Revista ARACÊ
ISSN: 2358-2472

CONVENTIONAL AMELOBLASTOMA, BEYOND A CLINICAL AND RADIOGRAPHIC ANALYSIS: A HISTOLOGICAL REVIEW OF ITS VARIANTS

https://doi.org/10.56238/arev7n2-301

Date of submission: 27/01/2025 **Date of publication:** 27/02/2025

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ISSN: 2358-2472

ABSTRACT
Ameloblastoma is a tumor of odontogenic origin that arises from remnants of the dental lamina. Conventional ameloblastoma is the most common subtype of ameloblastoma. It primarily occurs in adult patients, affecting the posterior region of the mandible more frequently. Generally, the tumor is asymptomatic and slow-growing. Radiologically, it presents as a radiolucent/hypodense image with well-defined and scalloped borders, either unilocular or multilocular. When multilocular, it may exhibit small locules, referred to as "honeycomb," or larger locules resembling "soap bubbles." Histologically, six subtypes can be identified: follicular, plexiform, acanthomatous, desmoplastic, granular cell, and basal cell ameloblastoma. This study aims to conduct a literature review of the histological variants of conventional ameloblastoma. The present study is characterized as a documentary, retrospective, and applied research of the narrative literature review type. The selected database for this research was PubMed. The search terms used as descriptors were "Ameloblastoma", "histological" and "variants." A total of 962 articles were retrieved, and after applying a time frame filter of five years (2020-2025), 253 articles were listed. Articles unrelated to the topic, without full text, and those including theses and dissertations were excluded. In the end, 10 articles were used for this study. The results indicate that the main pattern found is the follicular type, characterized by the formation of nests of epithelial cells within the tumor stroma. The plexiform pattern shares similar characteristics but presents epithelial cords within the connective tissue. The acanthomatous pattern displays keratin pearls within its connective tissue, while the granular cell pattern shows the presence of cells with eosinophilic cytoplasm and nuclei displaced towards the periphery. The desmoplastic pattern is marked by scarce odontogenic epithelium and a more fibrous stroma. Finally, the basal cell pattern presents ameloblastic epithelium with more eosinophilic columnar cells along with the presence of blood vessels in its stroma. This study highlights a significant diversity in the histological presentations of conventional ameloblastoma, suggesting that these differences may influence both diagnosis and therapeutic strategies. Understanding these histological variants of conventional ameloblastoma is essential for a better comprehension of the clinical behavior of the lesion, as well as treatment modalities and prognosis.

Keywords: Histological Variant. Conventional Ameloblastoma. Benign Tumor.

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INTRODUCTION

The World Health Organization defines ameloblastoma as a benign intraosseous epithelial odontogenic neoplasm characterized by progressive growth with destruction of surrounding tissues and a tendency for local recurrence if not adequately removed (RAMANADKA; KAMATH; KUDVA, 2018). This pathology has been classified since 2022 into five types: conventional ameloblastoma (formerly known as multicystic or solid), unicystic ameloblastoma (6%), extraosseous/peripheral ameloblastoma (2%), metastatic ameloblastoma (1%), and adenoid ameloblastoma, a type designated in the 5th edition (GHAI, 2022).

With an approximate incidence of 1% of all oral tumors and about 9–11% of all odontogenic tumors (GONZÁLEZ *et al*., 2020), its etiology and pathogenesis remain subjects of research. It has been considered a neoplastic transformation of dental lamina remnants; elements of the enamel organ, the epithelial lining of certain odontogenic cysts, or basal epithelial cells of the oral mucosa may serve as the histological component for its pathogenesis (SHI *et al*., 2021).

Clinically, it presents as an asymptomatic growth or a volume increase accompanied by expansive bone destruction or even cortical perforation, with root divergence or resorption (MATHEW, 2020).

It is common for this benign neoplasm to be detected during routine radiographic examinations, revealing multilocular or unilocular radiolucent lesions. When the tumor reaches large proportions, deformity, masticatory dysfunction, facial asymmetry, limited mouth opening, or airway obstruction may be observed (KANG *et al*., 2020). These characteristics make clinical diagnosis more predictable; however, at these stages, the prognosis and the patient's quality of life become uncertain, as radical surgical intervention is the primary treatment option (DANDRIYAL *et al*., 2022).

