

Unicystic Ameloblastoma - A Case Report with a Brief Review of Molecular Pathogenesis

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Abstract: Ameloblastoma is the second most common odontogenic tumor. These are usually benign, slow growing and locally aggressive, with a high recurrence rate, representing 11% of all odontogenic tumors. 61.5% of odontogenic neoplasm in India is ameloblastoma. Its incidence, combined with its clinical behavior and tendency for recurrence, makes ameloblastoma the most significant odontogenic neoplasm. Various studies have been conducted to understand the molecular pathogenesis of ameloblastoma better and thus aid in proper treatment. This article focuses on a case of a 34-year-old male diagnosed with unicystic ameloblastoma with mural proliferation.

Keywords: Ameloblastoma, odontogenic tumor, recurrence

1. Introduction

Odontogenic tumors represent a surprisingly diverse group of pathologic lesions of the jaws and overlying soft tissues.¹ These neoplasms are lesions derived from epithelial, ectomesenchymal, or mesenchymal elements that are or have been a part of the tooth-forming apparatus.² In many instances, the exact tissue of origin (histogenesis) may only be inferred from its site and structure³.

Ameloblastoma comprises 11% of odontogenic tumors, with less than 1% of all tumors affecting the jaws³. It has a wide age range, with clusters of cases occurring between 20 to 60 years. No significant sex predilection has been seen, and the Asian population show susceptibility. 80% of cases effects the mandible, 66% of which occurs in the mandibular angle-ramus region⁴.

Radiographically, ameloblastoma appears as either a unilocular or a multilocular radiolucency. Unilocular radiolucency may or may not be associated with an unerupted tooth. Multilocular radiolucency show soap-bubble radiolucency and are aggressive lesions.² The treatment of choice is complete surgical removal with adequate margins.

2. Case Report

A 34-year-old male patient reported to the Department of Oral Pathology and Microbiology with a chief complaint of swelling in the lower right back tooth region since 1 month. Patient was apparently normal 1 month back when he noticed a swelling on the right side of the face that gradually increased to the present size.

On extra-oral examination, Facial asymmetry was present [Figure 1]. Swelling could be seen on the right side of the face. Swelling was firm on palpation and non-tender. Intra-oral examination, on inspection revealed a well-circumscribed swelling on the labial aspect, extending from 36 obliterating the labial sulcus till the ramus of mandible [Figure 2]. On palpation, the swelling was firm, bony-hard, non-compressible and non-tender in nature.



Figure 1: Extra-oral examination showing facial asymmetry on the right side



Figure 2: Intra-oral examination revealing a swelling on the labial aspect

Orthopantomogram (OPG) shows a unilocular radiolucency present i.r.t 46, 47 and impacted 48 [Figure 3].



Figure 3: OPG revealing a unilocular radiolucency i.r.t 46, 47, 48

Based on clinical and radiological features, a provisional diagnosis of ameloblastoma was made and an incisional biopsy was recommended to rule out the lesion.

Macroscopically, two bits of tissue mass was received which was grayish white in color, firm in consistency measuring 1×0.7 cm and 0.7×0.5 cm approximately in 10% formalin [Figure 4].



Figure 4: Incisional biopsy grossing specimen

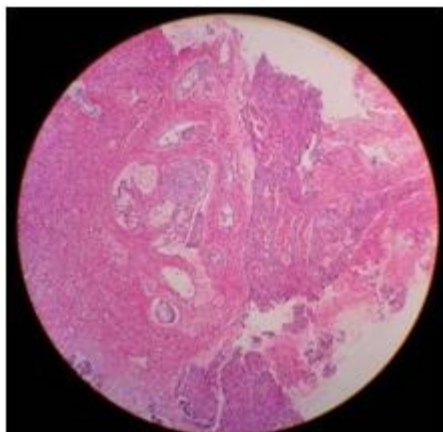


Figure 5: Photomicrograph at 10x revealing odontogenic epithelium and connective tissue stroma with numerous am. Follicles

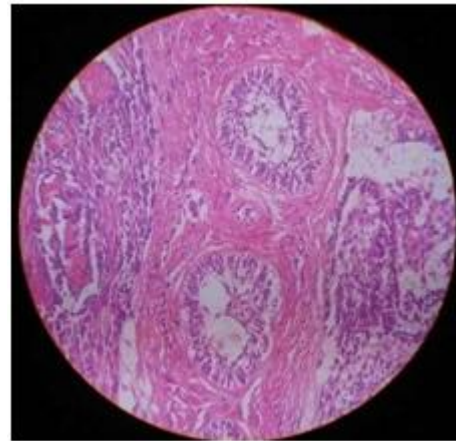


Figure 6: Photomicrograph at 40x revealing follicles with peripheral ameloblasts like cells and central stellate reticulum like cells

