Oncologic profile of maxillary odontogenic myxoma: A rare case

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Abstract

Odontogenic myxoma (OM) is an ectomesenchyme derived neoplasm, almost exclusively found in jaws. This article presents a maxillary OM with a brief review of the molecular and proteomic antecedents of OMs, capturing its histopathogenesis.

Keywords: Ectomesenchyme, extracellular matrix, immunohistochemistry, odontogenic myxoma, proteomic analysis, stem cells

Introduction

Mucoid tumors of soft-tissue represents a heterogeneous group of lesions that exhibit significant differences in biological behavior, ranging from harmless to malignant neoplasms. As an osseous entity odontogenic myxomas (OMs) are found in the bones of the jaws and are considered slow growing tumors with potential for extensive bone destruction.[1] With mandible being affected more than the maxilla, the premolar molar region of jaws are affected. Females are more affected.[2] Radiographic features are described as small unilocular to large multilocular tumors that displace teeth or less frequently resorb roots of teeth.[1]

A case of maxillary myxoma occurring in the maxilla of a 34-year-old female patient is described followed by molecular review with emphasis on histogenesis and biological behavior.

Case Report

A 34-year-old female patient approached the department for an opinion regarding a swelling in the left upper jaw. Past dental history revealed an episode of trauma 1 year back with a subsequent slow growing swelling in the posterior region of left maxilla

When patient reported to the department, she had a bony hard non-tender diffuse swelling of approx. 2.5 cm × 2 cm on the left middle third of face obliterating the nasolabial fold. Intra-orally, the lesion obliterated the vestibule and extended from 23 to 26 regions. It was approx. 3 cm × 2 cm × 1 cm in dimension. Overlying mucosa showed no color change. The associated teeth showed grade 1 mobility. [Figure 1].

Orthopantamograph revealed a unilocular radiolucent lesion in 23 to 26 regions. Root resorption was observed [Figure 2]. None of the teeth were absent in maxillary jaw. Missing teeth were 37 and 46. Fine needle aspiration failed to show any cellular yield

An excisional biopsy harvested multiple small pieces of the lesional tissue. Gross specimen was yellowish white, glistening, gelatinous, lobulated mass [Figure 3].

Histopathological examination revealed typical features of myxoma, with loosely arranged stellate or spindle shaped cells within a myxoid matrix. At places, tumor showed collagen fiber bundles. Islands of odontogenic epithelium were seen. The findings were found consistent with OM [Figures 4 and 5].

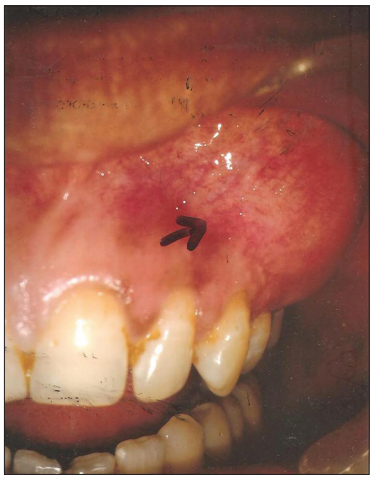

Figure 1: Intraosseous swelling extending from 23 to 26 region obliterating buccal vestibule

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Although the incidences of recurrences are high, a 12 month asymptomatic follow-up has been recorded. [Figures 6 and 7]

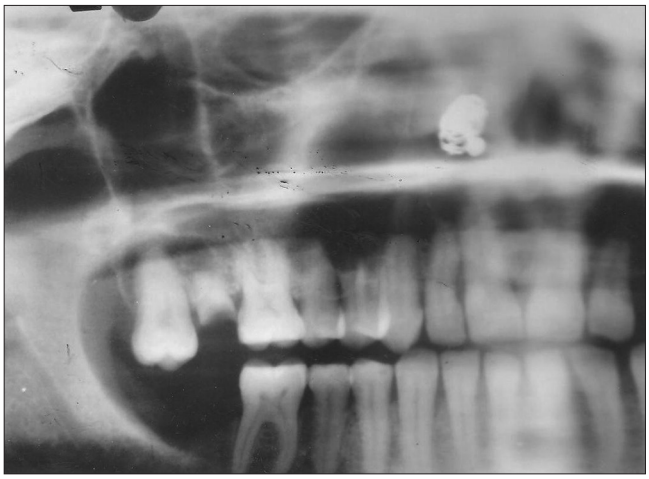

Figure 2: Orthopantomograph showing unilocular radiolucent lesion extending from 22 to 26 regions