Regarding its histological findings, conventional ameloblastoma presents a total of six variations, which are classified as plexiform, folicular, desmoplastic, acanthomatous, basal cell, and granular cell (RAJENDRAN, 2020). Thus, the objective of the present article was to analyze and present the main histological variants of conventional ameloblastoma.

METHODS

For the development of this narrative review, A bibliographic search was conducted in January 2025, in the PUBMED and Virtual Health Library (VHL) databases using the

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descriptors: "Ameloblastoma," "histological," and "variants." Initially, 253 published studies were identified, from which those written in English and published between 2020 and 2025 were selected. During the selection process, priority was given to studies that included clinicopathological evaluations and case reports, provided they were available in full text. Articles that were not directly related to the review topic, those in which ameloblastoma did not present in its conventional type, as well as monographs, theses, and dissertations, were excluded from the analysis.

After a thorough review, 10 articles were deemed relevant for inclusion in this review. These articles are listed in Table 1. It is important to note that no classification system was applied to assess the level of evidence of the analyzed studies.

The authors selected the following topics to create a suitable chronological narrative: Follicular variant; Plexiform variant; Desmoplastic variant; Acanthomatous variant; Basal cell variant; Granular cell variant.

RESULTS AND DISCUSSION

Table 1: *List of articles selected for the narrative review.*

Title	Author	Year	Type of study	Topic adressed
A case report on granular cell ameloblastoma – A rare histological entity.	Anju Mathew	2020	Case report.	It discusses a clinical case regarding the rare histological variation of ameloblastoma.
Maxillary Ameloblastoma: A Review with Clinical, Histological and Prognostic Data of a Rare Tumor.	Zoi Evangelou	2020	Literature review.	It comprehensively depicts the histological variants of ameloblastoma.
Histopathological patterns and	Phenehas Bwambale	2022	Literature review.	It presents both information
biological characteristics of ameloblastoma: A retrospective cross- sectional study.				regarding the histological characteristics of ameloblastoma and meticulously

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ISSN: 2358-2472

				outlines it patterns.
Histopathologic Feature of Hyalinization Predicts Recurrence of Conventional/Solid Multicystic Ameloblastomas.	Dominic Augustine	2022	Clinicopathological evaluation.	Evaluations of hyalinizations characteristics regarding ameloblastoma recurrence.
An unusual case report of basal cell ameloblastoma and a detailed review of literature.	Kirti Buva	2022	Clinical case.	It addresses information regarding the uncommon basal cell variant of ameloblastoma.
Ameloblastoma: Retrospective Study and Analysis of 102 Cases Over 10 Years, Single Centre, Institutional Experience.	Ramakant Dandrival	2022	Literature review.	Evaluation of 102 cases of ameloblastoma in the last 10 years.
Conventional Ameloblastoma. A Case Report with Microarray and Bioinformatic Analysis.	Emiliano Jurado-Castañeda	2022	Clinical case.	It discusses a clinical case report with the aid of bioinformatics.
Desmoplastic Ameloblastoma – A Case Report.	Saranya Manikandan	2023	Clinical case.	Case report of histological subtype: desmoplastic.
ARetrospective Analysis of 129 Ameloblastoma Cases: Clinical and Demographical Trends from a Single Institution.	Stefan Vila	2024	Clinicopathological evaluation.	It presents a review of 129 cases of ameloblastoma
Desmoplastic ameloblastoma of anterior maxilla - A case report.	Madhur Manak	2024	Clinical case.	It presents a report on the desmoplastic variant of ameloblastoma.