Routine hematoxylin and eosin stain was done which revealed odontogenic epithelium interspersed in connective tissue stroma [Figure 5]. Epithelium was arranged in the form of follicles with peripheral ameloblast like cells and central star-shaped stellate reticulum like cells [Figure 6]. Connective tissue stroma revealed dense collagen bundles, chronic inflammatory infiltrate chiefly lymphocytes and plasma cells and endothelial lined blood vessels. Based on the overall histopathological findings, a final diagnosis of follicular ameloblastoma was given.

Excisional biopsy specimen was received. Multiple bits of hard & soft tissue specimen, firm in consistency, yellowish-brown in color, largest soft tissue bit measuring 4×3 cm approximately and remaining smaller bits together measuring 6×5 cm approximately. Hard tissue measuring 5×2 cm approximately and 45,46,47,48 also received in 10% formalin.



Figure 7: Grossing of excisional biopsy specimen

Routine hematoxylin and eosin stained section revealed odontogenic lining epithelium with underlying connective tissue stroma [Figure 7]. Epithelium was 3-4 cell layer thick. Odontogenic epithelium showed basal cell layer composed of cuboidal to columnar cells displaying hyperchromatic &

palisaded nuclei with loosely arranged cells resembling the stellate reticulum like cells [Figure 8, Figure 9]. Discrete follicles of odontogenic epithelium composed of peripheral ameloblasts like cells and central stellate reticulum like cells seen in the fibrous connective tissue stroma [Figure 10]. Connective tissue stroma reveals dense bundles of collagen fibers with fibroblast interspersed, chronic inflammatory cells chiefly lymphocytes & plasma cells, endothelial lined blood vessels with extravasated RBCs. Overall histopathological features were suggestive of 'Unicystic ameloblastoma with mural proliferation'.

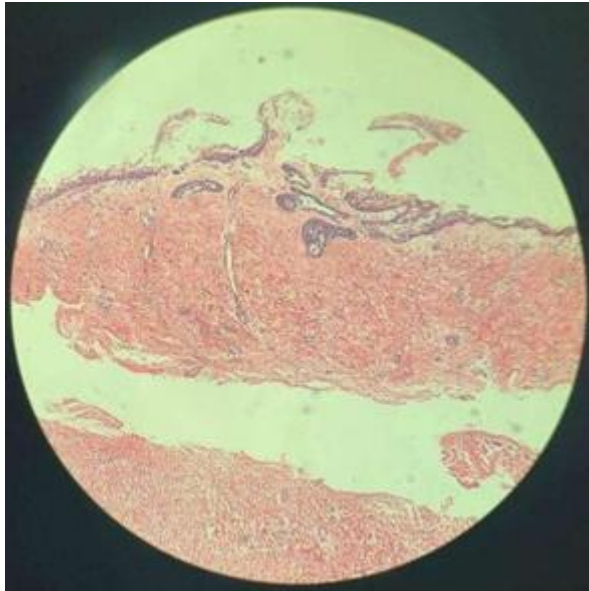


Figure 7: Odontogenic lining epithelium and underlying connective tissue stroma (10x)

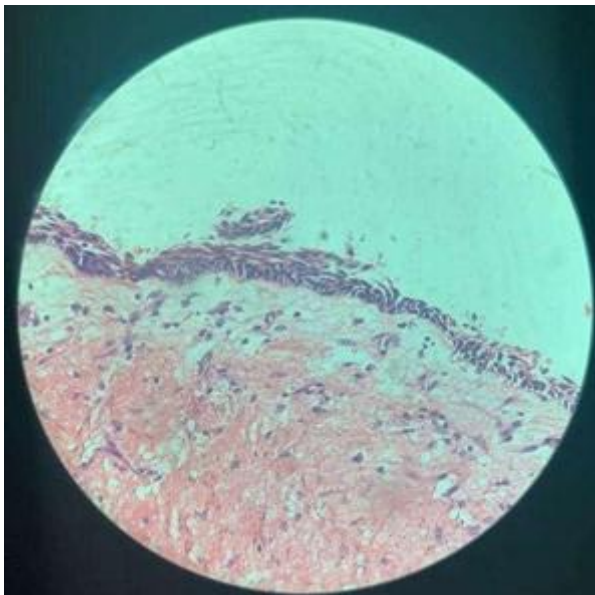


Figure 8: Epithelium is 3-4 cell layer thick (40X)

