

Clinical, imaging, histopathological, immunohistochemical, and molecular profile of adenoid ameloblastoma: a scoping review

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Abstract:

Adenoid ameloblastoma is a rare odontogenic tumor with locally aggressive behavior, overlapping histologic features, and heterogeneous molecular findings. This study described its clinical, imaging, histopathological, immunohistochemical, and molecular profile through a PRISMA-ScR-based scoping review of case reports and series. A total of 109 patients were included, with male predominance and peak incidence between 20–50 years. The mandible was most affected. Swelling and prolonged symptom duration were common, with lesions >30 mm appearing as well-defined radiolucencies. Histologically, dentinoid material and duct-like structures predominated. β -catenin showed high positivity, whereas CTNNB1 mutations were variable, and BRAF V600E and KRAS alterations were infrequently detected. Treatment was heterogeneous, mainly surgical. Recurrence occurred in 57.14%, though most patients were disease-free at last follow-up. Despite supporting its recognition as a distinct entity, gaps in molecular data, reporting heterogeneity, and lack of standardized management limit clinical decision-making.

Keywords: Adenoid ameloblastoma; Odontogenic tumors; Immunohistochemistry; Molecular pathology; Scoping review.

INTRODUCTION

Adenoid ameloblastoma (AA) is a distinct tumor within the spectrum of odontogenic and maxillofacial bone tumors, recognized in the 2022 World Health Organization (WHO) classification of head and neck tumors¹. It is defined as a rare, benign, yet locally aggressive epithelial odontogenic tumor^{1–4}. It was initially described by Waldron in 1959, who contributed to delineating its distinctive morphological profile^{3,4}. Originally termed “dentinoameloblastoma” by Slabbert et al.^(apud 4), its current nomenclature derives from the term “adenoid ameloblastoma with dentinoid,” introduced by Brannon in 1994^(apud 4).

Clinically, AA typically presents as a slow-growing swelling, predominantly affecting the mandible, with a slight male predilection and a higher incidence in the fourth decade of life. Radiographically, it appears as a radiolucent lesion, generally unilocular and well defined^{1,2}, and may mimic other benign odontogenic entities.

AA is thought to arise from remnants of the dental lamina or enamel organ. Histologically, it shows ameloblastoma-like patterns with adenoid, duct-like, and

Statement of clinical significance

Adenoid ameloblastoma is a rare, locally aggressive odontogenic tumor with overlapping histologic features and heterogeneous molecular findings. Diagnosis requires clinicopathologic correlation, while treatment is variable, with recurrence risk underscoring the need for standardized management strategies.

cribriform structures, along with morules and dentinoid areas, forming a hybrid architecture^{1–4}. Immunohistochemically, it supports odontogenic epithelial differentiation, with variable, often focal expression of CK7, CK8, CK14, and CK18, and more diffuse positivity for CK19, p16, p40, and p53^{1,4}. Nuclear β -catenin indicates Wnt pathway activation, consistent with dentinogenesis and dentinoid formation, while Ki-67 is generally low, reflecting its biological behavior¹.

Molecularly, AA typically lacks BRAF (p.V600E) and KRAS (p.G12V, p.G12R) mutations seen in ameloblastoma and AOT^{1,4}. Instead, CTNNB1 exon 3 alterations have been reported, linking to Wnt activation and also seen in DGCT, though not in all cases, suggesting

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additional events such as APC mutations. FGFR2 and SMO mutations have also been described, but evidence remains limited and heterogeneous^{2,4}.

Despite its recognition by the WHO in 2022, AA has attracted increasing interest because many of its biological aspects remain poorly defined, posing diagnostic and therapeutic challenges. In this context, comprehensive characterization is essential to guide clinical management, particularly given its high recurrence rate and locally invasive behavior. However, the available evidence remains limited and heterogeneous. Therefore, the aim of the present study is to describe the clinical, imaging, histopathological, immunohistochemical, and molecular profile of adenoid ameloblastoma reported in the literature.

METHODS

This scoping review aimed to describe the clinical, imaging, histopathological, immunohistochemical, and molecular features of adenoid ameloblastoma, a recently recognized entity in the 2022 WHO classification, through analysis of published case reports and series in English. The study followed PRISMA-ScR guidelines. No formal risk-of-bias assessment was performed, and only descriptive analysis was conducted due to data heterogeneity, representing a study limitation.

