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Ameloblastic fibroma: a series of 10 cases from South America

Abstract:

Objective: Ameloblastic fibroma (AF) is a rare odontogenic tumor composed of ectomesenchymal tissue and epithelial components, without the formation of dental hard tissues. Despite its recognition, data on AF from South America remain limited. This study describes a series of 10 AF cases from Venezuela and Colombia. **Methods:** Clinicopathological data, radiographic characteristics, and treatment modalities were analyzed descriptively. **Results:** The series comprised seven (70%) female and three (30%) male patients, with a mean age of 12.9 years. Lesions were predominantly located in the posterior mandible (80%). Radiographic findings revealed radiolucent lesions associated with bone expansion and involvement of adjacent teeth. Treatment modalities included mandibular resection and hemimandibulectomy, accounting for 66.6% of cases. Recurrence was observed in one case (16.7%). **Conclusion:** This study provides novel data on AF in South America, particularly in pediatric patients, and highlights the need for long-term surveillance and optimized treatment strategies due to the potential for recurrence.

Keywords: Jaws; Odontogenic tumors; Oral diagnosis; Oral medicine; Oral pathology.

INTRODUCTION

Ameloblastic fibroma (AF) is a rare odontogenic tumor composed of ectomesenchymal tissue resembling dental papilla, interspersed with epithelial strands and nests that mimic the dental lamina

and enamel organ, but without the formation of dental hard tissues¹. Since its initial description by Kruse in 1891², the nature and behavior of AF have remained subjects of ongoing debate and uncertainty. In the most recent World Health Organization (WHO) classification of odontogenic tumors and cysts of the

Statement of Clinical Significance

This study provides valuable contributions into ameloblastic fibroma in South America, highlighting its occurrence in pediatric patients and emphasizing the need for vigilant surveillance and tailored treatment strategies to mitigate the risk of recurrence.

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jaws, AF is categorized as a benign mixed epithelial and mesenchymal odontogenic tumor¹.

The global incidence of AF ranges from 0.6 to 16%³, with fewer than 300 well-documented cases reported in the literature⁴. AF typically manifests during the first two decades of life, with a mean age of 15.2 years, and predominantly affects males (58% of cases)⁴. Radiographically, AF is characterized by a unilocular radiolucent lesion with bone expansion, typically without cortical perforation, and most commonly involves the posterior region of the mandible⁴.

Reports on AF from South America are scarce and primarily consist of case reports^{5,6} or retrospective studies on odontogenic tumors^{7,8}, which provide limited clinicopathological, radiological, and treatment information. The purpose of the present study was to describe the clinicoradiographic features and management of a series of AF cases from Venezuela and Colombia as part of a collaborative South American effort.

MATERIAL AND METHODS

The present series comprised a convenience sample of 10 AF cases retrieved from the archives of two oral pathology and medicine services: Universidad Central de Venezuela in Caracas, Venezuela (n=7) and Universidad Nacional de Colombia in Bogotá, Colombia (n=3). The study was approved by the local research Ethics Committee (No. 18-23/57829), and Material Transfer Agreements were established to formalize the collaborative framework. Participants provided written informed consent in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants in accordance with the Declaration of Helsinki.

Clinicodemographic data, including sex, age, lesion duration (in months), anatomical location, symptoms (e.g., pain and swelling), radiographic features (e.g., radiolucent, mixed, or radiopaque; unilocular or multilocular), cortical bone alterations (e.g., expansion or perforation), association with a tooth (e.g., impaction, displacement, or root resorption), lesion size, treatment modalities, and recurrence (when available), were retrieved from patients' records.

A 4 µm-thick section was obtained from each paraffin block and stained with hematoxylin and eosin. The diagnosis was reviewed by at least one oral and maxillofacial pathologist from each service, following the 2022 WHO Classification of Odontogenic and Maxillofacial Bone Tumors (5th edition)⁹. Synchronous tumors and

hybrid odontogenic lesions were excluded from the study.

Data were tabulated using Microsoft Office Excel 2019 (Microsoft®, Redmond, WA, USA) and analyzed descriptively with GraphPad Prism version 8.0.0 for Windows (GraphPad Software, San Diego, CA, USA).

RESULTS

The series comprised seven (70%) female and three (30%) male patients, with a mean age at diagnosis of 12.9±6.8 years (range: eight months to 25 years). The lesions were predominantly located in the posterior mandible (80%), with one case (10%) in the parasymphysis and another in the anterior maxilla (10%), extending into the nasal fossae and infraorbital floor (Table 1).

