Follicular-acanthomatous ameloblastoma and impact on intervention

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Abstract
Ameloblastoma is the second most common benign neoplasm of odontogenic origin. It occurs commonly in third to fifth decade of life with no sex predilection. The clinical presentation of tumor includes swelling and facial disfigurement. Here we present a case report of 48 year old male patient reported with a chief complaint of pain and swelling in lower left front tooth region of the jaw since one month. Various investigation modalities were performed which assured the diagnosis of Follicular-acanthomatous ameloblastoma.

Keywords: Ameloblastoma, Odontogenic tumor, Follicular, Acanthomatous.

Introduction
Ameloblastoma is a common, benign, slow-growing but locally invasive neoplasm of enamel organ-type tissue which has not undergone differentiation to the point of hard tissue formation.[1] First described by Cusack in 1827, the term Ameloblastoma was derived from the English word 'amel' meaning enamel and the Greek word 'blastos', which means germ or bud. Other names suggested for this tumor are cystosarcoma, adamantine epithelioma, adamantinoma, adamantinoblastoma, multilocular cyst and finally ameloblastoma.[2]

The term 'ameloblastoma' was given by Churchill in 1934, in order to replace the term 'adamantinoma' coined by Malassez in 1885, because the latter term implies on hard tissue formation but no such material is present in this lesion.[3] In 1879, Falkson gave the first detailed description of this lesion.[4] Robinson defined it as being a tumor that is 'usually unicentric, nonfunctional, intermittent in growth, anatomically benign and clinically persistent'.[1] In 1991, World Health Organization (WHO) defined it as a benign but locally aggressive tumor with a high tendency to recur, consisting of proliferating odontogenic epithelium lying in a fibrous stroma.[5] In 2017, the WHO updated the classification on ameloblastomas based on the current genetic studies. Ameloblastomas were earlier classified as solid/multicystic, extraosseous/peripheral, desmoplastic, and unicystic types in the 2005 WHO classification of odontogenic lesions. In the most recent WHO classification (2017), it has been reclassified as ameloblastoma, unicystic ameloblastoma, and extraosseous/peripheral types. The term solid/multicystic was removed because most conventional ameloblastomas show cystic degeneration with no biologic differences. According to latest WHO (2017) classification, six histopathologic subtypes of solid ameloblastoma include follicular, plexiform, acanthomatous, basal cell, granular and desmoplastic.[6]

It is the second most common odontogenic neoplasm and only odontoma outnumbers it in reported frequency of occurrence.[3] Its incidence, along with its clinical behavior, makes it most significant odontogenic neoplasm to oral and maxillofacial surgeons.[4] The present case is a conventional ameloblastoma with mixed histopathological variants. The intention of this case-report is to shed some light on sub-classification of histopathological variant of ameloblastoma with mixed histopathological presentation and also to find the impact of identification of histopathologic variant on treatment modality. In the present paper, we describe a case of solid multicystic ameloblastoma – follicular-acanthomatous variant in 48-year-old male patient.

Case Report
A 48-year old male patient reported with a chief complaint of pain and swelling in lower left front tooth region of the jaw since one month. Initially, the swelling was small, pea-sized which gradually increased and reached the present size. No relevant medical and family history was reported. Patient had no complaint of fever, chills, loss of weight and paresthesia. On clinical examination, swelling was present in relation to lower left mandibular canine and first premolar with an approximate size of 2x3 cm. Swelling was bony hard and tender on palpation.

Further investigations included hematological investigation, radiological investigation and biopsy. Hematological investigation included complete blood count, erythrocyte sedimentation rate (ESR) and random blood sugar (RBS) which were in normal physiological range. Radiographic investigations included intra-oral periapical radiograph (IOPA) and OPG (Orthopantomogram). IOPA radiograph (Fig.1) revealed a well demarcated radiolucency in the canine - premolar region above the apical one-third of roots. A complete extent of lesion could be seen in OPG (Fig. 2) which showed a well demarcated radiolucency from distal aspect of lateral incisor to mesial roots of second molar. No sclerotic border could be ascertained. Excisional biopsy was submitted to the Department of Oral Pathology and Microbiology for histopathological examination.

