Original Article

Revisiting Vickers and Gorlin criteria in histopathological subtypes of ameloblastoma

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Abstract

Background: Ameloblastoma is a benign tumour of odontogenic epithelial origin arising from enamel organ tissue that has not undergone differentiation to the point of hard tissue formation.

Aims: This study was conducted with an aim to provide a baseline data to analyse whether various histopathological variants of ameloblastoma satisfies all the characteristic histopathological features of Vickers and Gorlin criteria.

Settings and Design: A retrospective study of 25 cases of intraosseous ameloblastoma was carried out in the Department of Oral Pathology and Microbiology in accordance with the Institutional Ethics Committee.

Methods and Materials: Histopathological slides of ameloblastoma subtypes were analysed microscopically to assess Vickers and Gorlin criteria.

Statistical Analysis Used: Statistical analysis was done using the Chi-square test. A *P*- value of < 0.05 was set for statistical significance.

Results: Presence of hyperchromatic nuclei was seen in all the variants (100%), except for the desmoplastic variant which showed only 60% positivity. Basal cell palisading, reverse polarity and subnuclear vacuolization were seen predominantly only in acanthomatous (100%), and follicular variants (83%).

Conclusions: Vickers and Gorlin criteria have become an integral part of diagnosis of histopathological subtypes of ameloblastoma and should be applied vigilantly in the diagnosis as these may not always fulfill all the gold standard criteria when individual subtypes are assessed.

Keywords: Acanthomatous, ameloblastoma, desmoplastic, follicular, Vickers and Gorlin criteria

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Submitted: 19-Apr-2023, **Revised:** 19-May-2023, **Accepted:** 19-Jun-2023, **Published:** 12-Sep-2023

INTRODUCTION

Ameloblastoma is a benign tumour of odontogenic epithelial origin arising from enamel organ tissue that has not undergone differentiation to the point of hard tissue formation.[1] The term ameloblastoma is derived from the English word "Amel" which means enamel and" Blastos" which means "germs" in Greek. Ameloblastoma was first described in 1827 by Cusack. In 1884 and 1885, Malasezz gave the evidence of the lesion arising from odontogenic epithelial remnants and coined the term "Epithelioma Adamantin" for solid multicystic Ameloblastoma.[2] Ivey and Churchill in 1930 coined the term ameloblastoma, a

Access this article online

Quick Response Code:

Website: https://journals.lww.com/JPAT/

DOI: 10.4103/jomfp.jomfp_186_23

How to cite this article: Adyanthaya S, Begum S, Devasia J, Sasikumar R, Smitha T, Abdulla R. Revisiting Vickers and Gorlin criteria in histopathological subtypes of ameloblastoma. J Oral Maxillofac Pathol 2023;27:455-60.

currently accepted term.[3] The different sources considered for the pathogenesis of ameloblastoma are cell rests of enamel organ, cystic odontogenic epithelium, from the disturbances caused during the development of enamel organ, basal cell hamartias and heterotopic epithelium in the different parts of the body.[1]

Ameloblastomas account for about 1% of all oral tumours and about 9-11% of odontogenic tumours.[4] Ameloblastomas are locally aggressive and being able to reach large sizes if left untreated, causing facial disfiguration and functional problems.[5,6] The neoplasm can occur at any age group, but it has its peak incidence during the 3rd-4th decade of life with insignificant gender predilection.[5-7] Most common site for conventional ameloblastoma is mandibular molar-ascending ramus area (80%-85%) followed by 15%-20% in the maxillary posterior region.[8] Symptomatic cases show features of swelling, malocclusion, root resorption, pain and paresthesia of the affected region. Radiographically, it appears as a multilocular lesion having a resemblance to "honey coomb" or "soap bubble" appearance with the bucco-lingual expansion with thinning of the cortex.[9] In computed tomography, it shows features like the reduced thickness of bone, cortical plate destruction and local infiltration into surrounding areas.[1]

In 2005 WHO classification for head and neck tumours, the ameloblastoma had been categorized into (1) peripheral, which comprises an extraosseous tumour and shows continuity with the oral mucosal stratified squamous epithelium, (2) unicystic, comprises of single cystic intraosseous growth pattern (3) solid/multicystic, comprises of invasive tumour which permeates bone marrow spaces and may show multicystic foci (4) desmoplastic, comprising of an infiltrative intraosseous tumour dominated by the stromal component, radiographically reminiscent of a fibro-osseous lesion.[10] However, desmoplastic ameloblastoma was re-included only as a histological subtype in the 2017 WHO classification.[11] Histological variants of ameloblastoma include primarily follicular, plexiform, acanthomatous, granular, basaloid and desmoplastic ameloblastoma.[8]