Source: own authorship

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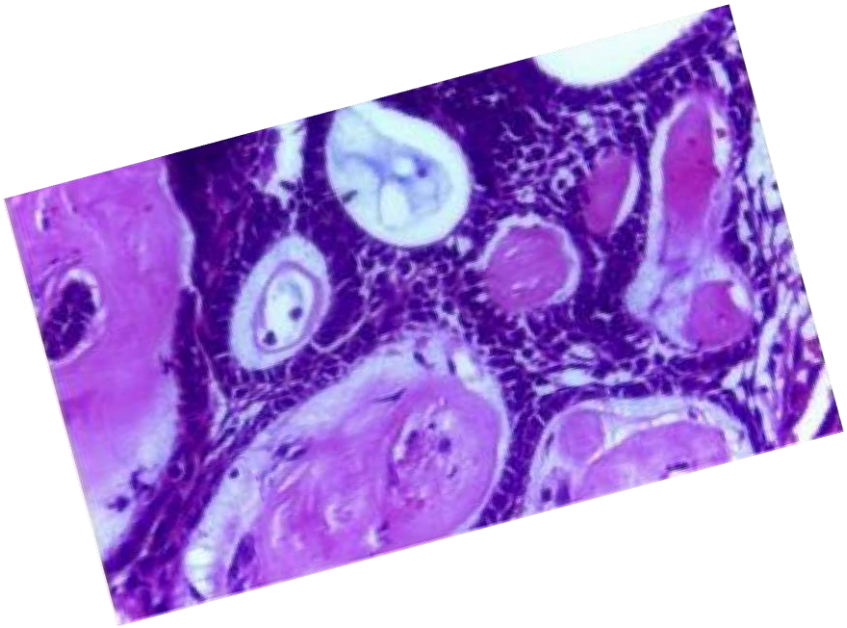
FOLLICULAR HISTOLOGICAL VARIANT

The follicular variant (Figure 1) is the most common histological pattern of ameloblastoma among the possible variations, representing 42.9% of all cases (DANDRIYAL *et al*., 2022). Histologically, it consists of nests or islands of neoplastic cells with a central loosening of short fusiform epithelial cells, resembling the stellate reticulum of the developing enamel organ, surrounded by columnar cells in a palisade arrangement with reversed nuclear polarity. These cells present hyperchromatic nuclei, indicating a high metabolic content (EVANGELOU *et al*., 2020).

Figure 1. Presentation of a conventional ameloblastoma follicular pattern slide, stained with hematoxylin and eosin (HE 200x), showing large cell nests with palisading cell layers and a central area of stellate reticulum.



Adapted from: BWAMBALE P., Yahaya JJ, Owor G, Wabinga H. Histopathological patterns and biological characteristics of ameloblastoma: A retrospective cross-sectional study. J Taibah Univ Med Sci. 2021.

PLEXIFORM HISTOLOGICAL VARIANT

The plexiform pattern (Figure 2) is the second most common subtype of conventional ameloblastoma, with an incidence of 30.2% according to Bwambale *et al.* (2021). In terms of its microscopic findings, most characteristics are similar to its “conventional” follicular variant (Figure 1), with the major differences being structural. It is represented by anastomosing cords arranged in a plexiform pattern, with loose centers and palisading basal cells embedded in a dense connective tissue stroma (JURADO-CASTAÑEDA *et al.*, 2022).

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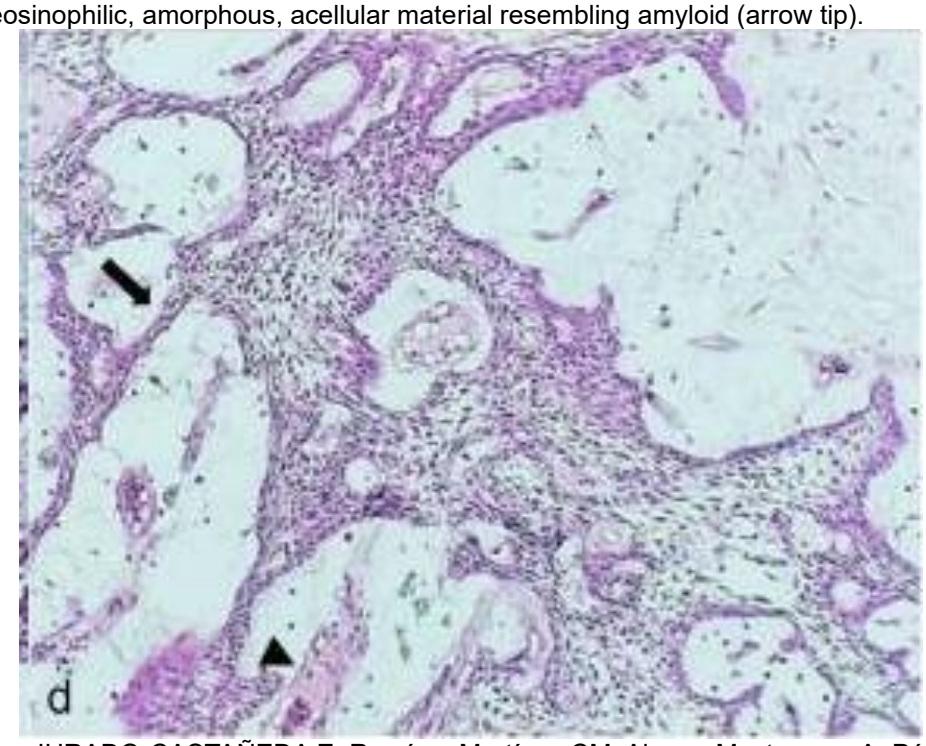
Figure 2. Presentation of a conventional ameloblastoma plexiform pattern slide, stained with hematoxylin and eosin (HE 200x), showing anastomosing cords (arrow) with cystic degeneration in a loose stroma, with the presence of eosinophilic, amorphous, acellular material resembling amyloid (arrow tip).