Clinically, swelling was observed in five patients (71.4%), pain in one (14.3%), and two were asymptomatic (28.6%). Symptom information was unavailable for three cases. The duration of the lesions ranged from three days to 12 months, with a median of six months. Figures 1A and 1B illustrate the clinical features of a patient with AF (case #10).

Radiographic analysis revealed one case with well-defined borders and one with ill-defined borders. The predominant internal findings were radiolucent/hypodense densities (80%), followed by mixed densities (10%) and radiopaque lesions (10%). Multilocular structures were identified in 30% of cases. Cortical bone expansion was observed in seven cases (70%), while cortical perforation was identified in three (30%). Tooth involvement was present in nine cases (90%), including unerupted teeth (n=2), displaced teeth (n=2), and/or root resorption (n=2). Lesion sizes ranged from approximately 20 to 70 mm, with a median of 30 mm (Figures 1C; 2A-B; and 3A-D).

Grossly, AF appeared as a solid, encapsulated mass with a smooth outer surface (Figure 4A). Microscopically, its mesenchymal component was myxoid and cell-rich, resembling the dental papilla of a developing tooth bud. The odontogenic epithelial cords exhibited a bilayer of ameloblast-like cells with thickened, rounded edges, creating a drumstick-like appearance (Figures 4B-C). These epithelial structures were characterized by peripheral cells with hyperchromatic nuclei arranged in a palisading pattern.

Treatment consisted of mandibular resection in four cases (44.5%), surgical removal (excisional biopsy) in three cases (33.3%), and hemimandibulectomy in two cases (22.2%). In one case, the lesion recurred following initial curettage, necessitating subsequent mandibular

resection. Treatment modality information was unavailable for one patient. Outcomes data were available for six patients, of whom 83.3% showed no recurrence.

DISCUSSION

Based on previous systematic reviews^{3,4,10}, AF is recognized as an uncommon odontogenic tumor with variable prevalence across different geographic regions. Reported frequencies include 0.6% in Chile¹¹, 1.7% in Brazil⁷, 4.5% in Nigeria¹², 6.1% in the USA¹³, and up to 16% in Estonia¹⁴. These variations are likely influenced by a combination of genetic predisposition, environmental factors, and differences in diagnostic criteria

and practices¹⁵. Additionally, evolving classification systems for odontogenic tumors may contribute to the discrepancies observed in the literature¹⁶. However, the clinical features of AF in our sample are consistent with those previously described⁴, suggesting that geographic variation may not significantly influence its clinical presentation. As far as we know, this is the first collaborative case series from South America to provide data on AF.

AF predominantly affected children and adolescents, with a mean age of 12.9 years, consistent with the findings of Chrcanovic et al.⁴ and Buchner and Vered¹⁷. However, this contrasts with other reports indicating that 65% of cases occur within the first decade of life¹³ or that peak incidence is observed in the third decade¹⁸.

Table 1. Clinicodemographic, radiographic, and treatment characteristics of ameloblastic fibromas.

Case	Sex	Age	Evolution time	Anatomical location	Symptoms	Radiographic aspects	Size (mm)	Treatment	Recurrence
#1	F	14 years	NI	Right posterior mandible (body and ramus)	NI	Well-defined radiolucent lesion with multiple radiopaque foci, associated with unerupted and displaced teeth	NI	Surgical removal (excisional biopsy)	NI
#2	F	14 years	NI	Right posterior mandible (body and ramus)	NI	Radiopaque lesion with a radiolucent halo and cortical bone disruption, associated with an unerupted tooth	NI	Surgical removal (excisional biopsy)	NI
#3	M	8 months	3 days	Anterior superior alveolar border (premaxilla) extending to nasal fossae and infraorbital floor	No	Ill-defined, expansile hypodense lesion, associated with tooth displacement	27.4×13.7×17.6	Surgical removal (excisional biopsy)	NI
#4	F	25 years	12 months	Left mandibular body	No	Radiolucent lesion with expansion, associated with a tooth	20	Mandibular resection	No
#5	F	21 years	6 months	Left parasymphysis	Swelling	Multilocular radiolucent lesion with expansion, associated with a tooth	30	Curettage/mandibular resection (second procedure)	Yes
#6	M	15 years	NI	Posterior mandible	Swelling	Radiolucent lesion with expansion, associated with a tooth	25	Mandibular resection	No
#7	M	16 years	5 months	Posterior mandible	Swelling	Radiolucent lesion with expansion, associated with a tooth	30	Mandibular resection	No
#8	F	7 years	6 months	Posterior mandible	NI	Radiolucent lesion	NI	NI	NI
#9	F	8 years	12 months	Posterior mandible	Swelling and pain	Multilocular radiolucent lesion with expansion and cortical perforation; root resorption present	50	Hemimandibulectomy	No
#10	F	8 years	3 months	Posterior mandible	Swelling	Multilocular radiolucent lesion with expansion and cortical perforation; root resorption present	70	Hemimandibulectomy	No

F: female; M: male; NI: not informed.

