Case Report

A curious case of central odontogenic fibroma: A novel perspective

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Abstract

We appraise a case of central odontogenic fibroma (COF) with unusual histologic features of entrapped neural elements and mast cells. The presence of mast cells attributed to the release of stem cell factor, the principal growth and activating factor of mast cells. A putative role for C-kit and mast cells in the pathogenesis of COF is described.

Keywords: C-kit, central odontogenic fibroma, mast cells

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INTRODUCTION

Central odontogenic fibroma (COF) is described by the World Health Organization (WHO) as a benign fibroblastic neoplasm containing varying amounts of inactive odontogenic epithelium.[1] It has been subdivided into simple type and the WHO/complex type. However, the need for categorization has been questioned because of their similarity in biologic behavior.[2] COF is a rare tumor with uncertain histogenesis.[3] The classical histological picture of COF comprises of mature collagenous tissue with variable amount of myxomatous stroma containing proliferating fibroblasts. Nests of odontogenic epithelium and calcified material may be seen dispersed in the connective tissue.[4] Apart from these classical features, the occurrence of granular cells, giant cells and pleomorphic fibroblasts has also been reported in COF.[2] The closely related entities that need to be considered in the differential diagnosis include hyperplastic dental follicle, odontogenic myxoma and desmoplastic fibroma.[5] We report a case of COF with unusual histologic findings of entrapped neural elements and abundant mast cells.

The role of mast cells in tumorigenesis is known and has been attributed to the release of stem cell factor (SCF)[6] which binds to the SCF receptor, also known as proto-oncogene C-kit or tyrosine-protein kinase kit. It is an important cell surface marker specific for hematopoietic stem cells, multipotent progenitors and common myeloid progenitors.[7] This unusual presentation of COF was tested using C-kit marker to understand and unravel the possible role of mast cell.

CASE REPORT

A 25-year-old male presented with a swelling in the anterior maxilla of 1-year duration. There were no associated symptoms and no history of trauma. His

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medical and family history was noncontributory. Extraoral examination revealed a bulging facial contour on the left side. Intraorally, a 3 × 2 cm enlargement was noted in the maxilla in relation to the left central and lateral incisor extending into the sulcus. There was no apparent change in color of the overlying mucosa [Figure 1]. Palpation divulged a well-defined, firm and nontender swelling. There was no palpable lymphadenopathy, and routine blood investigations yielded values within normal limits.

A computed tomographic (CT) scan revealed a well-delineated isodense mass causing expansion and thinning of the buccal cortical plate and slight palatal expansion. Also noted was diversion and resorption of the roots of the incisors [Figure 2]. Owing to the size of the mass, the lesion was removed in toto and sent for histopathologic examination.

Gross examination revealed a glistening white round mass measuring 2.5 × 2 cm in dimension. Microscopically, the connective tissue stroma showed delicate collagen fibers disposed in a myxoid matrix containing stellate-shaped fibroblasts [Figure 3a]. A few nerve fibers and dilated blood vessels engorged with red blood cells were seen in the connective tissue [Figure 3b]. At places, a few odontogenic epithelial rests and foci of calcification were present [Figure 3c]. Distributed throughout the stroma were abundant mast cells [Figure 3d], and toluidine blue staining was performed for confirmation of the mast cells [Figure 3e]. The lesion was signed out as COF, complex type.

DISCUSSION

Odontogenic fibroma (OF) was introduced into the WHO classification of odontogenic tumors in 1971 as a rare neoplasm characterized by a variable amount of inactive odontogenic epithelium in a relatively mature fibrous stroma.[2] Depending on its primary location, it was further subdivided into central and peripheral.[8] COF is a rare benign tumor accounting for approximately 0%–5.5% of all odontogenic tumors.[9] It usually occurs in the 2nd to 6th decade of life with a predilection for females.[2] The maxilla and mandible have been found to be equally affected. The premolar/molar region is the preferred site in the mandible, as was seen in this case.[10] It usually manifests as a slow-growing asymptomatic swelling in the jaw occasionally associated with displacement and mobility of adjacent teeth.[5]

Radiographic features of COF are not very diagnostic. It can present as a unilocular or multilocular radiolucent lesion with well-defined borders. Features such as cortical expansion, displacement of adjacent teeth and the crown of an unerupted tooth may be associated with it.[10] In addition to these features, a feature that is not commonly associated with COF is the root resorption of the adjacent teeth, which was noted in our case.