Search strategy

This scoping review included studies published between January 1950 and January 2026, identified through searches in PubMed, Embase, BVS, Web of Science, and Scopus. The strategy combined MeSH terms and keywords such as “adenoid ameloblastoma,” “adenomatoid ameloblastoma,” and “dentinoameloblastoma.” The research question followed the PEO framework, focusing on clinical-radiographic, histopathological, immunohistochemical, and molecular features, as well as treatment and outcomes. Search strategies were managed in Rayyan[®] and are detailed in Supplementary Material 1.

Study selection

Study selection was performed using Rayyan[®]. After duplicate removal, studies were screened by title and abstract, followed by independent full-text assessment by two authors (CCTA and AFFM).

Inclusion criteria were:

1. Case reports or series with confirmed histopathological, clinical, and imaging diagnosis of adenoid ameloblastoma; and

2. Publications in English, without restrictions on sex, country, or race.

Exclusion criteria comprised conference abstracts, letters, in vitro, animal or cadaver studies, articles without full text, posters, and discussions. Disagreements were resolved by a third author (JPRM). Full-text screening involved CCTA, AFFM, and JPRM.

Data extraction

Included studies were fully reviewed for data extraction according to the research question. Variables included clinical and radiographic parameters (age, sex, tumor location, presentation, symptom duration, radiographic pattern, and lesion size), as well as treatment, follow-up, recurrence, and patient status. Histopathological, molecular, and immunohistochemical data were also collected.

Data were recorded in a Microsoft Excel[®] spreadsheet (Supplementary Material 2). Two authors (CCTA and AFFM), previously calibrated by a third (JPRM) through a pilot of five articles, independently performed extraction. Missing data were noted as “not reported.”

RESULTS

A total of 424 records were initially identified from PubMed, Scopus, Embase, BVS, and Web of Science, with an additional nine records identified through manual reference screening (Figure 1). In total, 38 articles were included for analysis (Supplementary Material 3), encompassing 109 patients; of these, 27 were case reports and 11 were case series. The findings presented here are based on descriptive synthesis and are not intended for causal inference.

Clinical and imaging characteristics

Sex

A total of 109 patients were included, of whom 75 were male (68.81%) and 34 were female (31.19%) (Table 1).

Age

Age was reported for 108 of the 109 patients. Distribution by age group showed that 11/108 patients (10.19%) were younger than 20 years, 61/108 (56.48%) were between 20 and 50 years, and 36/108 (33.33%) were older than 50 years (Table 1). The overall age range was 8 to 79 years. The mean age was 42.4 years, with a mean of 43.61 years in males and 41.32 years in females.

Location

Tumor location was reported in 107 of the 109 cases. Most lesions were located in the mandible (66/107; 61.68%). Among these, the affected region was not specified in 36/66 cases (54.55%), while 17/66 (25.76%) involved the posterior region, 11/66 (16.67%) the anterior region, and 2/66 (3.03%) showed extension involving both anterior and posterior regions.

In 41/107 cases (38.32%), lesions were located in the maxilla. Within this group, the posterior region was most frequently affected (18/41; 43.90%), followed by the anterior region (11/41; 26.83%), while in 14/41 (34.15%) the specific region was not reported. In 2 of the 109 cases (1.83%), the affected bone was not specified (Table 1).

Symptoms and duration

Clinical symptoms were reported in 44 of the 109 patients. The most common finding was swelling (36/44; 81.82%), followed by pain (11/44; 25%) and paresthesia (4/44; 9.09%). Less frequent findings included asymptomatic enlargement, mass, purulent discharge, mandibular deviation, and headache. In 65/109 cases (59.63%), this information was not reported (Table 1).

Symptom duration was reported in 41/109 cases (37.61%), ranging from 0.5 to 168 months. Most cases had a duration longer than 12 months (22/41; 53.16%) (Table 1).

Size

Lesion size was reported in 37 of the 109 cases. The greatest dimension ranged from 10 to 140 mm. Among cases with available data, most lesions were larger than 30 mm (28/37; 75.68%). This variable was not specified in 72/109 cases (66.06%) (Table 1).