Among pediatric odontogenic tumors, AF has been reported at a frequency of 3.2%¹⁹. Interestingly, our series included an 8-month-old patient. This is similar to a previously documented case of an 11-month-old male presenting with an expansive maxillary lesion involving the maxillary sinus and displacing the floor of the orbit²⁰. Moreover, two patients in our study were over 21 years old, which is unusual given that this age is well beyond the typical period of odontogenesis¹⁸. Females comprised 70% of our study population, in contrast to the 42% female prevalence reported elsewhere⁴. The reasons for this sex discrepancy remain unclear and may not be biologically significant, as suggested by a study from China¹⁸.

In the present study, the posterior mandible was affected in 80% of cases, consistent with previous

reports⁴. The tumors typically manifested as slow-growing, painless masses, with 80% appearing radiolucent and nearly the same proportion causing bone expansion⁴. Tooth involvement was noted in 90% of cases, often in association with unerupted permanent teeth⁴. Root resorption and cortical perforation were uncommon, occurring in 8.1 and 5.2% of cases, respectively^{4,18}.

Although jawbone lesions are rare in the pediatric population, clinicians should be aware of the broad differential diagnosis¹⁹. For solitary unilocular lesions, the differential diagnosis includes dental follicle, calcifying odontogenic cyst (COC), dentigerous cyst (DC), odontogenic keratocyst (OK), adenomatoid odontogenic tumor (AOT), unicystic ameloblastoma (UA), and primordial odontogenic tumor (POT). A Brazilian multicenter study reported that children and



Figure 1. Clinical and radiographic features of an ameloblastic fibroma. (A) A large, non-tender swelling measuring approximately 70 mm in diameter is observed in the right cheek. (B) Intraoral examination reveals an extension of the swelling into the mandibular labial fold, accompanied by erythematous and yellowish-gray areas. The right first molar is displaced. (C) A lateral view of a three-dimensional reconstructed computed tomography image reveals a lesion involving the body, ramus, and angle of the right mandible. The lesion exhibits an ill-defined, scalloped border with mixed areas of hypodensity and hyperdensity, creating a "soap bubble" appearance. The alveolar crest is disrupted, with involvement of the distal root of the first molar and the tooth germ of the second molar.

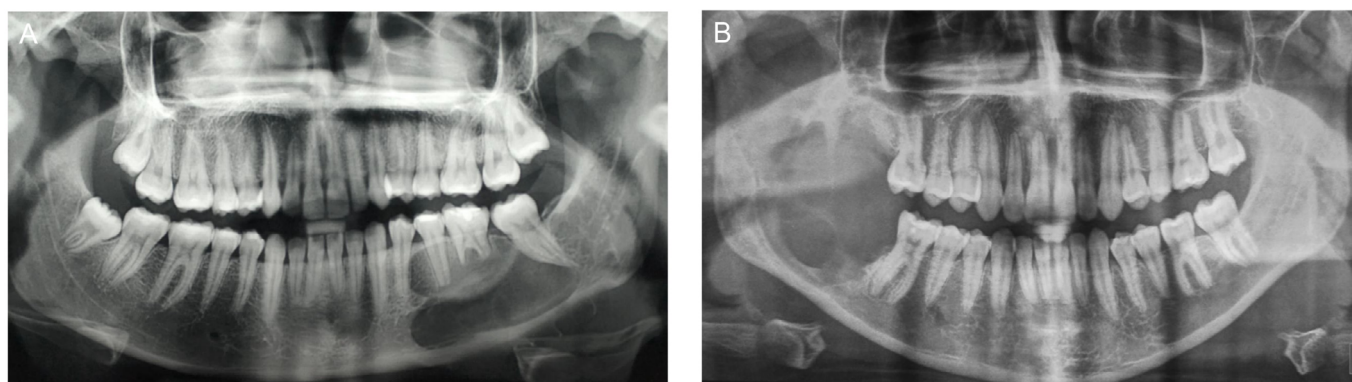


Figure 2. Radiographic features of an ameloblastic fibroma. (A) A panoramic radiograph reveals a multilocular lesion with an irregular shape, punched-out margins, and a radiolucent appearance. The lesion is located between the left premolars and molars, extending into the mandibular ramus. Root resorption of the second premolar and first molar, displacement of the second molar, and thinning of the cortical bone are observed. (B) A panoramic radiograph shows an ill-defined, multilocular radiolucent lesion with scalloped borders and cortical bone destruction, located near the distal region of the right first molar and extending into the mandibular ramus.

