Ameloblastoma – Adding perspectives

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Abstract:
Ameloblastomas are very common odontogenic tumours. The knowledge about this tumour is gaining greater importance because of its emerging variants. It is very essential to know the clinical, radiographical and histopathological features of all the subtypes of ameloblastoma along with their behavioural and prognostic characteristics. This article aims at reviewing and presenting the newer perspectives of the subtypes of ameloblastoma with more emphasis on UAs (unicystic ameloblastomas), DAs (Desmoplastic ameloblastomas), and HLAs (hybrid lesion of ameloblastoma) from the existing literature.

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Introduction
In humans, tumors of odontogenic tissues are comparatively rare, comprising of about 1\% of all jaw tumors. Ameloblastomas constitute almost half (48.9\%) of the odontogenic tumors with female-to-male and maxilla-to-mandible ratios of 1:1.7 and 1:8 respectively.\textsuperscript{1} The WHO defines it as locally invasive polymorphic neoplasm consisting of proliferating odontogenic epithelium, which usually has a follicular or plexiform pattern lying in fibrous stroma.\textsuperscript{2,3} This tumour is discussed to be derived from serre’s epithelial cell rests, the epithelial cell rest of malassez, epithelium of odontogenic cysts
Ameloblastoma and basal cell layer of gingiva or oral mucosa\(^4,5\)

Clinically ameloblastomas appear as aggressive odontogenic tumours often asymptomatic and slow growing with no evidence of swelling. It can even cause symptoms such as swelling, dental malocclusion, pain and paresthesia of affected area.\(^6\) Usually radiographs appears as a well demarcated unilocular or multilocular radiolucency that may or may not be associated with unerupted tooth. Histopathologically ameloblastoma exhibits proliferating odontogenic epithelium within a background of fibrous stroma.\(^7\) Since ameloblastoma shows histologic patterns which vary greatly, a number of subtypes can be distinguished.\(^5\)

Ameloblastoma is notorious for its recurrences although it is benign in nature. Due to this it is of great importance not only to the surgeons but also to the private practitioners of dentistry. Therefore this article aims at discussing the diversities of clinical, radiographical and histopathological features of subtypes of ameloblastoma reviewing from the existing literature.

**Discussion:**

Ameloblastomas are an enigmatic group of oral tumours.\(^8\) A series of genetic and molecular alterations appear to promote the development and progression of the odontogenic tumours via multiple steps. Some of these include Oncogenes eg. Fibroblast growth factor receptor, Transcription factors eg.myc, tumour suppressor genes eg. Retinoblastoma, Oncoviruses eg. HPV, EBV etc.\(^9\)

In the literature unicystic and desmoplastic variants are now recognized as clinically, radiographically and histopathologically distinct entities, with differing prognostic significance.\(^2, 10\). Hence, based on all these features along with
behavioural and prognostic characteristics, subtypes or variants of ameloblastomas can be presently distinguished as follows.\(^1\)

1. The classic solid/multicystic ameloblastoma (SMA)
2. The unicystic ameloblastoma (UA)
3. The peripheral ameloblastoma (PA)
4. The desmoplastic ameloblastoma (DA), including the so-called hybrid lesions.

In a recent study done on 3,677 ameloblastoma cases, clearly demonstrated that it is not appropriate to diagnose the ameloblastoma without specifying the type.\(^{11}\)

**Unicystic Ameloblastoma**

Unicystic Ameloblastoma was first described by Robinson and Martinez in 1977.\(^{12,13}\)

The term ‘unicystic’ is derived because of its macro- and microscopic appearance of the lesion.\(^{11}\) The incidence of UAs is 5-22\% of all types of ameloblastomas.\(^{14}\) Younger patients are commonly affected, with 50\% of cases being diagnosed during the second decade of life. The average age in one large series was found to be 23 years.\(^{15,16}\)

Slight male predilection with a male:female ratio of 1.6:1 is seen. However, when the tumor is not associated with an un-erupted tooth, the gender ratio is reversed to a male to female ratio of 1:1.8. Depending on the association of impacted tooth, UA can be divided into 2 categories.\(^{11}\)

1. Histologically verified UAs which are associated with an unerupted tooth (dentigerous variant)
2. UAs lacking an association with an unerupted tooth (non dentigerous variant).