The diagnostic criteria of Ameloblastoma were based on the Vickers and Gorlin (V and G) study using histopathological parameters in the year 1970. The criteria included hyperchromatism of basal cell nuclei, basal cell palisading with polarization which is referred to as reversal of polarity and cytoplasmic vacuolization with intercellular spacing of lining epithelium.[12] Future studies suggested that V and G criteria are indeed helpful for differential diagnosis, but not enough to establish the diagnosis of ameloblastomas in very incipient lesions.[13,14] Retrospective literature search revealed that no relevant studies were carried out to recognize the importance of V and G criteria in the histopathological diagnosis of ameloblastomas. This study was conducted with an aim to provide a baseline data to analyse whether various histopathological variants of ameloblastoma satisfies all the characteristic histopathological features of Vickers and Gorlin criteria.

MATERIALS AND METHODS

A total of 1152 retrospective lesions of the oral cavity and jaws were assessed and diagnosed between January 2014 and December 2019. Of these, 25 cases (2.17% %) satisfied the criteria to be included as intraosseous ameloblastoma taking into consideration both the clinical presentation as well as histopathology. The case history and biopsy report files and histopathological slides of these 25 cases were retrieved from the archives of the Department of Oral Pathology. The study has been conducted and reviewed by the Institutional review board (IRB). Two independent evaluators analysed the slides to avoid interobserver bias; in cases where there was disagreement a third evaluator was used and the result was established in consensus. The cases were evaluated for the presence of nuclear hyperchromatism, nuclear palisading with reverse polarization, and cytoplasmic vacuolization which are considered as the V and G criteria for the histopathological diagnosis of ameloblastoma. The data collected were statistically evaluated using the Chi-square test. A *P*- value of < 0.05 was considered for statistical significance.

RESULTS

In 25 cases of intraosseous ameloblastoma, histological variants included were plexiform 7 cases (28%), follicular 6 cases (24%), desmoplastic 5 cases (20%), granular cell 3 cases (12%), acanthomatous and basal cell ameloblastoma 2 cases (8%) each [Table 1].

Table 2 enlists the distribution of V and G criteria in histopathological subtypes of ameloblastoma. In

Table 1: Distribution of histopathological subtypes of ameloblastoma

Histopathological subtypes of amelolastoma	Number of cases
Plexiform Ameloblastoma	7 (28%)
Follicular Ameloblastoma	6 (24%)
Desmoplastic Ameloblastoma	5 (20%)
Granular cell Ameloblastoma	3 (12%)
Acanthomatous Ameloblastoma	2 (8%)
Basal cell Ameloblastoma	2 (8%)
Total number of cases	25 (100%)

Table 2: Evaluation of Vickers and Gorlin criteria in each histopathological subtypes of Ameloblastoma

Histopathological subtypes of ameloblastoma (*n*=25)	Hyperchromatic nuclei	Basal cell palisading	Reversal of polarity	Sub-nuclear vacuolization
Follicular ameloblastoma (*n*=6)	6 (100%)	5 (83%)	5 (83%)	5 (83%)
Plexiform ameloblastoma (*n*=7)	7 (100%)	3 (42%)	2 (28.5%)	1 (14%)
Acanthomatous ameloblastoma (*n*=2)	2 (100%)	2 (100%)	2 (100%)	2 (100%)
Granular cell ameloblastoma (*n*=3)	3 (100%)	3 (100%)	1 (33%)	0%
Basal cell ameloblastoma (*n*=2)	2 (100%)	1 (50%)	0%	0%
Desmoplastic ameloblastoma (*n*=5)	3 (60%)	0%	0%	0%
P=	0.1218	0.0271	0.0253	0.0041