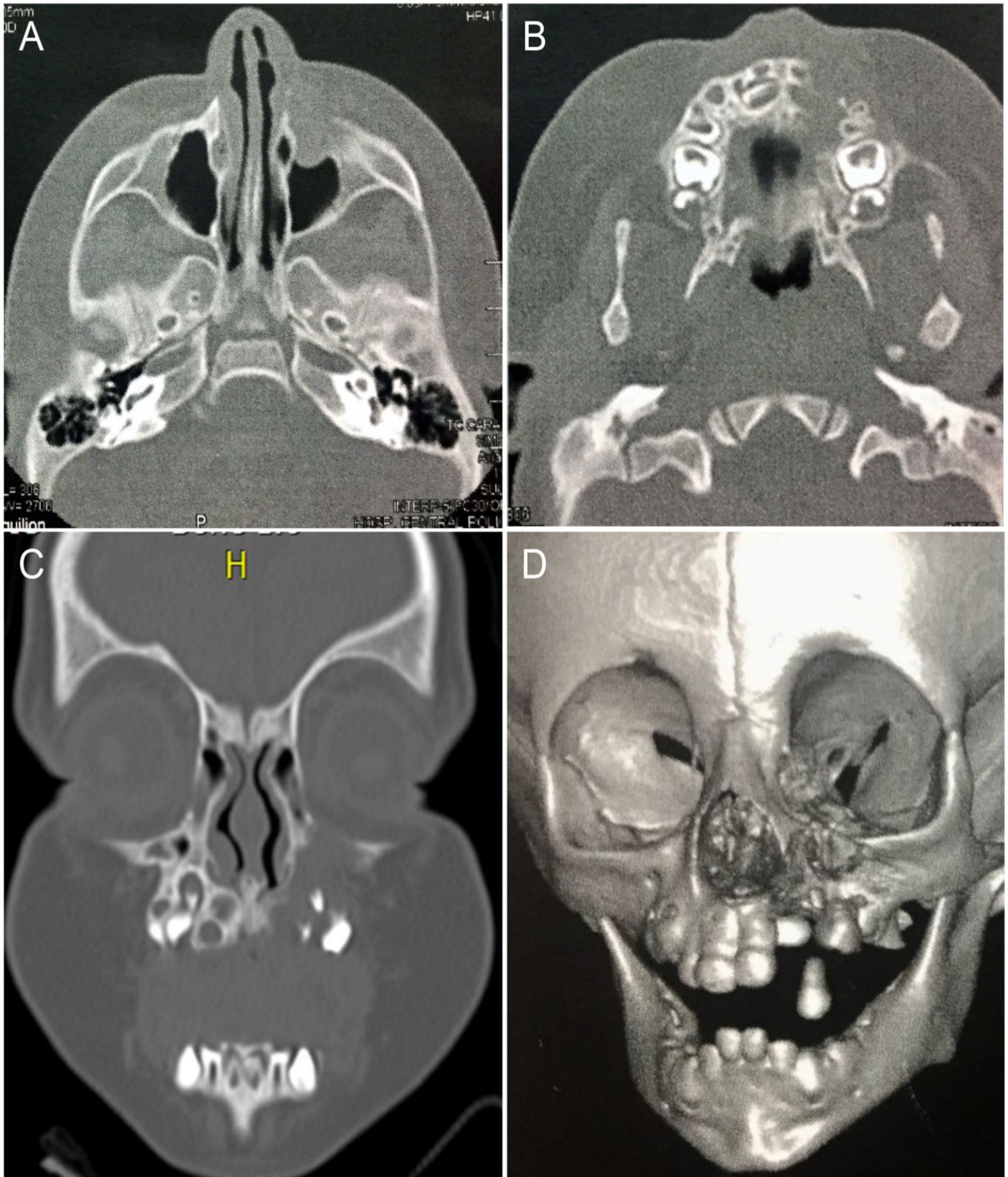


Figure 3. Imaging features of an ameloblastic fibroma. Computed tomography images show an intraosseous, multilocular, expansive hypodense lesion in the premaxilla and left maxillary region. The lesion is visible in the (A, B) axial view, (C) coronal view, and (D) three-dimensional reconstruction. It extends to the floor of the nasal fossae, partially obstructing the ipsilateral inferior meatus and affecting the left lateral nasal slope, but does not involve the infraorbital rim. Bulging of the vestibular and palatal cortices is observed without loss of continuity. The lesion measures 27.4×13.7×17.6 mm.