Radiographic pattern

Radiographic characteristics were reported in 25 of the 109 cases (22.94%), while in 84/109 (77.06%) they were not specified. Among cases with available data, most lesions were radiolucent (21/25; 84.00%), followed by mixed-density lesions (3/25; 12.00%); no purely radiopaque lesions were reported. In 4/25 cases (16.00%), lesion density was not specified.

Regarding lesion margins, 16/25 (64.00%) were well defined and 3/25 (12.00%) were poorly defined. In terms of internal architecture, 9/25 (36.00%) were unilocular and 5/25 (20.00%) multilocular. Absence of bone involvement was reported in one case. These categories were not mutually exclusive (Table 1).

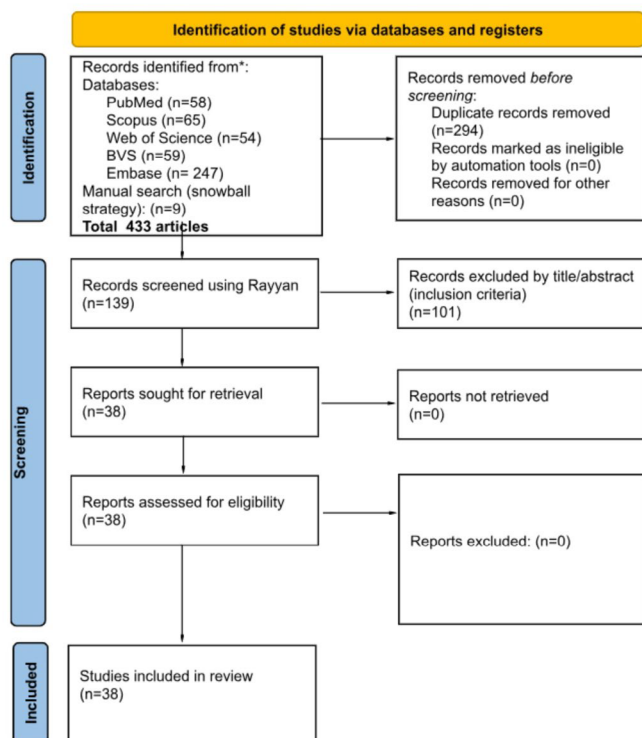
Histopathological characteristics

Histopathological findings were reported in 94 of the 109 cases. Dentinoid material was the most frequent finding (66/94; 70.21%), followed by duct-like structures (51/94; 54.25%), clear cells (40/94; 42.55%), and morules (40/94; 42.55%). Other findings, such as ghost cells (36/94; 38.29%), cribriform pattern (33/94; 35.10%), and ameloblastoma-like components (26/94; 27.65%), were observed with moderate frequency. These categories were not mutually exclusive. In 15 cases (13.76%), detailed histopathological features were not reported (Table 1, Figure 2A).

Immunohistochemistry

The use of immunohistochemical markers was reported in 65 of the 109 cases. β -catenin was the most frequently evaluated marker (43/65), showing positivity in 93.02% (40/43) of cases. CK19 was assessed in 20/65 cases, with 16 positive results (80%), while CK14 was reported in 15 cases, with 13/15 showing positivity (86.67%).

Ki-67 expression was documented in 22/65 cases; in seven of these, the proliferative index was reported, ranging from 10 to 20%, while in one case it was less



Source: Authors' own elaboration.

Figure 1. PRISMA-ScR flowchart.

Table 1. Summary of clinical, radiographic, and histopathological findings from case reports and case series of adenoid ameloblastoma.