follicular ameloblastoma, hyperchromatic nuclei of basal cells were observed in all the cases (100%), but basal cell palisading, reversal of polarity and subnuclear vacuolization was observed only in 83% of the cases respectively. Similarly, in plexiform ameloblastoma, hyperchromatic nuclei of basal cells were observed in all the cases (100%), but basal cell palisading, reversal of polarity and subnuclear vacuolization was demonstrated in 42%, 28.5% and 14% of the cases respectively. Interestingly, both the acanthomatous ameloblastoma cases studied showed all the standard microscopic features of V and G criteria (100%). Granular cell variant showed hyperchromatism and basal cell palisading in all the cases (100%), reversal of polarity in 33% of cases but did not exhibit subnuclear vacuolization in any of the cases. In basal cell variant, hyperchromatism of basal cell nucleus was observed in both the cases studied (100%), basal cell palisading was seen in only one case (50%) but did not exhibit reversal of polarity and subnuclear vacuolization in any of the cases. The desmoplastic variant did not fulfil the gold standard microscopic features of V and G criteria for basal cell palisading, reversal of polarity and subnuclear vacuolization except for the presence of hyperchromatism of basal cell nucleus (60%). The interesting findings to be noted in this study are that the presence of hyperchromatic nuclei was seen in all the variants (100%), except for the desmoplastic variant which showed only 60% positivity. Basal cell palisading, reverse polarity and subnuclear vacuolization were seen predominantly only in acanthomatous (100%), and follicular variants (83%). Statistical analysis showed no association between histopathological subtypes of ameloblastoma and the presence of hyperchromatic nuclei (Chi-square = 8.695, $P = 0.1218$). There was association between histopathological subtypes of ameloblastoma and presence of basal cell palisading (Chi-square = 12.631, $P = 0.0271$), histopathological subtypes of ameloblastoma and presence of reversal of polarity (Chi-square = 12.798, $P = 0.0253$), histopathological subtypes of ameloblastoma and presence of sub-nuclear vacuolization (Chi-square = 17.2313, $P = 0.0041$) respectively [Table 2].

Combinations of various histopathological features demonstrated by some of the cases of ameloblastoma variants [Figures 1-3] as analysed in Tables 1 and 2.

DISCUSSION

The incidence of ameloblastoma, combined with its clinical behaviour, makes it the most significant odontogenic neoplasm. Furthermore, the histomorphological diversity exhibited by the tumour and its possible clinical implications make it even more captivating.[15] The accurate histopathological diagnosis especially in the absence of classical pathological characteristics plays a pivotal role in the management of ameloblastoma. This study has attempted to understand the importance of V and G criteria in the diagnosis of histopathological subtypes of ameloblastoma.

The main histopathologic variants of solid ameloblastoma include follicular, plexiform, acanthomatous, basal cell, granular and desmoplastic ameloblastoma. Mixtures of different histological patterns are commonly observed and the lesions are frequently classified based on the predominant pattern present. The epithelial component of the neoplasm proliferates in the form of islands, cords and strands. The connective tissue stroma comprises moderate to densely arranged bundles of collagen fibres. A prominent budding growth pattern comprising small, rounded epithelial extensions projecting from larger islands, recapitulates the various stages of enamel organ formation.[9] The classical histological pattern of ameloblastoma described by Vickers and Gorlin is characterized by a peripheral layer of tall columnar cells with hyperchromasia, reverse polarity of the nuclei and sub-nuclear vacuole formation.[12]

Follicular type is composed of many small islands of peripheral layer of cuboidal or columnar cells with a reversely polarized nucleus. Cyst formation is relatively common in follicular type. Plexiform ameloblastoma is composed of anastomosing odontogenic epithelial islands with double rows of columnar cells in back-to-back arrangement. In acanthomatous type, the cells occupying

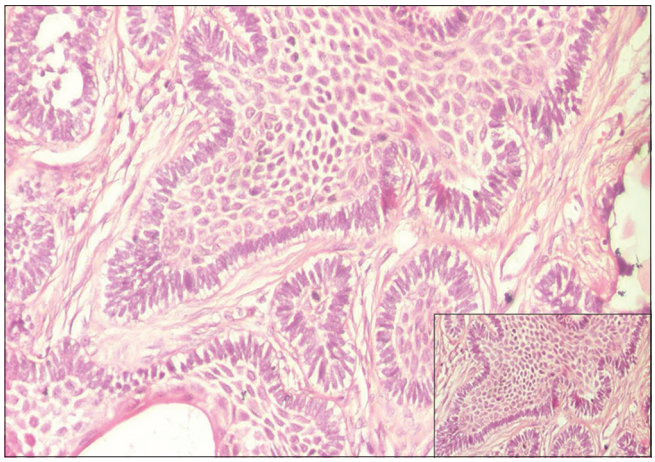

Figure 1: Photomicrograph of follicular ameloblastoma showing Vickers and Gorlin criteria.(H&E, × 40x) and inset showing tumour islands with hyperchromatic nuclei, basal cell palisading, reversal of polarity and subnuclear vacuolization