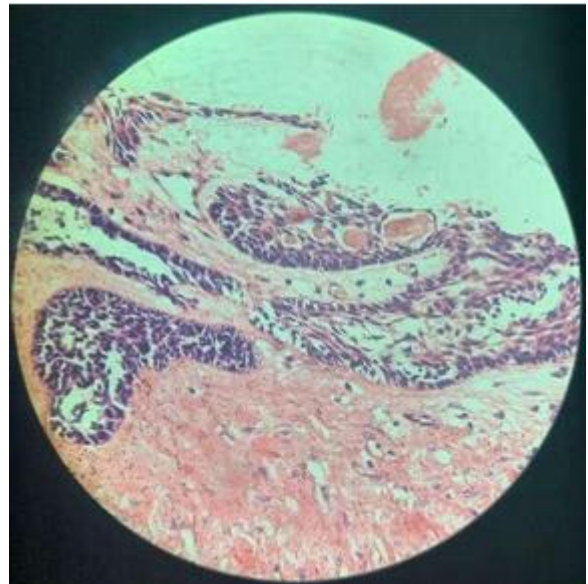


Figure 9: Peripheral ameloblast like cells and central stellate reticulum like cells (40x)

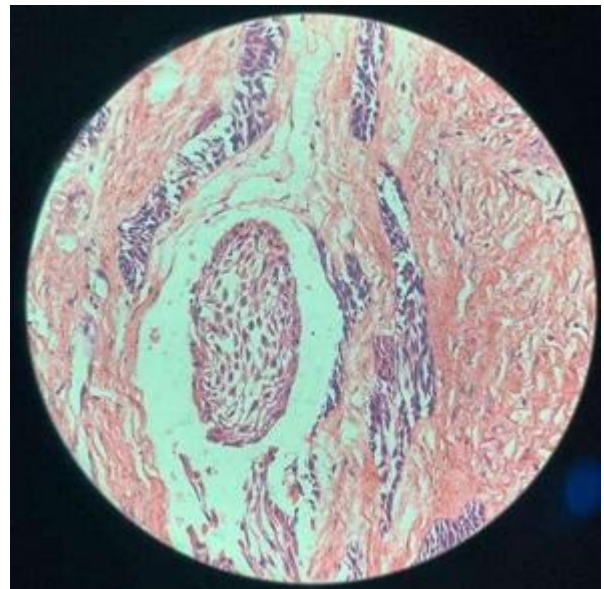


Figure 10: Discrete follicles showing ameloblastic features 40X

3. Discussion

The World Health Organization classifies ameloblastoma as a benign entity arising from odontogenic epithelium. Ameloblastoma is a true neoplasm of enamel organ type tissue which does not undergo differentiation to the point of enamel formation. According to Robinson, these are usually unicentric, non-functional, intermittent in growth, anatomically benign, and clinically persistent.⁴ Based on clinical, radiographic, and histologic prognostic aspects, ameloblastomas are classified as (1) classic/ solid/ multicystic, (2) unicystic, (3) peripheral, and (4) desmoplastic.³ 2017 modified WHO classification reclassified ameloblastoma as (1) Unicystic type and (2) peripheral type. Solid/multicystic was dropped because most conventional ameloblastomas show cystic degeneration with no biological differences. The desmoplastic type was left under the histopathologic subtype instead of becoming a separate entity.⁵

During and after the formation of teeth, most of the epithelium breaks down, but some epithelial residues remain throughout life in the periodontal membrane (the epithelial rests of Malassez). It is believed that most ameloblastomas

are derived from these epithelial residues⁸.