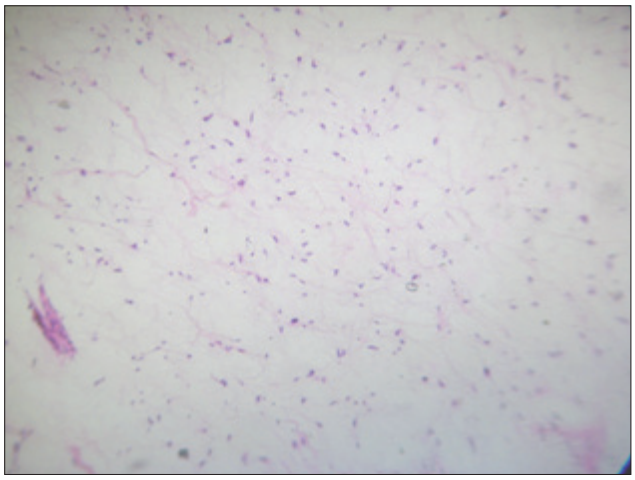

Figure 4: Stellate and spindle shaped cells in a myxomatous background. H and E, ×100

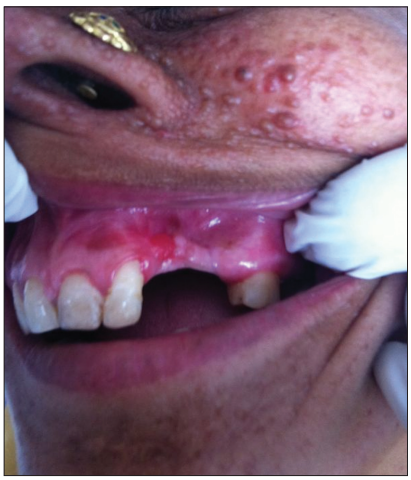

Figure 6: Intraoral view follow up 12 months later (complete healing)

Discussion

Myxoma of head and neck is a rare tumor.[3] The OM is a rare benign tumor that represents about 3% of all odontogenic tumors.[4] In Asia, Europe and America, relative frequencies between 0.5 and 17.7% have been reported. There is no gender predilection and it is seen in ages between 10 and