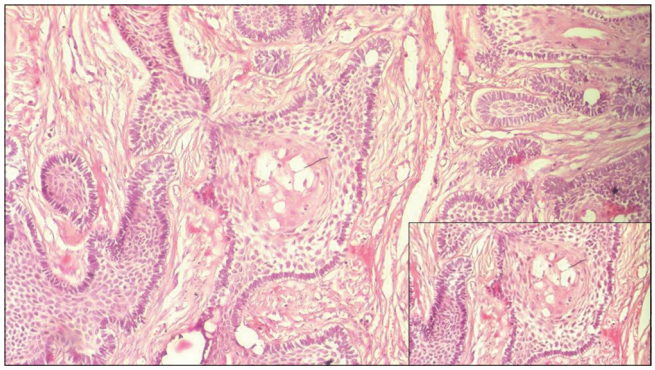

Figure 2: Photomicrograph of acanthomatous ameloblastoma showing Vickers and Gorlin criteria. (H&E × 40x) and inset showing tumour islands with hyperchromatic nuclei, basal cell palisading, reversal of polarity and subnuclear vacuolization

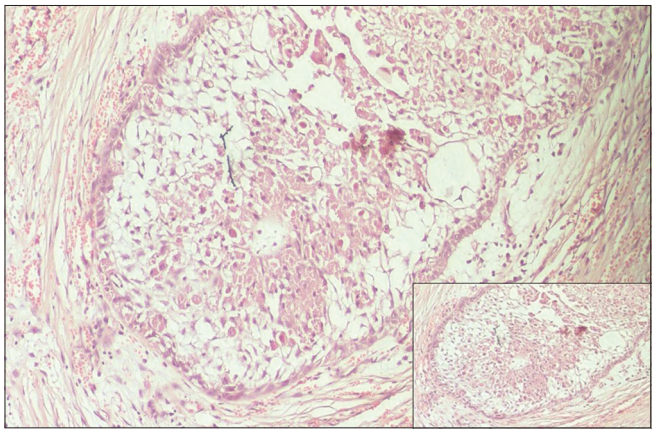

Figure 3: Photomicrograph of granular cell ameloblastoma showing only hyperchromatic nuclei and basal cell palisading (H&E × 40x) and inset showing tumour islands not exhibiting typical Vickers and Gorlin criteria

the position of stellate reticulum undergo squamous metaplasia in the center of tumour islands. In granular cell ameloblastoma, stellate reticulum-like cells comprise granular and eosinophilic cytoplasm. In basal cell type, the epithelial tumour cells are less columnar and arranged in sheets. The desmoplastic variant is composed of the dense collagen stroma, which appears hypocellular and hyalinized.[8]

Looking for the delineation of histopathologic features of early ameloblastoma, a classic work performed by Vickers and Gorlin gave birth to the so-called Vickers and Gorlin (V and G) criteria which are still largely utilized. V and G criteria state that nuclear hyperchromatism, nuclear palisading with reverse polarization, and cytoplasmic vacuolization with intercellular spacing constitute histopathologic evidence of neoplasia when observed together.[12]

Palisading is the term used to describe the orderly arrangement of epithelial cells with their long axes oriented at right angles to the basement membrane. Polarization is a term describing the apparent. movement of cell nuclei, especially nuclei of embryonic inner dental organ epithelium (preameloblasts).[12] In the original study done by Vickers and Gorlin, palisading and polarization were considered together but, in this study, we analysed these two features separately as in many of the cases these two features were not observed simultaneously.