Adapted from: JURADO-CASTAÑEDA E, Ramírez-Martínez CM, Alonso-Moctezuma A, Páramo-Sánchez JT, Rivera-Reza DI, Chanes-Cuevas OA, Ortiz-Solís CL, Téliz-Meneses MA, Hernández-Ortega OR, Vizzuete-Bolaños MX, Olmedo-Bastidas P, Jacinto-Alemán LF. Conventional Ameloblastoma. A Case Report with Microarray and Bioinformatic Analysis. Diagnostics (Basel). 2022.

DESMOPLASTIC HISTOLOGICAL VARIANT

The desmoplastic ameloblastoma (Figure 3) is a rare variant that accounts for approximately 4-13% of ameloblastomas (MANAK *et al.*, 2024). It is one of the variants with a high degree of hyalinization and increased tumor progression due to the presence of myofibromas in its stroma (AUGUSTINE *et al.*, 2022). This variant also has an unusual location for ameloblastomas, which typically have a predilection for the mandible (93.1%) (VILA; OSTER; JAMES, 2024), but this pattern is most often found in the maxilla (EVANGELOU *et al.*, 2020). Histologically, it shows epithelial islands surrounded by a dense connective tissue stroma, resembling odontogenic epithelium, consisting of cuboidal cells arranged peripherally to some columnar cells with hyperchromatic nuclei, and centrally placed squamous cells. The surrounding stroma is moderately cellular with abundant thick collagen fibers compressing the odontogenic islands. The stroma's periphery consists of metaplastic bone with active osteoblast borders (MANIKANDAN *et al.*, 2023).

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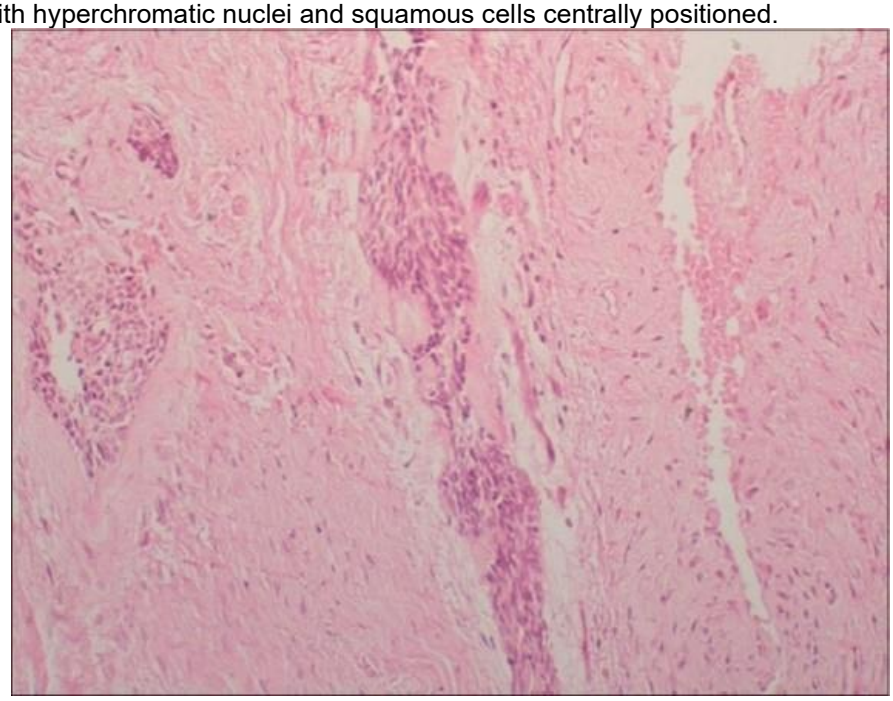
Figure 3. Presentation of a conventional desmoplastic ameloblastoma slide, stained with hematoxylin and eosin (HE 200x), showing odontogenic epithelium with cuboidal cells arranged peripherally around a few columnar cells with hyperchromatic nuclei and squamous cells centrally positioned.

