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AMELOBLASTOMA: A PROPOSED CLASSIFICATION BASED ON CLINICAL, RADIOGRAPHIC, AND HISTOPATHOLOGICAL FEATURES

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ABSTRACT:

Odontogenic tumors (OTs) originate from the epithelial/ectomesenchymal tissues, which are part of the odontogenic apparatus. Ameloblastoma is a true benign neoplasm of enamel organ-type tissue that does not undergo differentiation to the point of enamel formation. Ameloblastoma is an OT that is relatively rare and comprises about 11% of OTs and 1% of all jaw tumors. Whereas, ameloblastoma is the most common odontogenic tumor in the Indian sub-continent. The literature has described different clinical and histopathological cases of ameloblastoma separately. Various classifications have been proposed for ameloblastoma, but the classifications are incomplete and create confusion among new readers, undergraduate and postgraduate students. So here, we are presenting a complete classification of ameloblastoma for easy understanding. This classification in the form of a flowchart is simple and will give an idea about such an important and the most common odontogenic tumor at a glance.

Keywords: Ameloblastoma, classification, odontogenic tumors

INTRODUCTION:

Odontogenic tumors of the jaw are a group of lesions that originate from remnants of epithelium or ectomesenchyme associated with tooth development. It ranges from hamartomas to true neoplasms. The fifth edition of WHO histological typing of odontogenic tumors classifies them as benign and malignant. Then, they are subdivided according to the cell of origin to epithelial, ectomesenchymal, or mixed.[1] Ameloblastoma is sub-categorised under the epithelial odontogenic tumours. Ameloblastoma is a benign progressively growing, locally aggressive intra-osseous epithelial odontogenic neoplasm characterized by expansion and a tendency for local recurrence if not removed with an adequate surgical margin, beyond the radiological margin. Ameloblastoma is the second most common odontogenic tumor after odontoma (11%) and is commonly found in the lower jaw, near the angle of the mandible. Ameloblastoma, an epithelium-derived

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odontogenic tumor, has an origin in the prehistoric era. [2] In 1827, Cuzack was the first one to report the case of ameloblastoma, whereas Broca, in 1868 gave the first detailed description of ameloblastoma. During 1884 and 1885 Malassez studied odontogenic tumours and proposed the name "epithelioma adamantin" for ameloblastoma. The term adamantinoma was changed in 1930, to the more appropriate term ameloblastoma, which is still in current use. Various terminologies used for ameloblastoma are enlisted in Table 1. [2] The term adamantinoma may be considered a misnomer in as much as adamantin (enamel) is not a product of this tumor. The characteristic peripheral cylindrical cells of the tumor islands are not true ameloblasts in that these cells are not capable of producing enamel stroma. In particular, because the tumor islands are embedded in a mature, fibrous connective tissue. An account of the terminology (with historical aspects) of ameloblastoma was published by Baden in 1965. [3] It occurs most often between the third and fifth decades of life. According to clinical and radiographic features, ameloblastoma is classified into conventional solid or multicystic, extraosseous or peripheral, and desmoplastic or unicystic types. Histopathological variants include follicular, plexiform, acanthomatous, granular, basaloid, and desmoplastic types. [4] Various classification systems have been proposed for ameloblastoma, but no classification has compiled all the clinical, radiographical as well as histopathological features and given the classification on that basis. We have come up with a new classification considering the different aspects of ameloblastoma. To our knowledge, this is the first comprehensive classification for ameloblastoma, in which, clinical, radiographical, and histopathological features have been considered.

Classification

Figure 1 shows that ameloblastoma can be classified on various bases like clinical, radiographical & histopathological types.