Grossly, the specimen (Fig. 3) consisted of four bits of soft tissue specimen and one hard tissue specimen. The tissue was grayish white in color, firm in consistency and smooth to

rough in texture. Soft tissue mass collectively measured 1.5x1.5x1.0 cm whereas hard tissue measured 1x0.8x0.7cm. Microscopically, the submitted H & E stained sections showed partially encapsulated and overall well-delineated mass exhibiting abundant nests and islands of odontogenic tumor cells in a stroma of varying consistency (Fig. 4). Islands of tumor follicles exhibited peripherally palisaded, tall columnar, ameloblast-like cells arranged in two to three layers with central loose, stellate reticulum-like cells (Fig. 5). Multiple follicles exhibited extensive squamous metaplasia (Fig. 6, 7) centrally with or without the presence of keratin pearls. The proportion of follicles with or without squamous metaplasia appeared to be equal. The intervening stroma was myxoid (in the vicinity of tumor follicles) to moderately dense showing mature fibrous stroma. Based on histopathological features, a final diagnosis of Follicular-Acanthomatous Ameloblastoma was given.

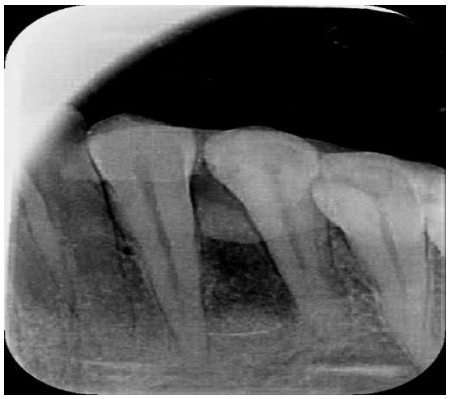

Fig. 1: IOPA radiograph showing a well demarcated radiolucency in the left mandibular canine - premolar region above the apical one-third of roots

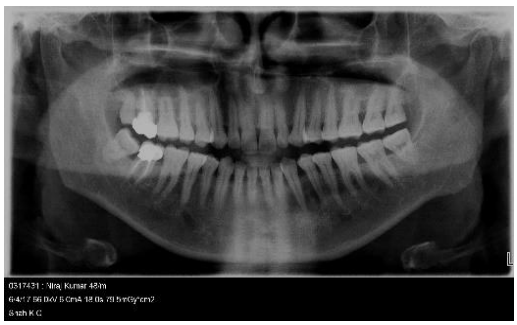

Fig. 2: OPG showing a well demarcated radiolucency from distal aspect of permanent left mandibular lateral incisor to mesial roots of permanent left mandibular second molar

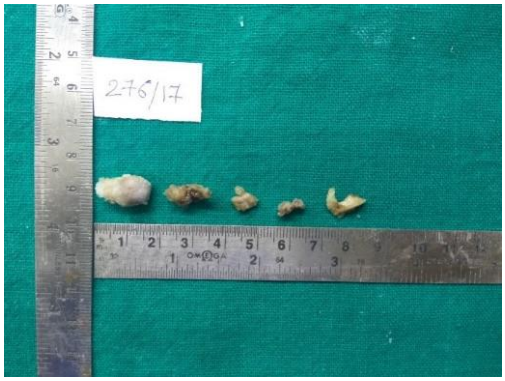

Fig. 3: Gross examination showing four bits of soft tissue and one bit of hard tissue specimen respectively

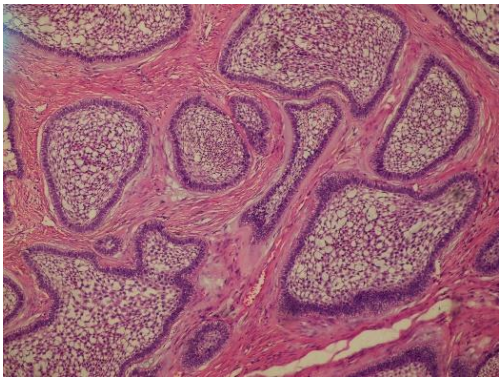

Fig. 4: Photomicrograph depicting multiple ameloblastic follicles (H & E stain, 10x magnification)

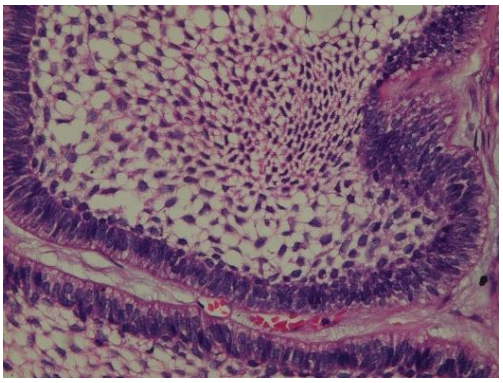

Fig. 5: Photomicrograph depicting ameloblastic follicle having tall columnar cells at periphery along with stellate reticulum like cells in the center (H & E stain, 40x magnification)