	n	%		n	%
Total, studies	38	100.00	Radiolucent	21	84.00
Case reports	27	71.05	Radiopaque	0	0.00
Case series	11	28.95	Mixed	3	12.00
Total, patients	109	100.00	Not specified	4	16.00
Sex	109	100.00	No bony involvement	1	4.00
Male	75	68.81	Margins		
Female	34	31.19	Well defined	16	64.00
Not mentioned	0	0.00	Ill defined	3	12.00
Age (years)	108	99.08	Internal architecture		
<20	11	10.19	Unilocular	9	36.00
20–50	61	56.48	Multilocular	5	20.00
>50	36	33.33	Not mentioned	84	77.06
Not mentioned	1	0.92	Effects on bone	17	15.60
Age mean	42.39		Expansion	12	70.59
Location of tumor	107	98.17	Thinning	4	23.53
Maxilla	41	38.32	Erosion	8	47.06
Anterior	6	14.63	Soft tissue involvement	2	11.76
Posterior	18	43.90	Not mentioned	92	84.40
Anterior and posterior	3	7.32	Root resorption	8	7.34
Not specified	14	34.15	Yes	7	87.50
Mandible	66	61.68	No	1	12.50
Anterior	11	16.67	Not mentioned	101	92.66
Posterior	17	25.76	Histopathological features	94	86.24
Anterior and posterior	2	3.03	Clear cells	40	42.55
Not specified	36	54.55	Ghost cells	36	38.30
Not mentioned	2	1.83	Dentinoid material	66	70.21
Symptoms	44	40.37	Duct-like structures	51	54.26
Swelling	36	81.82	Cribriform pattern	33	35.11
Asymptomatic swelling	4	9.09	Morules/whorls	40	42.55
Mass	2	4.55	Ameloblastoma-like component	26	27.66
Pain	11	25.00	Stellate reticulum-like cells	17	18.09
Asymptomatic	2	4.55	Reverse polarity	14	14.89
Paresthesia	4	9.09	Squamous metaplasia	5	5.32
Purulent discharge	1	2.27	Hyperchromatism	17	18.09
Headache	1	2.27	Mitoses	5	5.32
Mandibular deviation	1	2.27	Spindle cells	7	7.45
Not mentioned	65	59.63	Cystic degeneration	10	10.64
Evolution time (months)	41	37.61	Calcifications	6	6.38
12	2	4.88	Hyalinization	1	1.06
<12	17	41.46	Inflammation	5	5.32
>12	22	53.66	Necrosis	1	1.06
Not mentioned	68	62.39	Atypia	2	2.13
Tumor size (mm)	37	33.94	Not mentioned	15	13.76
30	4	10.81	Follow-up (months)	41	37.61
<30	5	13.51	<12	6	14.63
>30	28	75.68	>12	34	82.93
Not mentioned	72	66.06	Lost to follow-up	1	0.92
Radiographic pattern	25	22.94	Not mentioned	68	62.39

Source: Authors' own work.

than 2%. The BRAF V600E marker was rarely assessed, reported in only three cases, with positivity in one. These categories were not mutually exclusive (Table 2, Supplementary Material 4, Figure 2B–F).

Molecular profile

Molecular analysis was reported in 58 of the 109 cases. CTNNB1 was the most frequently evaluated gene (43/58; 74.14%), with mutations identified in approximately half of the cases, predominantly in exon 3 (e.g., p.Ser33Cys, p.Ser37Phe, p.Gly34Arg), while the remaining cases were wild-type.

BRAF was assessed in 39/58 cases, showing a low frequency of V600E mutations (3/39). KRAS alterations were rare, with most cases exhibiting wild-type status. Other mutations, including TP53, ERBB2, SMURF1, NEDD4L, KRT13, APC, and PIK3CA, were sporadically reported in 6/58 cases, without a consistent pattern. These categories were not mutually exclusive (Table 3, Supplementary Material 5).