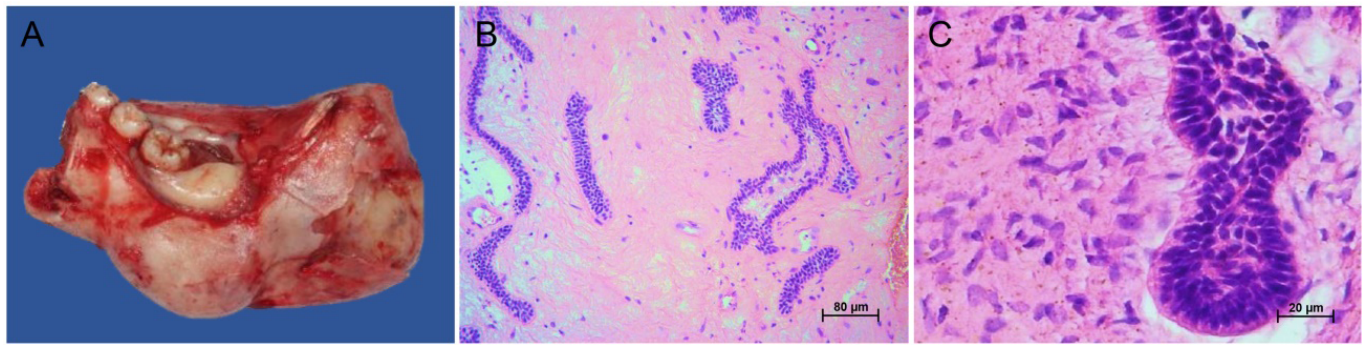


Figure 4. Macroscopic and histopathological features of an ameloblastic fibroma. (A) Gross specimen of a partial mandible showing irregular hard tissue with embedded teeth and areas of hemorrhage. (B) Cords of odontogenic epithelium exhibit a bilayer of ameloblastic-like cells with thickened, rounded edges, creating a drumstick-like appearance. (C) The epithelial component resembles the enamel organ, with peripheral cells exhibiting hyperchromatic nuclei arranged in a palisading pattern. These peripheral cells enclose a central core resembling the stellate reticulum, surrounded by cell-rich connective tissue (hematoxylin and eosin staining; original magnifications: 100× and 400×).

adolescents accounted for 35.1% of COC cases, with 40.7% occurring in the posterior mandible²¹, a pattern similar to that observed in AF. DCs represent 39% of odontogenic cysts in pediatric populations¹⁹ and have a 2.1% prevalence in impacted third molars²². OKs predominantly affect the posterior mandible in 77% of cases, with 22.6% diagnosed in the second decade of life, despite a mean age at diagnosis of 34.2 years²³. AOTs are more common in females during the second decade of life and are often asymptomatic. Unlike AF, these tumors are associated with impacted canines in nearly 70% of instances²⁴. Although UA is uncommon in children, it shares similarities with AF, as both primarily affect the mandible and often present as unilocular radiolucencies²⁵. POT is a rare mixed odontogenic tumor, with approximately 27 well-documented cases in the literature. It is more frequently reported in males (55%), with a mean patient age of 12 years, and typically presents as an asymptomatic swelling in the posterior mandible in 70% of cases²⁶. Notably, these features closely resemble those observed in AF cases.

For multilocular lesions, the differential diagnosis includes odontogenic myxoma, ameloblastoma, central giant cell granuloma (CGCG), and intraosseous hemangioma. CGCG is particularly relevant, as nearly 50% of cases occur in children and adolescents, with 70% diagnosed in the mandible²⁷. Radiographically, CGCG typically appears as a slow-growing, asymptomatic, well-defined radiolucency, occasionally associated with root resorption²⁷. These features align with the cases reported in this series. Regarding malignancies, although ameloblastic fibrosarcoma (AFS) primarily affects young adults, it is more frequently

observed as a multilocular radiolucency compared to AF (52.3% vs. 39.4%)⁴.