Histopathologically, COF has been divided into two types: an epithelium poor type or simple type and an epithelium rich type or WHO type.[9] The 1992 WHO classification subsequently replaced the term WHO type with odontogenic fibroma complex type or fibroblastic odontogenic fibroma. The basic difference between the two types lies in the connective tissue where the simple type often resembles the dental follicle whereas the complex type does not. In addition, the simple type is relatively less cellular, contains less odontogenic rests and areas of calcification in comparison to the complex type. Although there are some differences microscopically, the

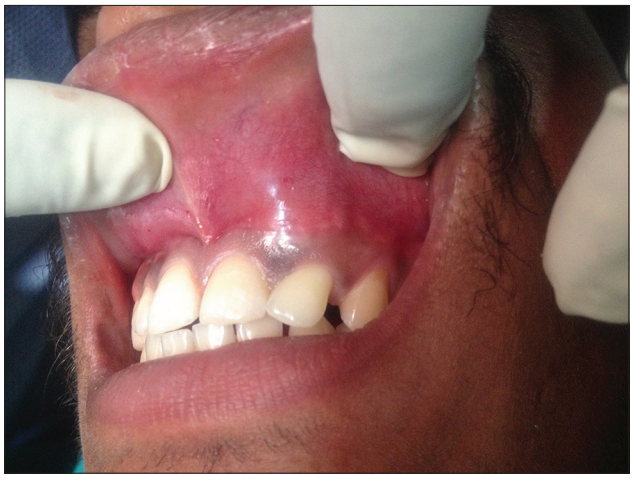

Figure 1: Intraoral view showing a 3 cm × 2 cm enlargement in the maxilla

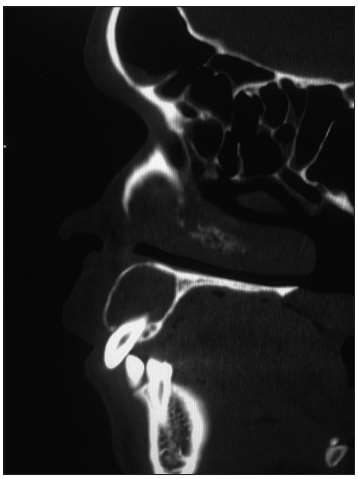

Figure 2: Sagittal computed tomography scan revealing a well-delineated isodense mass with thinning of the buccal cortical plate and slight palatal expansion

classification of COF into simple and complex type has remained contentious.[2]

The final diagnosis should however be given after exclusion of entities that form distinct differential spectrum of either subtype. These include odontogenic myxoma, hyperplastic dental follicle and desmoplastic fibroma.[5] Odontogenic myxoma/myxofibroma is a typically infiltrative lesions[2] and was ruled out due to the absence of any infiltration and overall paucity of myxomatous areas. Hyperplastic dental follicle is associated with an unerupted or missing tooth,[1] and desmoplastic fibroma does not contain odontogenic rests. The presence of mast cells was a confounding factor in ascertaining a final diagnosis in lieu of their ubiquitous presence in neurofibromas and nerve sheath myxomas. However, negative S100 staining helped in ruling out the possibility of a nerve tumor. Based on the presence of a numerous odontogenic rests and calcifications along with a fibrous stroma, a final diagnosis of mast cell-rich COF (complex type) was rendered.

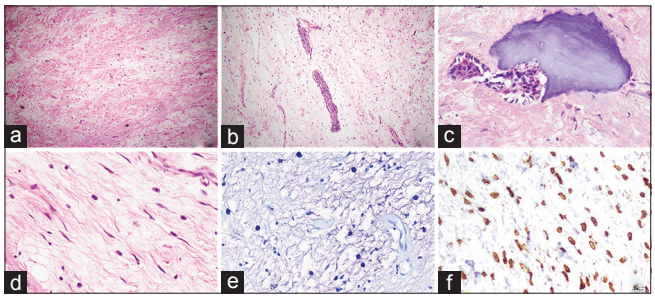

Figure 3: Photomicrographs of histology (a) Stroma showing delicate collagen fibers disposed in a myxoid matrix with focal distribution of neural elements, rests of odontogenic epithelium with areas of calcification and mast cells (H&E, ×4), (b) Focal distribution of neural elements in the connective tissue (H&E, ×10); (c) Rests of odontogenic epithelium with areas of calcification (H&E, ×20); (d) Stroma showing the presence of numerous mast cells (H&E, ×20); (e) Confirmation of mast cells with special stain (Toluidine blue, ×20); (f) Strong positive expression of mast cells and fibroblasts for C-kit (Anti C-kit, ×20)