As per clinical sites involved, it is categorized as ameloblastoma affecting the oral cavity. It can occur on the soft tissue of the oral mucosa e.g. gingiva or any other area of oral mucosa called soft tissue/peripheral/extraosseous type. Peripheral ameloblastoma (PA) is a benign odontogenic tumor arising from the odontogenic epithelium with no influence of the ectomesenchyme. [5] It has the same histologic characteristics as a solid/ multicystic ameloblastoma (SMA), but it occurs in the soft tissues overlying the tooth-bearing areas of the maxilla and mandible. PAs do not invade the underlying bone. [6] The term “peripheral ameloblastoma” was first coined by Kuru in 1911. [7] Ameloblastoma involving the jaw bone can be seen as central/intraosseous ameloblastoma. Apart from the oral cavity, it can also involve different other sites like the pituitary gland or long bone or lymph nodes labeled as metastasizing ameloblastoma. Metastasizing ameloblastoma is clearly defined by the World Health Organization (WHO) as a

histologically benign typical ameloblastoma that metastasizes to distant sites. [8]

Based on radiographical findings, ameloblastoma can be classified as radiolucent or a combination of radiolucent, radiopaque, or mixed lesions which can be seen as a unilocular or multilocular radiolucent area.

Depending on histopathological findings ameloblastoma can be classified as benign and malignant. Benign can be further divided as neoplastic as - conventional/solid/multicystic and cystic can be as unicystic ameloblastoma(UA). This "classic" intraosseous ameloblastoma commences as a solid epithelial tumor. In some cases, the epithelial islands remain relatively small, and consequently, there is little tendency toward cystic degeneration of the epithelial component. The tumors remain solid. In other cases, the neoplastic epithelial islands grow and become cystic; this degenerative process starts in the center of the islands where the cells cannot receive sufficient supplies of nutrients. This phenomenon may spread to several islands, where it is first recognized microscopically and later grossly. This has led to the use of the term solid multicystic ameloblastoma (SMA). [9] The unicystic ameloblastoma is a less encountered variant of the ameloblastoma, referring to those cystic lesions that show clinical and radiographic characteristics of an odontogenic cyst but in histologic examination show a typical ameloblastomatous epithelium lining part of the cyst cavity, with or without luminal and/or mural tumor proliferation. Eversole et al, 1984 were able to identify six radiographic patterns for UA, ranging from well-defined unilocular to multilocular appearance.(Figure 2) [3]

In conventional ameloblastoma, 3 basic microscopic pictures as follicular, plexiform, and mixed type of ameloblastoma are seen. In any of the above 3 basic types, it can show changes in the stellate reticulum-like cells (epithelial component) such as granular cells, acanthomatous change, basaloid type, papilliferous, keratinizing, clear cell variant or adenoid variant. In connective tissue, it can show desmoplastic, hemangiomatous change, or dentinoid formation. Follicular variant is the most common and diagnostic pattern where the central areas of the neoplastic islands are loose and resemble the stellate reticulum of the developing tooth germ and the peripheral cells are columnar (palisaded) and display reverse nuclear polarity. [10]

The plexiform variant consists of thin lamina-like strands but there are two distinct patterns. One where the cells are basaloid and often arranged in a double row of basaloid cells without peripheral palisading or reverse nuclear polarity. In the second pattern of plexiform, the cords are thicker, and the central cells are more squamous but without peripheral palisading or reverse nuclear polarity. [11] Acanthomatous ameloblastoma shows squamous metaplasia of the stellate reticulum and

the formation of keratin within the tumor islands. [12]

Histopathologically, the granular cell variant has numerous large eosinophilic granular cells. Transformation of the cytoplasm of stellate reticulum-like cells into a coarse, granular eosinophilic appearance imparts the granular appearance. Granular cells form central masses of the epithelial tumor islands and cords. The periphery of islands consists of the non-granular tall columnar cell. [13]

The basal cell variant is a rare variant that tends to grow in an island-like pattern. The characteristic color gradation in other ameloblastomas is often difficult to appreciate in basal cell types because basaloid-appearing cells rather than stellate reticulum-like cells occupy the center portion of the tumor island. The basaloid cells stain deeply basophilic and equivalent in staining intensity with a peripheral layer of cells. [14]