Histopathologically, AF is characterized by a cell-rich mesenchymal tissue resembling dental papilla, interspersed with strands or islands of proliferating odontogenic epithelium^{1,18,28}. The epithelial component resembles both the dental lamina and the follicular stage of the enamel organ, with mitotic figures being rare, consistent with the tumor's benign nature²⁸. While the 2005 WHO classification stated that AF lacks hard tissues such as enamel or dentin, the 2017 WHO classification acknowledges that AF may occasionally exhibit dental hard tissue formation²⁸. This reflects an evolving understanding of AF, with ameloblastic fibro-odontoma (AFO) and ameloblastic fibro-dentinoma (AFD) now recognized as lesions that may progress into odontomas rather than being distinct entities¹. Sánchez-Romero et al.²⁸ proposed that AFD and AFO should be more accurately classified as “developing odontomas” rather than as mixed odontogenic tumors, as previously categorized.

The molecular pathogenesis of AF remains only partially understood, although mutations in genes of the MAPK/ERK pathway have been identified in these tumors²⁹. The *BRAF* p.V600E mutation is present in 40% of AF cases, a frequency comparable to that observed in AFD and AFO but distinct from odontomas³⁰. This finding supports the notion that AF, AFD, and AFO may represent distinct neoplastic entities³⁰. However, the histological and molecular overlap raises uncertainty as to whether AFD and AFO are truly separate entities, intermediate lesions leading to odontoma formation, or a combination of developing odontomas and AF⁹.

Additionally, histopathological features observed in POT, such as odontogenic epithelium invaginations and subepithelial ectomesenchymal cell condensation, have prompted efforts to distinguish POT from AF and odontomas²⁶. The neoplastic potential of AF and its related entities is further supported by their biological behavior and potential for malignant transformation into odontogenic sarcomas. This is exemplified by approximately 103 documented cases of AFS, where over 50% had a prior history of AF, suggesting a stepwise process of malignant transformation⁴.

Conservative surgical removal is recommended for pediatric patients with AF, as the lesion may represent an early stage of a “developing odontoma”, often referred to as AFO¹⁸. However, Chrcanovic et al.⁴ emphasize that simple enucleation is associated with a high recurrence rate in AF. For individuals older than 20 years, more radical surgical approaches should be considered, particularly in cases of large tumors or multiple recurrences^{4,18}. In the current study, 44.4% of cases underwent mandibular resection, and 22.2% had hemimandibulectomy, with recurrence observed in 16.7% of cases. Chen et al.¹⁸ reported that four of 11 patients with AF (36.4%) experienced recurrence. Overall, evidence indicates that the recurrence rate for AF is 19.8%, with specific rates of 33.3% for curettage, 20.4% for enucleation, 22.2% for marginal resection, and 6.3% for segmental resection⁴. Nonetheless, while these findings suggest that more aggressive surgical management may reduce recurrence, direct comparisons are limited due to variations in follow-up duration and treatment protocols across studies. It is important to note that the available literature on AF is primarily based on single cases or small case series. Furthermore, the lack of long-term follow-up data is a drawback of this study. Long-term follow-up is essential for AF due to the potential risk of recurrence or malignant transformation into AFS^{4,18}.

CONCLUSION

This study presents novel data on 10 AF cases from two South American countries, primarily affecting female adolescents with a mean age of 12.9 years. The tumors were predominantly located in the posterior mandible. Radiographic findings were consistent with established patterns, typically presenting as expansive radiolucent lesions with involvement of adjacent teeth. Our findings suggest that radical surgical approaches are effective for managing AF in pediatric patients.

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AUTHORS' CONTRIBUTIONS

JAAA: Conceptualization, Methodology, Supervision, Validation, Writing – review & editing. JVLV: Data curation, Investigation, Writing – original draft. MEZB: Data curation, Investigation, Writing – original draft. MVD: Resources, Investigation, Writing – review & editing. CPPV: Resources, Investigation, Writing – review & editing. JPRM: Resources, Investigation, Writing – review & editing. ACVPS: Investigation, Writing – review & editing. ILC: Data curation, Investigation, Writing – original draft. IBV: Conceptualization, Methodology, Supervision, Writing – review & editing. ESSA: Conceptualization, Methodology, Supervision, Writing – review & editing. GCS: Conceptualization, Methodology, Supervision, Writing – review & editing. JRT: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. BABA: Conceptualization, Data curation, Formal analysis, Methodology, Supervision, Validation, Visualization, Writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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