The pathogenesis of COF has been ambiguous due to its rarity. Dunlap *et al*. (1984) implicated the role of neural crest cells in its pathogenesis.[3] Our case had an interesting finding; an overwhelming presence of mast cells. Based on the association of mast cells with C-kit and the importance of C-kit in the pathogenesis of tumors such as gastrointestinal stromal tumor and adenoid cystic carcinomas,[7] we tested the sample for C-kit expression [Figure 3f]. With the stromal cells of COF showing expression of C-kit in the present case, we postulate a possible aberration in C-kit that causes its overexpression and resultant activation of tyrosine kinase leading to unchecked initiation of intracellular signal transduction pathways involving phosphatidylinositol 3'-kinase (P13'-kinase), mitogen-activated protein (MAP) kinase, Src family kinases and phospholipases. The uncontrolled activation of tyrosine kinase channeled pathways results in excessive proliferation and imbalance between the proapoptotic and antiapoptotic molecules thereby conferring the neoplastic fibroblasts immortality and unhindered proliferation leading to tumor formation.[11] One could even propose that the release of the SCF by these fibroblasts has a chemotactic effect on mast cells thus leading to their accumulation and activation. The mast cells then contribute to a change in the microenvironment

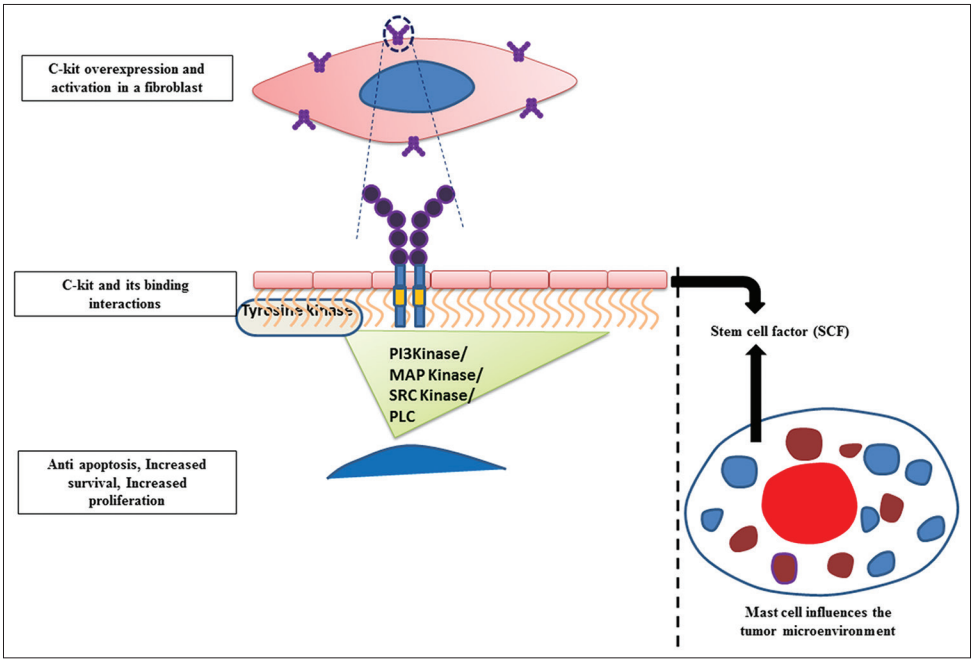

Figure 4: Role of C-kit and mast cells in central odontogenic fibroma - a tumor progression model

by releasing substances, namely histamine, cytokines, growth factors and metalloproteinases causing eventual progression of the tumor [Figure 4]. Ultimately, the entire process may also be associated with the downstream regulation of Ras suppressor protein as it has a direct effect on C-kit.[6] Although our attempt to explain the role of mast cells in the pathogenesis of COF is based on the earlier work, where its role has been emphasized in changing tumor microenvironment, definitive role of mast cells in tumor progression and prognosis is yet to be established. The management of COF entails complete surgical removal. Recurrences are infrequent following postsurgical follow-up as was with our case. However, a regular follow-up for 5-year posttreatment is advisable.[10]

In summary, the unusual presentation of COF with mast cells with a possible role of C-kit in its pathogenesis is highlighted. Whether the present finding delineates a specific subset of COF or if all COF express C-kit needs to be elucidated. The prospect of using C-kit inhibitor drugs such as imatinib could be tried in cases where surgery is contraindicated.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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