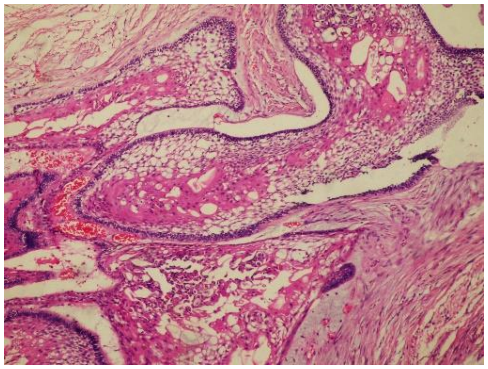

Fig. 6: Odontogenic islands exhibiting extensive central squamous metaplasia with areas of parakeratin formation. (H&E stain, 10x magnification)

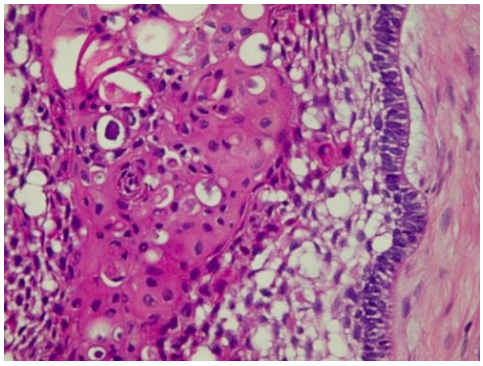

Fig. 7: Layer of stellate reticulum like cells separating peripheral ameloblast-like cells from central squamous cells. (H&E stain, 40x magnification)

Discussion

Conventional ameloblastoma is characterized by follicles consisting of peripheral cell layer of ameloblast like cells and central stellate reticulum like cells. The three main clinico-patho-radiological types of ameloblastoma have various histological variants. The solid multicystic type with six variants may have differing occurrence, recurrence rates and clinico-pathological behaviors. This probably makes the variant identification of ameloblastomas significant and not just of academic interest.

The criteria for diagnosing the histopathological variant has been loosely mentioned in the literature and so is the importance of the same. Presence of predominant pattern appears to be the only statement for diagnosing variants which is ironically ignoring the multiple patterns, if present within the one lesion. The two variants seen commonly are follicular and acanthomatous and were seen in our case as well with almost equal preponderance. Acanthomatous, granular cell, desmoplastic and basal cell types are the uncommon variants.[2]

As per the literature, most prevalent type is follicular ameloblastoma, representing 64.9% of the total cases followed by plexiform type with 13% and desmoplastic with 5.2% cases. The least prevalent of all is acanthomatous type having an occurrence of 3.9%. Histological presentation of these lesion does not alter its clinical or biological behavior, the degree of invasiveness or predisposition to the occurrence of metastases. These were only reported as differentials which help in diagnosis and research.[7]

Histopathologically, the follicular variant consists of many small discrete islands of tumor which consist of peripheral layer of cuboidal or columnar cells with well polarized nuclei resembling preameloblasts. These cells enclose a central mass of polyhedral, loosely arranged cells which resemble stellate reticulum.[8] The acanthomatous variant shows central area with squamous cell differentiation along with keratin formation.[9] In these cases, squamous metaplasia is thought to be attributed by chronic irritation due to calculus and oral sepsis.[10] Takegawa et al. had done a study on rats in which transition of squamous metaplasia into squamous cell carcinoma in submandibular salivary gland by application of potassium iodide had been emphasized. They observed the development of squamous metaplasia in proliferative ductules and interlobular ducts. Further conversion of squamous metaplasia in to squamous cell carcinoma take place and explained by the mechanism via a non-genotoxic, proliferation-dependent mechanism.[11]

According to some researchers, histologic subtype may have prognostic implications for recurrence of lesion. Follicular ameloblastoma shows the highest recurrence rate of 29.5%. In contrast, the acanthomatous type shows only a 4.5% recurrence rate.[3]

Some researchers believe that if left untreated, acanthomatous type of ameloblastoma may develop into an invading and metastasizing squamous cell carcinoma. There is controversy related to the biological behavior of the acanthomatous type. Some investigators believe that this variant is locally aggressive and frequently invades in to the alveolar bone and even recurs after marginal surgical excision. Some of aspects, related to pathogenesis and the invasive growth of ameloblastoma are still unclear. So study related to molecular mechanisms of cell proliferation can be helpful to predict aggressiveness of ameloblastoma and especially p16 (cyclin-dependent kinase inhibitor) tumor suppressor protein encoded by CDKN2A gene.[9]

Although, the literature does not appear to emphasize upon the importance of sub classifying the histopathological variants of ameloblastoma but the presence of squamous metaplasia in a follicle might actually have an aggressive impact on the disease course. The presence of squamous metaplasia has been correlated with malignant transformation when stimulated with noxious agents. Thus, sub-classification

of tumor must always be accomplished with due importance to criteria of sub-classification.

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