Most common site is the mandible, irrespective of the variant. The ratio of the maxilla:mandible is 1:7 for the dentigerous
variant, versus 1:4.7 for the nondentigerous type.\(^{17}\)

Radiographically, unilocular and multilocular patterns of UAs exist. Unilocular pattern seen predominantly. Eversole LR et al identified predominant radiographical patterns for UA: unilocular, scalloped, macromultilocular, pericoronal, interradicular, or periapical expansile radiolucencies. \(^1\)When the UAs associated with impacted tooth the differential diagnosis is dentigerous cyst. UAs that are not associated with an impacted tooth may mimic a residual cyst or a keratocyst.\(^{14}\)

Histologically, the minimum criterion for diagnosing a lesion as UA is, the demonstration of a single cystic sac lined by Odontogenic (ameloblastomatous) epithelium often seen only in focal areas. UA should be differentiated from odontogenic cysts because the former has higher rate of recurrence than later. In a clinicopathological study of 57 cases of UA, Ackerman et al classified this entity into 3 histolologic groups.\(^{12}\)

**Group I: Luminal UA** [tumour confined to the luminal surface of the cyst: (Fig.1)]

![CTW AE](image_url)  
**Fig.1:** Photomicrograph shows cystic wall lined by ameloblastomatous epithelium and stellate reticulum like cells (CTW: Connective tissue wall, AE: Ameloblastomatous epithelium) [Haematoxyllin & Eosin stain x10]

**Group II: Intraluminal/plexiform UA** [nodular proliferation in to the lumen without infiltration of the tumour cells in to the connective tissue wall: (Fig.2)]
Histological subgroups (modified after Ackerman et.al) by Philipsen and Reichart.\textsuperscript{11}

Subgroup 1: Luminal UA
Subgroup 1.2: Luminal and intraluminal
Subgroup 1.2.3: Luminal, intraluminal and intramural
Subgroup 1.3: Luminal and intramural.

Therefore when UAs removed in toto, the surgical specimen is that of partially or totally collapsed cystic sac. By careful examination of the inner and outer aspects of the cyst wall, it may be possible to spot characteristics of UA features such as one or several intraluminal papilloma-like tissue proliferation and/or intramural focal thickenings or nodules. Lack of these findings does not however exclude a diagnosis of UA. The diagnosis of UA can only be made histologically and cannot be predicted preoperatively on clinical or radiographic grounds. Examination of the entire lesion through sectioning at many levels is
mandatory for securing the final diagnosis. The UAs diagnosed as subgroups 1 and 1.2 may be treated conservatively where as subgroups 1.2.3 and 1.3 showing intramural growths must be treated radically same as SMA. Recurrence is also related to histological subtypes of UAs with those invading fibrous wall having the rate of 35.7% but others only 6.7%. Recurrence rate for enucleation alone is 30.5%, where as 3.6% for resection, compared to 0-25% chances in conventional ameloblastoma after resection. 

Desmoplastic Ameloblastoma

Recently, the desmoplastic variant of ameloblastoma is considered as a distinct clinical, radiographical and pathologic entity and classified as separate category by WHO classification of odontogenic tumours. DAs comprises of 4 to 13% of all the ameloblastomas. Eversole and co-workers are, credited for the first publication on DA in English literature It is named so because of unusual histomorphology, including the extensive collagenisation or desmoplasia.