A multitude of studies can be found in the literature regarding the molecular pathogenesis of ameloblastoma.^(6, 7)

<i>Molecular</i>	<i>Expression</i>	<i>Function Marker</i>
Ki67	Peripheral ameloblast-like cells in solid/multicystic. Basal cells in unicystic.	Indicates that the cellular proliferation and consequently the ameloblastoma growth are concentrated in the peripheral areas composed of ameloblast-like cells.
Telomerase	Increased	Reflects the proliferative potential of ameloblastoma cells. Ability of local invasion and high recurrence rates.
P53	Increased	Increased cellular proliferation and malignant potential.
Caspase 3 (pro-apoptotic)	Diffusely distributed in the central area of tumour islands.	Confirms the presence of two distinct patterns of ameloblastoma cells; • an anti-apoptotic proliferating area correspondent to its peripheral basal cell layer, • a pro-apoptotic site in the central layers of the tumor islands.
Bcl-2 (anti-apoptotic)	The peripheral basal cell layer of ameloblastoma	
Ameloblastin	Not expressed in ameloblastoma.	The tumour cells do not attain functional maturation as secretory phase ameloblasts.
Enamel matrix proteins (sheathlin, amelogenin, enamelin, tuftelin)		Ameloblastin-null mice– developed an odontogenic tumour of dental epithelium origin in the buccal vestibule of the maxilla. Odontogenic tumour cells expressed enamel matrix proteins (amelogenin, enamelin, tuftelin) but did not express ameloblastin. Based on this, the authors concluded that ameloblastin deficiency was the cause of the tumourigenesis seen in null mice.
RANKL	Increased	Induces osteoclastogenesis.
TNF- α	Activated	In turn, provides the space for ameloblastoma to expand in the bone. Tumor aggressiveness.
Matrix metalloproteinases	Increased	Matrix degradation during tumor growth, invasion and induction of angiogenesis.
MMP-2		Degrades type IV collagen, resulting in the promotion of tumor invasion and metastasis.
MMP-14	Higher in recurrent and solid /multicystic ameloblastoma tissues than in primary and unicystic ameloblastoma tissues.	Local invasive capacity.

We hereby reported a case of a unicystic subtype of ameloblastoma. The term ‘unicystic’ is derived from the macro and microscopic appearance. The lesion is essentially a well-defined, often large monocystic cavity with a lining and constitutes approximately 6% of all ameloblastomas.⁴ Presenting symptoms may include a slow-growing submucosal mass, loose teeth, malocclusion, paresthesias, and pain.⁹ For the present case, the patient had reported with a swelling that was slow growing in nature and radiograph revealed resorption of the involved teeth roots. As seen in the present case; 58.3% of cases appear radiographically as a unilocular radiolucency with unerupted tooth involvement. A slight male predominance is noted with a ratio of 1.6:1.² The average age for presentation of unicystic ameloblastoma is 22.1 years compared with 35.9 years seen in conventional ameloblastoma which abides with the case discussed above.¹⁰

A histological subgrouping of unicystic ameloblastoma have been introduced as luminal (subgroup 1), luminal and intraluminal (subgroup 1.2), luminal, intraluminal, and intramural (subgroup 1.2.3), and luminal and intramural (subgroup 1.3).² The present case was diagnosed as

subgroup 1.3. This intramural unicystic ameloblastoma exhibits ameloblastomatous invasion into the underlying connective tissue wall of the cyst which may or may not involve the lining epithelium. The intramural pattern is analogous to a superficially invasive carcinoma.¹⁰ The extent and depth of the infiltrative growth may vary considerably; necessitating careful and extensive sampling of the tumor.¹⁰ Histopathologically, the characteristic appearance is a lining epithelium exhibiting Vickers and Gorlin’s criteria as representing early ameloblastomatous changes - peripheral tall columnar cells with hyperchromatic nuclei, reverse polarity of nuclei, nuclei showing a palisading pattern, and subnuclear vacuole formation between the nuclei and basement membrane.² Ameloblastomatous lining epithelium proliferating into the connective tissue wall (luminal & intramural) and islands of ameloblastoma occurring isolated in the connective tissue wall (intramural).² The treatment of choice is adequate tumor removal including uninvolved tissue margin. Since the unicystic variant of ameloblastomas is less aggressive, the recurrence rate is distinctly lower than that for the characteristic ameloblastoma.⁴

4. Conclusion

Ameloblastoma is a benign, locally invasive odontogenic tumor with a high rate of recurrence. With its poor symptoms and low prevalence, it is usually diagnosed late. Though a benign lesion, due to its locally aggressive property, it can cause extensive thinning and expansion of cortical plates. This lesion also demonstrates a wide variety of histological patterns. Timely recognition and surgical interventions may improve treatment outcomes and reduce recurrence and morbidity.

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