Treatment

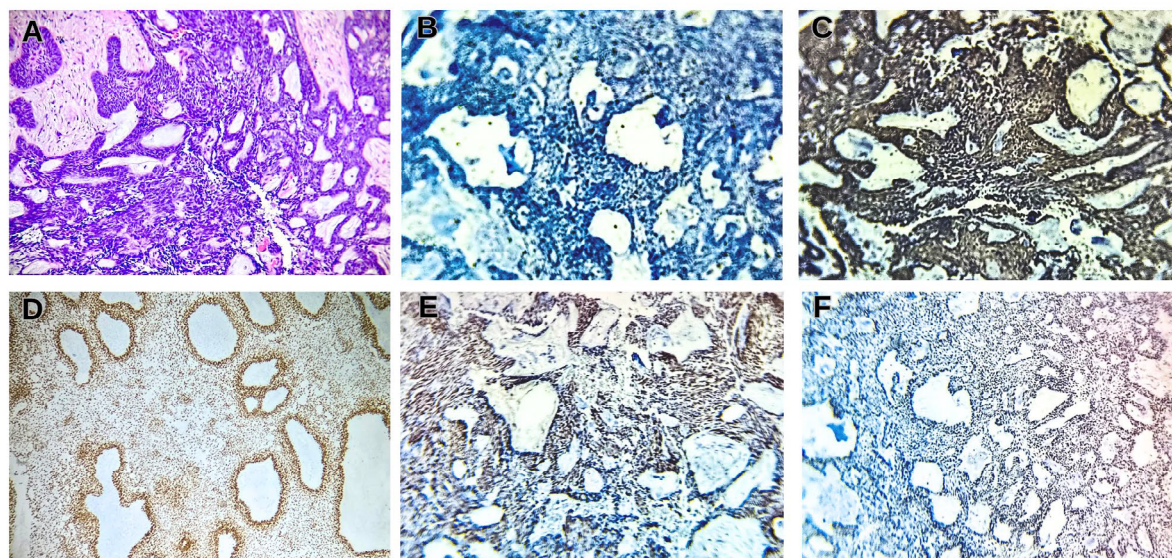
Treatment was reported in 50 of the 109 cases (45.87%), while in 59/109 (54.13%) this information was not available. Among cases with available data, there was marked heterogeneity in therapeutic approaches.

Table 2. Summary of immunohistochemical markers reported in the literature.

Immunohistochemical marker	Reactive (n)	%	Non reactive (n)	%
Betacatenin	40	93.02	3	6.98
BRAF V600E	1	33.33	2	66.67
CK14	13	86.67	2	13.33
CK19	16	80.00	4	20.00
Ki67	21	95.45	1	4.55
CK7	7	41.18	10	58.82
CK8	3	60.00	2	40.00
CK18	3	60.00	2	40.00
PanCK	1	100.00	0	0.00
P53	6	40.00	9	60.00
P63	4	100.00	0	0.00
P40	1	100.00	0	0.00
Calr	3	42.86	4	57.14
IMP3	0	0.00	8	100.00
CD56	0	0.00	2	100.00
SOX10	1	33.33	2	66.67
Pod	1	100.00	0	0.00

Abbreviations: β -catenin: Beta-catenin; BRAF V600E: B-Raf proto-oncogene V600E mutant protein; CK1: Cytokeratin 14; CK19: Cytokeratin 19; Ki-67: Ki-67 proliferation marker; CK7: Cytokeratin 7; CK8: Cytokeratin 8; CK18: Cytokeratin 18; PanCK: Pan-cytokeratin; p53: Tumor protein p53; p63: Tumor protein p63; p40: Δ Np63; Calr: Calreticulin; IMP3: Insulin-like growth factor 2 mRNA-binding protein 3; CD56: Neural cell adhesion molecule; SOX10: SRY-box transcription factor 10; Pod: Podoplanin.

Source: Authors' own work.



Source: Courtesy of Claudia Patricia Peña-Vega, DDS, Oral Pathologist, Private Practice.

Figure 2. (A) Hematoxylin and eosin, 10 $\times$. Cribriform architecture is observed with numerous prominent duct-like, pseudocystic spaces containing mucinous material and eosinophilic dentinoid deposits within the lumina. Focally, cellular areas resembling Homer Wright-type rosettes are identified. The stroma shows segmental fibro-hyalinized changes, partially lined by ameloblastoma-like epithelium, with focal hemorrhage. (B–F) Immunohistochemistry. (B) CK14 positive. (C) β -catenin (CTNNB1) positive. (D) p40 positive. (E) p16 positive. (F) BRAF V600E negative.

Conservative treatments included enucleation (4/50; 8.00%), curettage (6/50; 12.00%), excision (2/50; 4.00%), and marsupialization (1/50; 2.00%), collectively representing a minority of the approaches used. In some cases, these procedures were combined with adjuvant therapies, such as radiotherapy in one case treated with curettage, and peripheral ostectomy with Carnoy's solution in combination with enucleation in two cases.