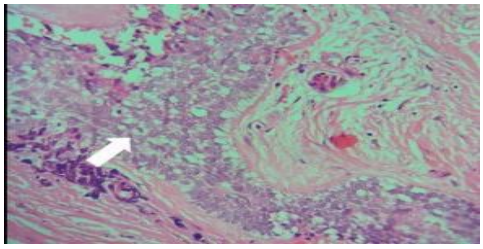


Adapted from: MANIKANDAN S, Vijayakumar G, Parthiban B, Kumarasamy B. Desmoplastic Ameloblastoma-A Case Report. J Pharm Bioallied Sci. 2023

ACANTHOMATOUS HISTOLOGICAL VARIANT

The acanthomatous variant (Figure 4) is also a rare variant, described in only 7.7% of cases in the literature (DANDRIYAL *et al.*, 2022). Histologically, the described variant shows the standard characteristics found in both the follicular variation (figure 1) and the plexiform variation (figure 2), presenting islands or cords of odontogenic epithelium with loosely arranged cells within these structures and cells with inverted polarity at the peripheral portion. Its distinguishing feature is the presence of extensive squamous metaplasia, sometimes with the formation of corneal pearls, found within the islands of tumor cells (VILA; OSTER; JAMES, 2024).

Figure 4. Presentation of a conventional acanthomatous ameloblastoma slide, stained with hematoxylin and eosin (HE 40x), showing peripheral cells exhibiting differentiation similar to ameloblastic cells, with the presence of keratin pearls.



Adapted from: *Singh R, Shrestha S, Acharya P, Shrestha A. Peripheral Ameloblastoma of Acanthomatous Variant: A Case Report. JNMA J Nepal Med Assoc. 2022*.

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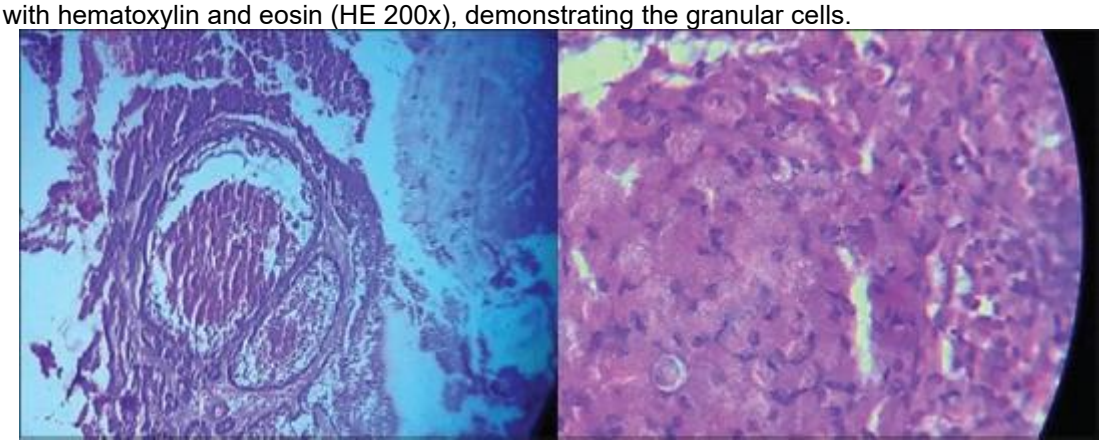
GRANULAR CELL VARIANT

