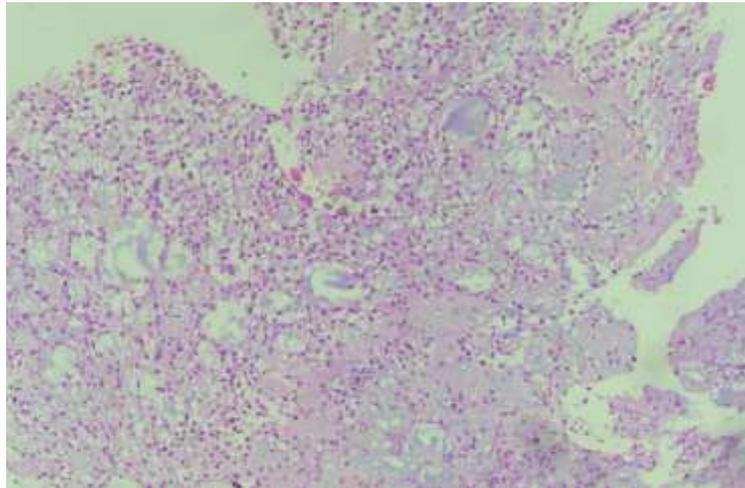


Fig. 3: a photomicrograph showing a lobulated tumor formed of hyaline cartilage, with areas of myxoid matrix and central relative maturation with endochondral calcification (x100).

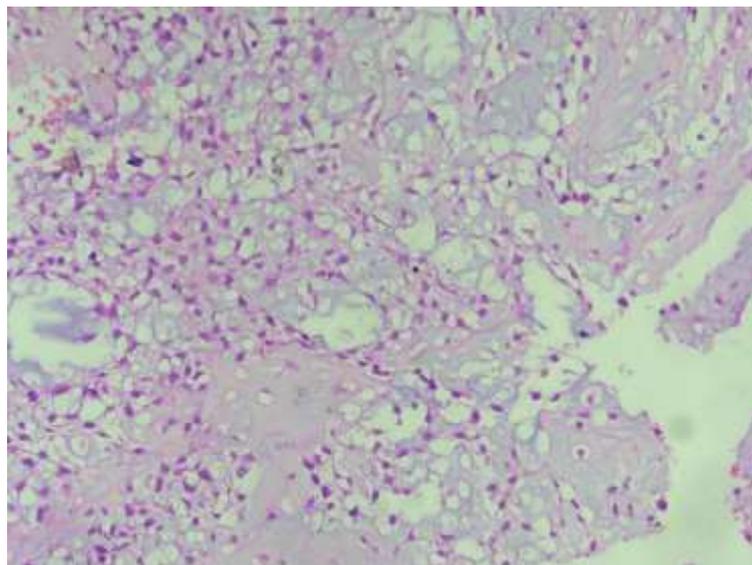


Fig.4: a photomicrograph showing malignant chondrocytes with nuclear atypia. Note the Binucleation, spindling of the chondrocytes and the irregular nuclear membrane (x200).

Discussion:

Chondrosarcoma is a malignant tumor in which the tumor cells produce cartilaginous matrix (Fletcher *et al.*, 2013). Chondrosarcoma of the jaw and facial bones is rare and represents about 11% to 12% of chondrosarcoma cases (Almansoori *et al.*, 2019).

On the basis of previous reports, the disease occurrence being more common in the third to fifth decades of life with no gender predilection. The incidence of chondrosarcoma in the maxilla more than in the mandible as the present case arises in the anterior maxilla. Regarding the mandible, the body and ramus of the mandible, were reported more than the coronoid process and

condyle. Chondrosarcoma may present with a wide variation of clinical manifestations, depending on the site of origin. Painless swelling was the most commonly reported complaint (Coca-Pelaz *et al.*, 2014; Almansoori *et al.*, 2019). However, in the present case the patient complains from painful swelling.

Some of the previous studies identified factors and conditions that may contribute to tumor formation, including multiple hereditary exostoses, Ollier disease, Maffucci syndrome, Paget disease, chondromyxoid fibroma, previous irradiation, previous trauma, and previous benign tumor (Pontes *et al.*, 2012). In the present case the patient familial and medical history were free of such conditions.

Chondrosarcoma may be Conventional chondrosarcoma, Periosteal chondrosarcoma, dedifferentiated chondrosarcoma or Clear cell chondrosarcoma. All of them except clear cell chondrosarcoma, harbour somatic mutations in the isocitrate dehydrogenase genes type 1 and 2 (*IDH1*, *IDH2*) (Almansoori *et al.*, 2019).

Conventional chondrosarcoma comprises the common subtype with 90% of cases, while the other variants account for the remaining 10% (Almansoori *et al.*, 2019). Evans *et al.* classified conventional chondrosarcomas into 3 grades (I, II, and III) according to mitotic rate, cellularity, and nuclear size. Most authors consider grade I tumors as low-grade tumors and grade II and III tumors as high-grade tumors (Evans, Ayala and Romsdahl, 1977; Fletcher *et al.*, 2013). In the present case the

patient was diagnosed with conventional chondrosarcoma

Histologically chondrosarcoma has a lobular morphology and destructive growth pattern with entrapment of pre-existing trabecular bone. Low grade differentiated tumours are like hyaline cartilage with polygonal cells surrounded by lacunar spaces in a basophilic matrix as seen in the present case. The nuclei are uniform, with evenly distributed dense chromatin (Coca-Pelaz *et al.*, 2014). Nuclear atypia, increased cellularity with irregular distribution, decreased volume of cytoplasm, myxoid background, and mitoses are associated with higher tumor grade (Evans, Ayala and Romsdahl, 1977). In the present case there is minimal atypia and mitosis however, increased cellularity and prominent myxoid pattern is detected this made the tumor in intermediate grade (grade II).

Distinguishing chondrosarcoma from chondroblastic osteosarcoma must be considered with particular significance in jaws because of differences in prognosis and biological behavior of the two tumors. Osteonectin and various matrix metalloproteinases could be helpful in this aspect. Attention has been recently drawn to the immunohistochemical assessment of isocitrate dehydrogenase encoded by a mutant *IDH1* gene (Greene, 2002).

Surgical resection is the treatment of choice in the maxillofacial bone's chondrosarcoma. Histologic grade and complete resection are the most important prognostic factors. In the present case the patient showed no recurrence after surgical excision of the tumor without chemotherapy or radiotherapy.

Conflict of interest: No conflict of interest.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors

Ethics: This study protocol was approved by the ethical committee of the faculty of dentistry- Cairo university

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