Radical treatments, such as mandibular or maxillary resections of varying extent, were reported in 33/50 cases (66.00%). In 2/50 cases, surgical resection was combined with adjuvant radiotherapy and cervical lymph node dissection (Table 4).

Recurrence

Recurrence was reported in 56 of the 109 cases. Among these, recurrence occurred in 33/56 cases (58.93%), while no recurrence was observed in 23/56 cases (41.07%). Two cases experienced recurrence twice, and one case presented with multiple recurrences. In 53/109 cases (48.62%), this variable was not reported.

Patient status at last follow-up was reported in 39 cases. No evidence of disease (NED) was observed in 35/39 cases (89.74%), while 4/39 patients (10.26%) were alive with disease (AWD). In 33/109 cases (30.28%), patient status was classified as unknown, and in 37/109 (33.94%) this information was not reported (Table 4).

DISCUSSION

The available evidence on adenoid ameloblastoma (AA) is primarily based on case reports and case series⁵⁻²⁹ (Supplementary Material 3), which entails a high risk of bias and limited inferential strength. This is largely due to inter-study heterogeneity, variability in diagnostic criteria, and the frequent absence of key data, all of which compromise comparability and the accuracy of histopathological, immunohistochemical, and molecular

records. Consequently, significant underreporting and the potential inclusion of misdiagnosed cases cannot be ruled out²⁻⁴, particularly given the histopathological overlap with other odontogenic tumors such as adenomatoid odontogenic tumor (AOT), dentinogenic ghost cell tumor (DGCT), ameloblastic carcinoma, odontogenic carcinoma with dentinoid, aggressive AOT, clear cell odontogenic carcinoma, and ghost cell odontogenic carcinoma⁴.

Table 4. Therapeutic strategies reported for adenoid ameloblastoma.

	n	%
Treatment	50	45.87
Curettage	6	12.00
Curettage+Radiotherapy	1	2.00
Enucleation	4	8.00
Enucleation+Peripheral ostectomy+Carnoy's solution	2	4.00
Marsupialization	1	2.00
Excision	2	4.00
Surgical resection	33	66.00
Surgical resection+Radiotherapy	1	2.00
Surgical resection+Radiotherapy+Neck dissection	1	2.00
Not mentioned	59	54.13
Recurrence	56	51.38
Yes	33	58.93
No	23	41.07
Not mentioned	53	48.62
Status at last follow-up	39	35.78
No evidence of disease	35	89.74
Alive with disease	4	10.26
Unknown	33	30.28
Not mentioned	37	33.94
Total patients	109	100

Source: Authors' own elaboration.

Table 3. Molecular profile reported in case reports and case series of adenoid ameloblastoma.

Molecular finding	No. of patients reported	%	Main findings
<i>CTNNB1</i>	43	74.14	Predominantly <i>wild-type</i> ; recurrent variants included <i>p.Ser33Cys</i> , <i>p.Gly34Arg</i> , <i>p.Ser37Phe</i> and <i>p.Leu31Leu</i>
<i>BRAF</i>	39	67.24	Mostly <i>wild-type</i> ; <i>BRAF V600E</i> was identified in a limited number of cases
<i>KRAS</i>	35	60.34	Predominantly <i>wild-type</i> ; <i>p.G12V</i> and <i>p.G12R</i> were reported in some cases
Other molecular alterations	6	10.34	Alterations involving <i>TP53</i> , <i>APC</i> , <i>ERBB2</i> , <i>PIK3CA</i> , <i>SMURF1</i> , <i>KRT13</i> and <i>NEDD4L</i>

Source: Authors' own elaboration.

Despite these limitations, the analyzed data suggest a relatively consistent clinical pattern characterized by male predominance, higher frequency in middle-aged individuals, preferential localization in the posterior mandible, and a prolonged clinical course — typically exceeding 12 months — often accompanied by swelling and pain, with infrequent neurological manifestations such as paresthesia². However, given the small sample size and descriptive nature of the evidence, generalizability remains limited.

Regarding imaging features, discrepancies across studies suggest heterogeneity in the radiographic presentation of this tumor. While some authors describe radiolucent lesions with poorly defined margins⁴, others report well-circumscribed borders², which may be explained by differences in tumor stage, imaging modality, or interpretative criteria. To date, only one case has been reported without bone involvement¹³. Similarly, variability between unilocular and multilocular patterns suggests a broader radiographic spectrum than previously recognized.