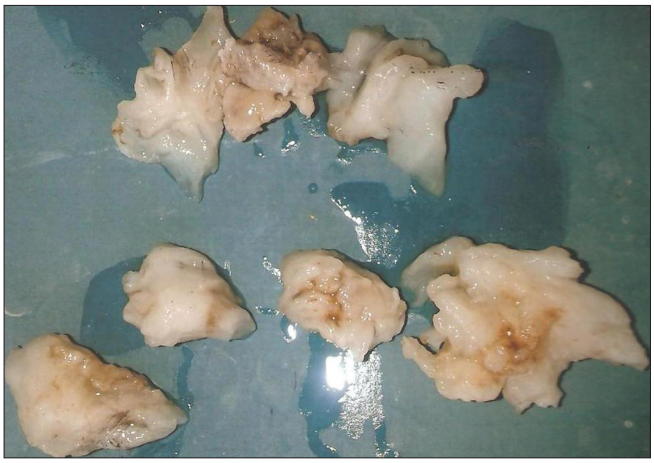

Figure 3: Gross specimen showing multiple gelatinous masses

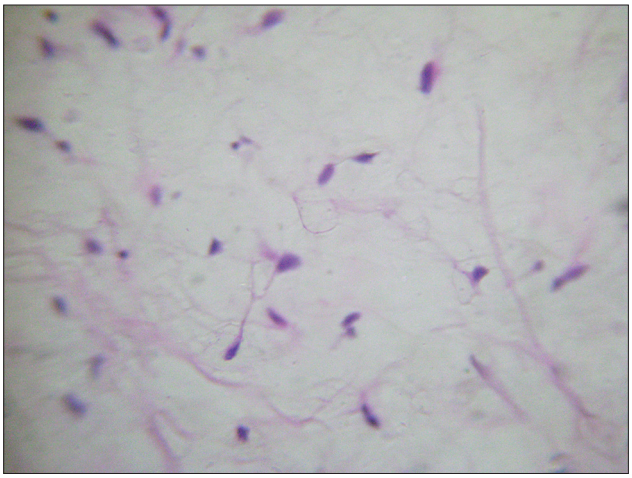

Figure 5: Tumor tissue H and E, ×450

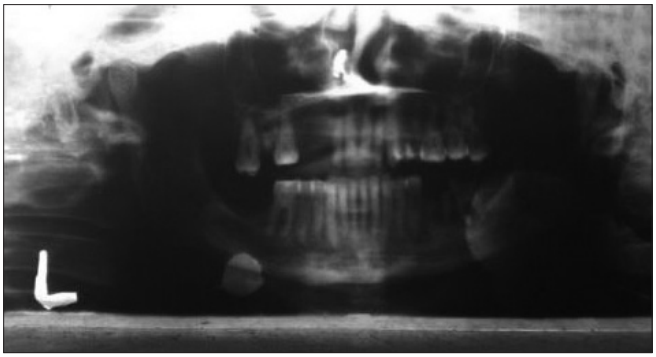

Figure 7: Orthopantomogram follow up 12 monthly (uneventful no recurrence)

40 years. Mandible is reportedly more affected than maxilla. The premolar molar region is the site of predilection in the maxilla and root resorption is rare. Radiologically, its unilocular or multilocular with cortical expansion and tooth displacement.[5] Macroscopically, OM appears as a soft, lobulated non-encapsulated mass which has graying yellow, glistening, firm, mucoid surface. Microscopically, there are stellate or spindle shaped cells of mesenchymal origin, loosely arranged in a soft, mucoid matrix composed of glycosoaminoglycans (GAGs). Hyperchromatic nuclei and mitotic figures are rare. The epithelial odontogenic rests that may be seen are not necessary for diagnosis. They have been shown to be identical to epithelial rests of Malassez found in the periodontal ligament surrounding teeth. Presently authors have started to hypothesise that myoblasts may have developed due to inductive effect of this odontogenic epithelium.[6]

Bryant, in 1802, introduced the term myxosarcoma, which he described as a mucous transformation of round cell sarcoma, malignant and of large volume, usually attacking the omentum and skin. Furthermore, myxomas were described under the name of collenemas by Johannes Miller in 1838. In his 1858 article titled cellularpathologie, Rudolph Virchow introduced the term "myxoma" to describe a soft-tissue tumor, resembling the structure of the umbilical cord.[2] OM was first described by Thoma and Goldman in 1947. There are two divisions observed those that are observed in jaw bones and those that are observed in soft-tissues of that area. It's slow growing locally aggressive.[5] In 1948, Stout labeled the myxoma as a true neoplasm.[3]

This tumor has an extremely rare malignant version called odontogenic myxosarcoma.[6]

The current knowledge of the OM still has significant gaps. One of them is related to the histogenesis of the odontogenic neoplasms.[7] Majority of tumors occur in jaw bearing areas therefore the word odontogenic is prefixed to reflect its odontogenic origin. The resemblance to mesenchyme of developing tooth or the periodontal ligament suggests its histogenesis. However, this tumor is also seen in extragnathic bones. This prompts investigators to think on alternatively that central myxomas are osteogenic in origin.[4] It has been previously been associated with a myxomatous change of an odontogenic fibroma or residual foci of embryonic tissue.[5]

Myxoid changes in other neoplasms may mimic OMs. Such appearances may be found in myxoid neurofibromas, myxoid lipoma and chondromyxoid fibroma. Dental follicle or papillae, normal developmental structures removed in conjunction with unerupted or impacted teeth, may be misinterpreted as a myxoma.[1]

A minority of OM and enlarged follicles but not normal odontogenic mesenchyme may stain positively for s100 protein. The finding that myxomas did not contain s100 may help in differentiating myxomas from enlarged myxoid follicles.[8] Neoplastic cells of myxomas were positively stained for transferrin, ferritin, alpha 1 antichymotrypsin, alpha 1 antitrypsin, s-100 protein, vimentin and actin. It's a tumor of dual fibroblastic histiocytic origin and cells may be of myofibroblastic origin as described by Sivakumar *et al*.[9]

Ultrastructural studies show that the neoplastic spindle cells are fibroblast like cells called myxoblasts. They have the capacity to synthesize large quantities of mucopolysaccharides. The cells show positivity to vimentin, muscle specific actin.[6]