Keratoameloblastoma is a rare variant of ameloblastoma exhibiting surface para keratinization and central keratinization in a so-called lamellated pattern. It is characterized by cystic and solid epithelial follicles in a fibrous stroma. The follicles consist of discohesive polygonal or angular cells resembling the stellate reticulum. [15]

Desmoplastic variants exhibit an "animal-like" configuration or flying kite appearance. Peripheral cells are cuboidal with hyperchromatic nuclei. The center of the epithelial islands appears hypercellular with spindle-shaped or squamatoid, occasionally keratinized, epithelial cells. Extensive stromal desmoplasia is noted. [6]

Hemangiomatous ameloblastoma is an ameloblastoma that has many spaces filled with blood or large endothelial-lined capillaries in its stroma. One of the theories for its origin states that during amelogenesis, capillaries associated with the outer enamel epithelium providing necessary nutrition for enamel completion are abnormally induced and result in their abnormal proliferation. Such proliferated vessels possibly turn into a tumor component. Another theory suggests that any traumatic incident such as a tooth extraction may provide the stimulus for the proliferation of epithelial cell rests in the periodontal ligament and subsequent tumor development. [16]

Clear cell odontogenic tumor is an uncommon or unusual neoplasm of the jaw. They show unusual histologic biphasic patterns with areas of acceptable ameloblastoma (follicular, basaloid cells, acanthomatous) together with the conspicuous clear cell component in the ameloblastic follicles. The presence of clear cell components may represent a sign of dedifferentiation and possibly a malignancy with or without metastases. [17]

Adenoid ameloblastoma (AA) is the only new entity added to the odontogenic lesions and it represents the most important change. It is defined as an epithelial odontogenic neoplasm composed of cribriform architecture and ductlike structures and frequently

includes dentinoids. Approximately 40 cases have been reported in the literature so far. It usually presents as a painless swelling with an incidence peak in the 4th decade and a slight male predilection. The essential diagnostic criteria have been described as an ameloblastoma-like component, duct-like structures, whorls/morules, and cribriform architecture, while dentinoid, clear cells and focal ghost-cell keratinization are reported as desirable features. [18]

In cystic it can be divided as multicystic with any histological picture as described above whereas unicystic is further classified as luminal, intraluminal, and mural histological variant.

Malignant is labeled ameloblastic carcinoma. Ameloblastic carcinoma (AC) is considered a primary odontogenic carcinoma histologically resembling ameloblastoma. BRAF p.V600E mutations, the most common activating mutation in conventional ameloblastoma, have been reported in AC. [19]

CONCLUSION

The last decades have witnessed a tremendous increase in the knowledge of the various diagnostic methods. This has challenged the traditional way of classification of ameloblastoma. In the wake of this, we here proposed a new classification of ameloblastoma based on clinical location, radiographic appearance & based on histopathology. To our knowledge, neither the textbooks nor the literature has described the classification of ameloblastoma based on different aspects. Hence our proposed classification is inclusive of consideration of clinical, radiographic & histopathological features of the important entity, i.e., ameloblastoma. In reviewing the previous classification, this classification also provides systematic additional information regarding the treatment approach.

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TABLE:

Sr.No.	Year	Author	Terminology
1.	1654	Scultet	Tumeurs liquides de la machoire
2.	1832	Dupuytren	Corps fibreux de la machoire
3.	1840	Forget	Maladie kystique de machoires
4.	1859	Forget	Tumeur fibreuse
5.	1859, 1862	Robin	Tumeur fibreuse provenant du follicule dentaire
6.	1867	Broca	Odontomes embryoplastiques
7.	1870	Wedl	Cystosarcoma/colloid Tumor/cystosarcoma adenoides
8.	1876	Heath	Cystic sarcoma of the lower jaw
9.	1877	Kolaczekin	Cystic adenoma
10.	1877	Busch	Cystic epithelioma
11.	1877, 1879	Falkson	Follicular cystoids or cystoma proliferum folliculare
12.	1882	Brasseur	Sarcoma kystique avec cylindres epitheliaux
13.	1884	Malassez	Epithelioma adamantin
14.	1885	Bernays	Enamelogenous cyst
15.	1888	Bland-Sutton	Epithelial odontome
16.	1888	Audry	Epithelioma oligokystique
17.	1889	Nasse	Cystome central paradentaire
18.	1889	Tapie	Cystodermoid
19.	1890	Derujinsky	Adamantinom
20.	1890	Derujinsky	Epithelioma adamantinoma
21.	1891	Bennecke	Central solid epithelial tumour
22.	1893	Becker	Central papilloma of the jaw
23.	1895	Tapic	Carcinoma adamantinum
24.	1901	Blumm	Adamantinom
25.	1902	Borst	Cystadenema adamantinum
26.	1904	Partsch	Soft odontoma and multilocular cystoma
27.	1904	Pirkus	Central cystadenoma
28.	1907	Dreybladi	Pseudoadenoma adamantinum
29.	1917, 1918	Krompecher	Epithelioma adamantinunmalignum & Basiloma
30.	1926	Melanotic epithelioma	Mummery and Pitts
31.	1929, 1932	Churchill and Ivy	Ameloblastoma
32.	1938	Cahn	Epithelioma of the basal variety
33.	1946	Thoma and Goldman	Adamantoblastoma
34.	1946	Byars and Sarnat	Pre-ameloblastoma
35.	1948	Willis	Carcinoma of tooth germ residues
36.	1948	Fischer and Waslas	Odontoma adamantinum
37.	1951	Schulenburg	Basal cell carcinoma of the jaws
38.	1954	Mathis	Epithelioma ameloblastoides
39.	1957	Treves	Pre-ameloblastoma metamorfo and pre-ameloblastoma protomorfo

Table 1: Different terminologies for ameloblastoma

FIGURES:

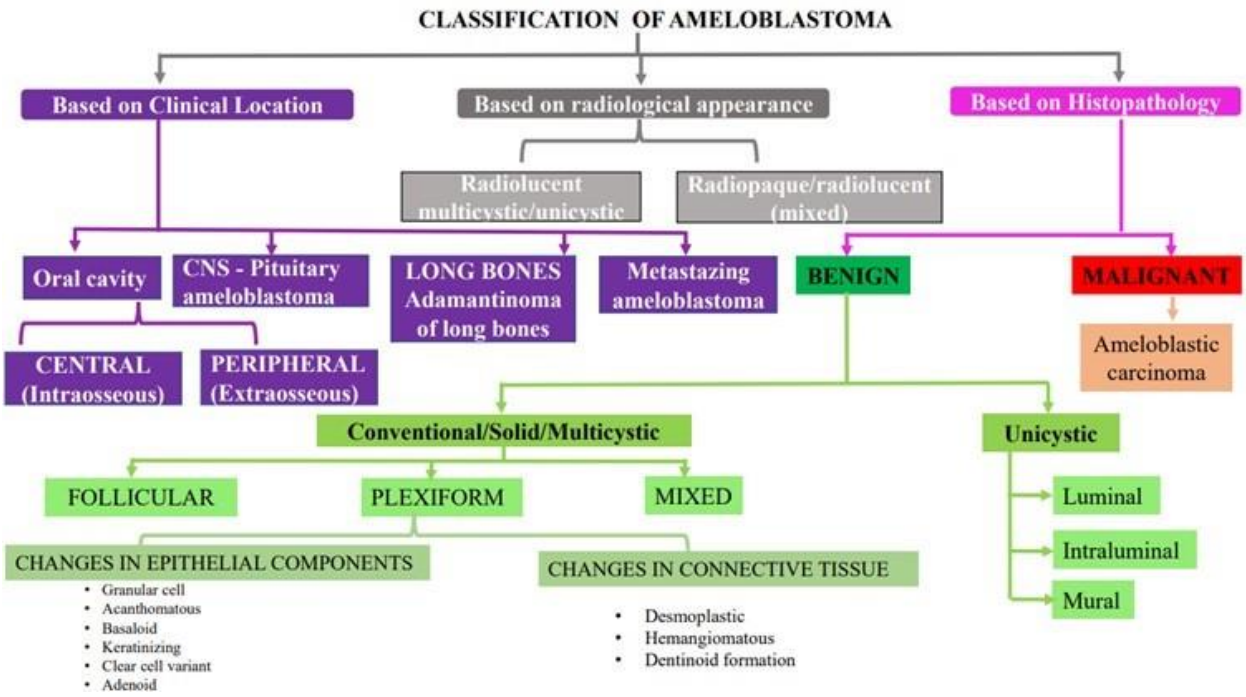

Figure 1: Classsificaaation Of Ameloblastoma

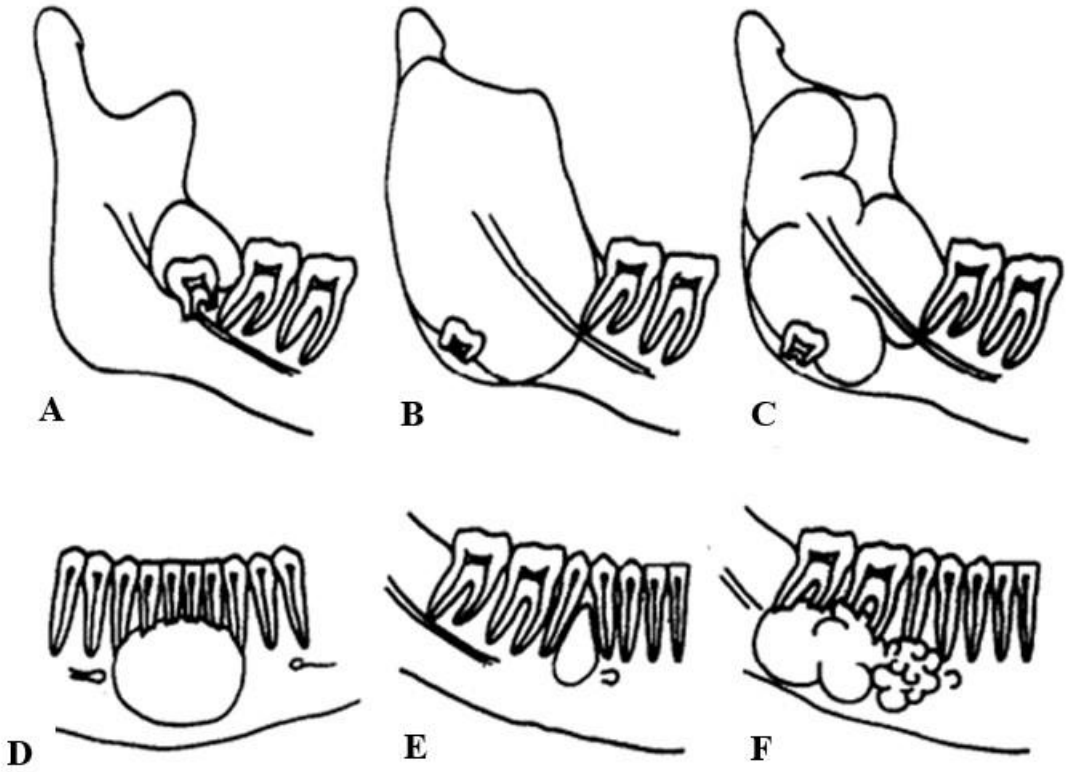

Figure 2