In this retrospective study conducted on 25 cases of ameloblastoma revealed that histopathological subtypes are not exhibiting all the characteristic features described in V and G criteria when assessed individually. This is in accordance with the study performed by Gardner who drew attention to the fact that not all ameloblastomas exhibit classic V and G criteria.[13] It has also been observed that all the features required by V and G criteria to diagnose ameloblastoma may not be exhibited by peripheral ameloblastoma.[14]

The follicular ameloblastoma is the most prevalent histological variant followed by the plexiform ameloblastoma in the literature.[1,16] In this study, follicular ameloblastoma showed a majority of the features of V and G criteria which is consistent with studies in the literature.[1,16,17] Out of 6 cases, only 17% did not exhibit characteristic basal cell palisading, reversal of polarity and subnuclear vacuolization. In plexiform ameloblastoma, the cells are arranged in interconnecting strands and cords with cuboidal or columnar basal cells exhibiting hyperchromatic nuclei, nuclear palisading with polarization and central stellate reticulum-like cells.[18] A study by Gardner concluded that the V and G criteria, although valuable, are too rigid for establishing the diagnosis of plexiform ameloblastoma.[13] In the present study, plexiform ameloblastoma did not

show V and G criteria in the majority of the cases except for nuclear hyperchromatism which was present in all the cases. This may be because of double rows of columnar cells in back-to-back arrangement which translates the tall columnar basal cells into a more flattened morphology and nuclear palisading with reverse polarization and subnuclear vacuolization becomes inconspicuous.

In acanthomatous ameloblastoma, V and G criteria are observed in all the cases studied and the cells in the centre of tumour islands showed squamous metaplasia. Similar findings were reported in other studies in the literature.[8,16] In granular cell ameloblastoma, granular cells are seen usually in the central area with the marked transformation of stellate reticulum cells into granular eosinophilic cells, surrounded by tall columnar cells. Sometimes, they extend to include tall columnar and cuboidal cells.[19] In our study, the typical reversal of polarity and subnuclear vacuolization was not observed in the tumour islands where granular cells have extended to embrace the peripheral tall columnar cells.

Many of the case reports related to desmoplastic ameloblastoma have pointed out that the peripheral cells of tumour nests are usually rimmed by cuboidal cells and occasionally hyperchromatic. The morphologic characteristics typical of multicystic and unicystic ameloblastomas such as palisaded columnar cells demonstrating the reversed nuclear polarity are rarely conspicuous. Also, a central zone resembling stellate reticulum is encountered only occasionally. Instead, this area appears hypercellular and is composed of spindle-shaped or polygonal epithelial cells.[20-22] Similar features were observed in our study wherein basal cell palisading with reversal of polarity and subnuclear vacuolization was not observed in any of the cases studied. The characteristic histopathological features of ameloblastoma will be masked in desmoplastic ameloblastoma because of extensive stromal desmoplasia which constricts the typical ameloblastic follicles. In such cases, the identification of more typical ameloblastoma elsewhere in the specimen is important. The diagnosis will be made based on a few of the tumour nests showing stellate cells in the central area and columnar cells with nuclear polarity in the peripheral layers in some areas.

Very few cases of basal cell ameloblastoma have been reported in the literature. In these few cases, it has been observed that the typical cellular morphology and nuclear orientation of the peripheral cells as seen in other ameloblastomas are often altered. They appear as low columnar to cuboidal and usually do not exhibit reverse nuclear polarity with sub-nuclear vacuole formation. However, hyperchromatism and palisading of the nuclei normally are retained.[23,24] Our histological findings were in accordance with the described features and the reversal of polarity and subnucleolar vacuolization was not observed in both the cases studied.

The most prominent V and G criteria are predominantly seen in acanthomatous, granular followed by the desmoplastic variant of ameloblastoma. The most significant inference from our study was that, follicular ameloblastoma which was the most common histopathological variant was not accomplishing all the gold standard criteria of ameloblastoma when compared to relevant literature.

There are only minimal studies conducted on Vickers and Gorlin criteria for histopathological subtypes of ameloblastoma. Further studies should be conducted on a larger cohort using this baseline data to analyse the significance of V and G criteria as the gold standard in the diagnosis of histopathological subtypes of ameloblastoma.

CONCLUSION

Vickers and Gorlin criteria were originally illustrated to help diagnose early ameloblastomas in cysts and had not considered the histopathological subtypes of ameloblastoma. But over the years, Vickers and Gorlin's criteria have become an integral part of the diagnosis of histopathological subtypes of ameloblastoma. Vickers and Gorlin criteria can be useful when diagnosing the lesions where ameloblastoma is considered as the histopathological differential diagnosis. Vickers and Gorlin criteria should be applied vigilantly in the diagnosis as these may not always fulfil all the gold standard criteria when individual subtypes are assessed.

Financial support and sponsorship

This study is funded by the Yenepoya University seed grant (YU/SEED GRANT /100-2021), Yenepoya (Deemed to be) University.

Conflicts of interest

There are no conflicts of interest.

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