Average age of occurrence is 42.9 yrs compared to 35.9 of SMA. No gender predilection. In most of the cases presents as painless swelling with tumour size varying between 1.0 and 8.5 cms at the greatest diameter. In the study of Phillipson, maxilla:mandible ratio was 1:0.9. This is in sharp contrast to the SMA showing 1:5.4. Vast majority of DAs are seen in the anterior region till premolar portions of the jaw. Approximately half of them are seen in the maxilla. Only about 5.4% cases were seen in the mandibular molar region as opposed to 39% of SMA. An association of DA and unerrupted or impacted tooth has been found in only about 3.4% of cases, as against the 8.7% among SMA.
The radiographic features of DA differ from those of SMA. DAs frequently presents as diffuse, mixed radiolucent-radio-opaque lesion with ill defined borders, often misdiagnosed as fibro-osseous lesion (Fig.4).\textsuperscript{23,24,25} The ill defined borders may explain the infiltrative behaviour of DA.\textsuperscript{22}

Waldron and El Mofty\textsuperscript{26} described histologic appearance of DA as small ovoid islands and narrow cords of odontogenic epithelium widely separated by dense, moderately cellular fibrous connective tissue. Typical ameloblastic columnar cells may be scant and the peripheral palisading may be absent. The center of the epithelial islands may appear hypercellular with spindle shaped or squamotoid epithelial cells.\textsuperscript{22,24} Extensive stromal desmoplasia (Fig.5) is a prominent feature, with abundant thick collagen fibres that seems to compress or squeeze the odontogenic epithelial islands from the periphery. Myxoid changes of the stroma may be observed surrounding the odontogenic epithelium. Formation of metaplastic bone trabeculae rimmed by active osteoblasts has been described in several cases. The desmoplastic stroma of DA is not scar tissue but newly produced connective tissue.\textsuperscript{22,27}

Fig.4: Radiograph showing ill-defined borders of the DA (Courtesy: J Can Dent Assoc 2004; 70(2):100–4)

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Fig.5: Photomicrograph showing extensive desmoplasia with compressed/squeezed odontogenic epithelial islands (magnification x5) [Courtesy: J Can Dent Assoc 2004; 70(2):100–4]
DA showed similar recurrence rate (15.9%) as that of SMA. Krezler even reported the higher recurrence rate than other types of ameloblastomas. The reason for this could be because radiographically DAs can be misdiagnosed as fibro-osseous lesions and also they present with ill-defined borders making it difficult to assess the exact interface of the lesion with normal bone. Along with all these, it is more commonly seen in maxilla which may produce early invasion of the adjacent structures. According to Phillipsen et al. radiographically ill-defined borders suggest an infiltrative process and aggressive nature with propensity to recur. Resection and enucleation are the main treatment modalities of DAs even though biological behaviour and prognosis, and the proper treatment strategies for DAs are not entirely defined so far. Prospective studies with regular and long term follow-up is required to provide the necessary information. Till then DAs has to be treated as that of SMA.

**Hybrid Lesion of Ameloblastoma (HLAs)**

The HLAs was first described by Waldron and El-Mafty. It is a tumour variant where histologically areas of follicular or plexiform ameloblastoma coexist with areas characteristics of DA. It has been suggested that the hybrid lesion should be considered a collision tumour. Whereas many more cases with detailed clinical and radiographic data and corresponding analysis are needed to clarify the biological behaviour of this tumour.

**Conclusion**

Eventhough ameloblastomas are common odontogenic tumours, they present challenge in both diagnosis and treatment, because of diversities in clinico-pathological and radiographic features. Therefore this article is an attempt at adding the current newer
perspectives, by discussing the clinico-pathological and radiographic variations of UAs, DAs and little about HLAs to the already existing types of ameloblastomas, 

**Conflict of Interest Statement:**
None Declared

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**References**

6. Gumgum S, Hosgoren B. Clinical and Radiographic Behaviour of


15. Neville BW, Damm DD, Allen CM, Bouquot JE. Odontogenic cysts and tumours, Chapter 15, in Oral and Maxillofacial


cases and review of literature. JADA 2002;133:1072-1075.


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