OMs stained positive for Nestin in half of study cases of Fujita *et al*. It is also suggested to be involved in the differentiation from pulp cells to odontoblasts in odontogenic tumor. Nestin is the one of the cytoskeleton constituting intermediate filament. It's a marker of neural stem cells or progenitor cells.[10]

Mutations of Gs alpha gene are rarely if ever, associated with sporadic jaw myxoma tumourigenesis. Furthermore, a mutation in the protein kinase A regulatory subunit type 1A (PRKAR1A) has been reported. Both mesenchymal cells as well as islands of odontogenic epithelium expressed MIB1 (mind bomb homolog 1 Drosophila). The cells of odontogenic epithelium were positive for Bcl-2 and p53 in OMs of the jaws.[6] PRKAR1A mutations have also been reported in OMs by Willems *et al*.[2]

Nakano compared notch signaling among OM and ameloblastic fibroma. Notch is a receptor for inhibitory signals and has a role to play in cytodifferentiation. It governs neoplastic cell differentiation in mesenchymal tumors. The authors said that the developmental stage of myxoma tumor tissue is less advanced than ameloblastic fibroma. The tumor tissue is differentiated to levels as seen in cap stage. The rate of differentiation is closely related to clinical behavior.[11]

Hyaluronic acid, which belongs to group of GAGs is the major contributor to the edematous appearance of the myxoid extracellular matrix (ECM). Their rigidity is responsible for the structural integrity of tissues facilitating diffusion of metabolites and cell migration.[2] The exuberance of ECM protein, hyaluronic acid observed *in vivo* and *in vitro* strongly suggests that it has a definitive role in the local invasiveness of this neoplasm. Other ECM molecules expressed by these cells are fibronectin, type 1 collagen and tenascin. These investigations points out that human immature dental papilla stem cells bear a strong resemblance to OM cells. A high degree of matrix metalloproteinases 2 (MMP2) expression was found in cell lines derived from OM tumor.[7]

Miyagi *et al*., also analyzed the expression and activity

of matrix metalloproteinases 2 and 9 involved in tumor expression. MMP are zinc dependent enzymes that can degrade structural components of the ECM facilitating invasion of tumor cells through normal tissues. These authors investigated the capacity of the cells to penetrate bony trabeculae and their relation with ECM. Fibroblasts, odontoblasts and osteoblasts produce MMPs. They concluded that MMP 9 can lend invasive character to OM.[12]

Moreira *et al*., attempted to investigate methylation pattern in OM. Deoxyribonucleic acid methylation is an epigenetic change occurring during the transcription. Tumor suppressor genes in both OMs and dental pulps were investigated. They were cyclin dependent kinase inhibitor genes p16, p21, p27, p53 and RB1(retinoblastoma1 gene). Cell cycle is dominated by interaction of cyclins and cyclin dependent kinases. Cyclin dependent kinase inhibitors are down-regulated cell cycle. Methylation of genes down-regulates protein expression and contributes to myxoma growth. p27, p53, RB1 showed hypomethylation in myxomas.[13]

García-Muñoz *et al.,* stated that orosomucoid protein is immunomodulatory and angiogenic and therefore results in invasive behavior of OM. It is anti-inflammatory, anti-neutrophil, anti-complement. Presence of orosomucoid protein justifies classical mucoid appearance of the tumor. This protein was present in the cytoplasm of stellate and spindle tumor cells as well as in endothelial cells of large and small blood vessels. Expression of carbonic anhydrase I and glutathione S-transferase was down-regulated in OMs. Carbonic anhydrase was proposed to have affected the balance between bone resorption and apposition. Glutathione transferase when inactivated was leading to loss of protective mechanism against genome damage and tumor suppressor protein.[14]

The histogenesis of OM is poorly understood. It still remains a debatable matter. Myxomas of the head and neck are rare tumors. This case report canvasses a maxillary OM, which again is considered as a rarity. A review of the current proteomic, immunohistochemical concepts has been attempted to update our understanding about the neoplasm.

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How to cite this article: Sarkar RR. Oncologic profile of maxillary odontogenic myxoma: A rare case. Contemp Clin Dent 2013;4:374-7.

Source of Support: Nil. **Conflict of Interest:** None declared.