The locally aggressive behavior of AA, consistently observed across analyzed cases, is supported by findings such as cortical bone erosion and perforation². The presence of root resorption in adjacent teeth further supports this interpretation as an indirect indicator of increased biological activity and potential infiltrative capacity. However, this feature may also be explained by mechanical effects associated with tumor size — often exceeding 30 mm, consistent with prior reports² — which may increase pressure on dental structures and promote root resorption. These hypotheses have not been systematically evaluated, and current evidence is insufficient to establish causal relationships. In this context, radiographic analysis remains a valuable but primarily adjunctive tool; its isolated interpretation may lead to diagnostic inaccuracies, particularly in lesions with overlapping features. Therefore, integration of clinical, imaging, and histopathological findings remains essential for accurate diagnosis, especially in rare and insufficiently characterized entities.

AA is characterized by marked histopathological heterogeneity, which has contributed to the lack of uniform diagnostic criteria¹⁻⁴. Nevertheless, integration of the available evidence allows the identification of relatively consistent features. Deorah et al. describe the presence of an ameloblastoma-like component — displaying plexiform, follicular, or unicystic patterns, with predominance of the plexiform type — associated with duct-like structures and polygonal cells

arranged in whorls or rosettes reminiscent of AOT, along with frequent identification of dentinoid, ghost cells, and clear cells⁴. Similarly, Odell et al. propose as essential criteria the presence of an ameloblastoma-like component, duct-like structures, whorled (morular) formations, and cribriform architecture, while considering dentinoid, clear cells, and ghost cell-type keratinization as desirable but non-essential features³. Morais et al. report a high frequency of the plexiform pattern as the predominant morphology, along with nearly constant duct-like structures and spiral cellular condensations, accompanied by cribriform architecture and odontogenic epithelium resembling stellate reticulum; they also document variable presence of dentinoid and diverse cellular phenotypes, including clear cells, ghost cells, and multinucleated giant cells².

In this review, a high frequency of dentinoid material was observed, followed by duct-like structures, clear cells, and whorled formations, as well as ghost cells, cribriform pattern, and an ameloblastoma-like component. Systematizing these features may help reduce diagnostic variability and improve differentiation from other odontogenic neoplasms with overlapping characteristics, such as conventional ameloblastoma, AOT, or DGCT³.

Immunohistochemistry and molecular pathology remain underexplored; however, the available evidence supports odontogenic epithelial differentiation, with variable expression of CK7, CK8, CK14, and CK18 — generally with focal distribution — and more diffuse positivity for CK19, p16, p40, and p53^{1,4}. In this review, β -catenin was the most frequently evaluated marker^{5,10,12,13,18,25}, showing nuclear positivity in some cases, suggesting activation of the Wnt pathway. This is consistent with its role in odontogenesis and dentin formation and may explain the presence of dentinoid material in this entity⁴.

At the molecular level, canonical MAPK/ERK pathway alterations, such as the BRAF V600E mutation — widely described in conventional ameloblastoma — are absent in most AA cases^{6,9,14}, consistent with prior literature³. In this review, BRAF was predominantly wild-type (WT)^{10,25}. Only three BRAF-mutated cases were identified: two reported by Xue et al.¹⁰ (GTG>-GAG) and one by Noda et al.¹¹ (c.1799T>A), both corresponding to the p.V600E mutation^{10,11}. Similarly, KRAS mutations (p.G12V, p.G12R), commonly associated with AOT, were not identified^{6,14}, with WT status predominating^{10,11,25}.

