High-grade chondrosarcoma of the mandible: A rare case report with immunohistochemical findings

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Abstract
Chondrosarcoma is an uncommon malignant neoplasm of the cartilaginous origin devoid of the tumor osteoid. It is an extremely rare primary tumor of head and neck with <10% of the cases occurring in the craniofacial region. Histological grades are pivotal in treating and managing the neoplasm. The high-grade variant is infrequently seen which makes this case interesting to discuss. Histopathology is the mainstay of diagnosis. A case of high-grade chondrosarcoma of the mandible is discussed herewith, with an emphasis on histopathology and immunohistochemical analysis.

Keywords
Cartilage, chondrosarcoma, immunohistochemistry

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Introduction
Chondrosarcoma is a malignant tumor characterized by cartilage formation. <7% of chondrosarcomas occur in the region of head and neck, comprising only 0.1% of all head and neck neoplasms, the larynx and maxillonasal areas are the preferred ones.[1] Chondrosarcomas of head and neck tend to be painless on presentation.

The pathogenesis and biologic behavior of this chondrogenic tumor is poorly understood, but it is evident that these lesions represent a spectrum from benign chondroma to the malignant chondrosarcoma, through varying degrees of intermediate type. In the head and neck region, chondrosarcomas of Grade I are frequently reported.[2] The present case was diagnosed as Grade III, which makes this important to document.

Case Report
A 51-year-old female visited the dental clinic with a chief complaint of swelling and pain on the left side of the jaw since 2 months (Figure 1a). On extra oral examination, a diffuse ill-defined swelling was seen on the left side of the mandible extending from the symphysis to the body of the left mandible causing facial symmetry. On palpation, the swelling was immobile, hard in consistency and slightly tender. The overlying and adjacent skin was normal; no regional lymphadenopathy was noted.

On intraoral examination, a solitary large swelling was seen extending from 31 to 36 obliterating the buccal and lingual vestibule (Figure 1b). It was firm in consistency, tender to palpate with overlying intact mucosa. Teeth, 32-35 were missing. The teeth in the region of the swelling showed Grade II mobility.

Orthopantomogram showed a large, ill-defined mixed lesion with focal patchy areas of calcification extending from the distal aspect 31 to the distal root of 36. Marked alveolar bone destruction was evident with ragged borders of the lesion (Figure 1c). A provisional diagnosis of osteosarcoma was arrived at. A differential diagnosis of aggressive ossifying fibroma and osteoblastoma was concluded.

Microscopic examination of the incisional biopsy revealed chondrocytes and lacunae in lobular patterns with pleomorphic and hyperchromatic nuclei. Mitoses were seen. A prominent cellular spindle cell proliferation was seen with minimal areas of chondroid (Figure 2a and b). A high grade chondrosarcoma was suspected.

Immunohistochemistry showed strong positivity for Ki-67 and proliferating cell nuclear antigen (PCNA) (Figure 3a and b). Strong
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positivity was also seen for CD34, which is a microvessel density marker associated with high-grade chondrosarcomas (Figure 3c).

All these features made us arrive at a final diagnosis of Grade III or high-grade chondrosarcoma.

Since this was a high-grade lesion a total mandibulectomy was planned and carried out under general anesthesia uneventfully. There was no evidence of recurrence of the tumor 1 year after surgery, and the patient is continuing to receive routine follow-up.

Discussion

Chondrosarcomas are malignant tumors arising from cartilage cells that tend to maintain their essentially cartilaginous nature throughout their evolution. These neoplasms mostly occur in the long bones, pelvis and the ribs.