The granular cell variant (Figure 5) is the most uncommon variation type, with an incidence of approximately 4% of cases (DANDRIYAL *et al.*, 2022). Although it exhibits biological behavior similar to other variants, this pattern has a higher recurrence rate (NIKITAKIS *et al.*, 2010). Histologically, granular cell ameloblastoma is characterized by the presence of granular cells, which typically occur in the central area of the tumor and progressively replace the stellate reticulum. Granular cells are oval to polyhedral in shape and tend to be large. The follicles may have a thin layer of stellate reticulum-like cells separating the granular cells from the peripheral columnar layer and the nucleus is displaced toward the periphery of the cells. Conspicuous coarse granules compact and distend the cytoplasm, showing a tendency to stain eosin, providing a remarkable manifestation. Occasionally, granular cell changes may also affect peripheral columnar cells (MATHEW, 2020).

Figure 5. Presentation of a histological slide of a conventional granular cell pattern ameloblastoma, (A) stained with hematoxylin and eosin (HE 40x), showing extensive cytoplasm with eosinophilic granules, (B) stained with hematoxylin and eosin (HE 200x), demonstrating the granular cells.



Adapted from: MATHEW A. A case report on granular cell ameloblastoma - A rare histological entity**. Indian J Radiol Imaging.** 2020 Apr-Jun;30(2):225-228.
Presentation of a histological slide of a conventional granular cell pattern ameloblastoma, (A) stained with hematoxylin and eosin (HE 40x), showing extensive cytoplasm with eosinophilic granules, (B) stained with hematoxylin and eosin (HE 200x), demonstrating the granular cells.

BASAL CELL HISTOLOGICAL VARIANT

Basal cell ameloblastoma (Figure 6) is the rarest variant, comprising only 2% of all histopathological variants of conventional ameloblastoma, with only 28 reported cases to date (KAUR; BHAT, 2020). Histopathologically, the tumor consists mainly of follicles and strands of basaloid cells. The peripheral cells exhibit hyperchromatic nuclei. The central cells of the islands of follicles lack stellate reticulum-like cells and instead contain only

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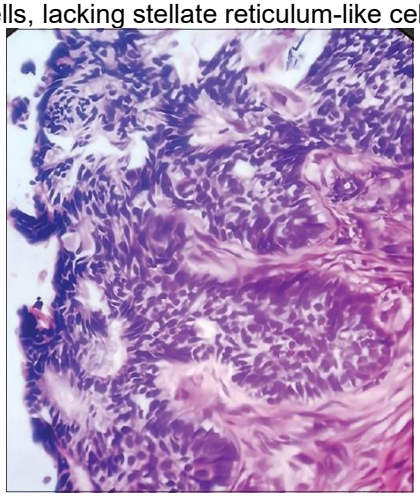
basaloid cells. Another distinguishing feature is the absence of a layer of columnar cells and palisaded nuclei, unlike other ameloblastoma variants. Some cases may show cystic degeneration. Nuclear alterations in the peripheral cells may also be observed (BUVA *et al.*, 2022). Histopathological knowledge of this lesion is crucial due to its differential diagnoses, which pose a higher risk, including intraoral cell carcinoma and basal cell adenoma (KAZAKYDASAN; ZAMHARI; ACHOL, 2019).

Figure 6. Presentation of a slide of conventional basal cell ameloblastoma, stained with hematoxylin and eosin (HE 10x), showing basaloid cells in a follicle without reverse nuclear polarity. The center of the follicle is filled with hyperchromatic basaloid cells, lacking stellate reticulum-like cells.



Adapted from: BUVA K, Deshmukh A, Kavle P, Gupta A. An unusual case report of basal cell ameloblastoma and a detailed review of literature. J Oral Maxillofac Pathol. 2022.

CONCLUSION

This study observed significant diversity in the histological presentations of conventional ameloblastoma, suggesting that these differences may influence both diagnosis and therapeutic strategies. Understanding these variants is crucial for the appropriate clinical management of patients, ensuring a more precise and targeted intervention. Therefore, it is concluded that conventional ameloblastoma comprises six histological variants, all occurring in bone tissue, each with distinct microscopic characteristics and varying degrees of aggressiveness. Consequently, knowledge of these variants is essential for an accurate histopathological diagnosis and appropriate treatment.

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ISSN: 2358-2472

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