In contrast, CTNNB1 findings show considerable variability, with a predominance of WT cases but

recurrent point mutations at key sites. Fonseca et al. report both WT cases and variants such as p.Ser33Cys, p.Gly34Arg, p.Ser37Phe, a synonymous mutation (p.Leu31Leu), and a truncating mutation (p.Gln68)⁵. Similarly, Bastos et al. identify recurrent mutations at codons 33, 34, and 37²⁵, suggesting potential mutational hotspots. Khalaj et al.⁹ and Xue et al.¹⁰ predominantly report WT cases, with isolated findings such as G34R^{9,10}, while Oh et al.¹² describe mostly WT profiles but report one frameshift variant (Y333fs)¹². Collectively, these findings suggest that although CTNNB1 mutations — particularly at codons 33, 34, and 37 — may play a role in AA pathogenesis, their presence is not consistent across all cases⁴, limiting their utility as definitive diagnostic markers and supporting the hypothesis of underlying molecular heterogeneity. Other isolated genetic alterations, including TP53 (p.Asp393Asn, p.P278S)^{5,12}, ERBB2 (p.Val782Ile)⁵, PIK3CA (p.His1048Tyr)⁵, APC (E789fs, Q1080*)¹², SMURF1 (L424fs)¹², KRT13 (Y281H, M239V)¹², and NEDD4L (N846fs)¹², were identified without a consistent molecular pattern.

Uncertainty surrounding multiple aspects of AA is particularly relevant for treatment planning. The analyzed cases show substantial variability in therapeutic strategies, with limited predominance of conservative approaches such as enucleation, curettage, local excision, and marsupialization. In some cases, these were combined with adjunctive measures such as peripheral ostectomy and application of Carnoy's solution^{6,7}, while one conservatively treated case included radiotherapy and was associated with multiple recurrences¹⁰. Conversely, radical approaches — including hemimandibulectomy, hemimaxillectomy, and segmental resections — were also employed, sometimes combined with radiotherapy with or without cervical dissection, with recurrence reported in these cases as well²⁹. Only one case reported two consecutive surgical interventions as the treatment strategy⁷.

Among the 56 cases (of 109 total) with follow-up data, 32 showed recurrence^{5,9,10,18,24–26,29}, suggesting a considerable recurrence rate. However, no bivariate analysis was performed in this review, precluding assessment of associations between treatment modality and recurrence risk. Furthermore, no clear definition of surgical margins was identified in the reviewed literature. Unlike conventional ameloblastoma, for which safety margins of 1–1.5 cm have been proposed³⁰, no such parameters have been established for AA. This lack of standardization may lead to both undertreatment — with increased

recurrence risk — and overtreatment, with implications for morbidity and quality of life. In this context, the limited understanding of AA's biological behavior and clinicopathological features remains a critical factor influencing not only diagnosis but also evidence-based clinical decision-making.

This review has several limitations, primarily related to the scarcity and quality of the available literature, which was characterized by a limited number of studies, small sample sizes, a predominance of case reports and case series, limited follow-up, and, in some instances, insufficient clinical, radiographic, histopathological, immunohistochemical, and molecular documentation. Considerable heterogeneity was also observed in clinical characteristics, diagnostic methods, immunohistochemical markers, and analytical techniques, which limited comparisons across studies and hindered the identification of consistent patterns. No major limitations were identified regarding the databases included in the search strategy; however, the restriction to English-language publications for practical reasons and variations in the terminology used to describe this entity may have resulted in the omission of potentially relevant studies. Finally, given the nature of the available evidence and the objectives of a scoping review, quantitative comparisons and statistical synthesis were not feasible; therefore, the findings should not be extrapolated or generalized. Future studies with larger sample sizes, longer follow-up, and standardized documentation are warranted. In particular, case reports should adhere to international reporting guidelines such as the CARE guidelines to promote more consistent characterization of the clinical, radiographic, histopathological, immunohistochemical, and molecular profile of this recently recognized entity, which is of increasing interest in oral and maxillofacial pathology.

CONCLUSION

Current evidence supports adenoid ameloblastoma as a distinct entity; however, limited molecular and immunohistochemical data weaken diagnostic criteria and expose inconsistencies. Case heterogeneity and poorly defined clinicopathological and therapeutic correlations create gaps that affect clinical decision-making. Thus, current literature is insufficient for a standardized approach. This review, the largest to date, provides a foundation for future robust studies to better define its behavior and guide management.

AUTHORS' CONTRIBUTIONS

CCTA: Data curation, Investigation, Writing – original draft. CPPV: Conceptualization, Supervision. AFFM: Data curation, Investigation, Writing – original draft. JPRM: Data curation, Investigation, Writing – original draft, Writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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