Though the pathogenesis is poorly understood, genetic factors are thought to play a role. Primary chondrosarcomas arise de novo whereas secondary chondrosarcomas are thought to arise from pre-existing lesions like Ollier’s disease, solitary osteochondroma, Maffucci syndrome, solitary enchondroma, Paget’s disease or radiation injury. It is now believed that cell cycle regulators p16, p53 and retinoblastoma play important roles in the development of this tumor.[3]

Chondrosarcomas are rare in the head and neck region which accounts for 4.2-6.7% of cases. Most chondrosarcomas of the head and neck region occur in the maxilla; others are found in descending order of frequency in the body of the mandible, the ramus, the nasal septum and the paranasal sinuses.[4] The present case occurred in the mandible.

The most common clinical finding is a painless swelling, expansion of the buccal and the lingual plates, premature eruption or exfoliation of teeth. The mass is usually rapidly growing and covered with mucosa which can ulcerate followed by pain at later stages.[5] These features were consistent with the present case, but no ulceration was seen.

The radiological pattern of chondrosarcomas is variable.[6] It includes single or multiple radiolucent areas. These lytic changes are prominent in more advanced cases.

Other findings are the pacification of air spaces, a densely calcified bone mass and root resorption. Some authors have reported an uniform widening of periodontal membrane space. Furthermore, it may reveal a ground glass appearance or a

Figure 1: (a) A diffuse ill-defined swelling was seen on the left side of the mandible extending from the symphysis to the body of the mandible causing facial symmetry. (b) Intraoral view of the swelling. (c) Orthopantomogram showing a mixed radiolucent lesion with focal areas of calcification

Figure 2: (a) Chondrocytes and bizarre cells with irregular nuclei (H and E, ×20). (Inset: ×40 shows an abnormal mitosis) minimal chondroid is observed. (b) A prominent spindle cell proliferation (H and E, ×20)

Figure 3: Immunohistochemical staining (a) Immunohistochemistry showing strong positivity for Ki-67 (×40 high power view). (b) Immunohistochemistry showing strong positivity for proliferating cell nuclear antigen (×40 high power view). (c) Immunohistochemistry showing strong positivity for CD34 (×10 low power view)
sunburst appearance. The present case revealed a mixed lesion with areas of patchy calcification.

Histopathology is the mainstay of diagnosis. Grade I chondrosarcomas closely mimic the appearance of a chondroma, composed of a chondroid matrix and chondroblasts that show only a subtle variation from the appearance of normal cartilage. Calcification or ossification of the cartilaginous matrix is often prominent and mitosis being a rare feature. Grade II chondrosarcomas show a greater proportion of moderately sized nuclei and increased cellularity. The cartilaginous matrix tends to be more myxoid. The mitotic rate is low. Grade III chondrosarcomas are highly cellular and show spindle cell proliferation with mitosis. Easily recognizable cartilage may be rare. They tend to have a higher proliferative index. This was confirmed in our case by the use of proliferative markers like PCNA and Ki-67 respectively which showed strong expression.

CD34 which is a microvessel density marker is overexpressed in high-grade chondrosarcomas. The expression of CD34 increases as the grade of chondrosarcoma increases, this has been proven by previous studies which have shown a positive correlation between microvessel density and histological grade. Expression of CD34 showed strong positivity in the present case.

The prognosis of the chondrosarcoma of the jaws is poor compared to any other part of the body Fatality is mainly due to the extension into the base of the skull or distant metastasis usually to lungs and bones. Wide surgical resection is the preferred choice of treatment as chondrosarcomas are traditionally radioresistant. However, radiotherapy can be opted as an adjunct for high-grade lesions.

The prognosis is good for low and intermediate grade chondrosarcomas. The recurrence of head and neck chondrosarcoma is frequent because of the complicated location preventing complete surgical excision of the lesion.

**Conclusion**

The prognosis for patients with chondrosarcoma appears to be related to the location of the tumor, the adequacy of the primary surgical resection and the histological grade of the neoplasm. In our case, there was no evidence of recurrence or metastasis of the tumor 1 year after surgery, and the patient is on a routine periodic screening. Chondrosarcomas should be considered in the differential diagnosis of mandibular masses. Immunohistochemistry is a useful adjunct.

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**References**
