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Ameloblastoma Differential Radiographic Findings in Children and Adolescents

Hallazgos Radiográficos Diferenciales de Ameloblastoma en Niños y Adolescentes

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ABSTRACT: The aim of this research was to investigate the radiographic, clinical, and histological features of cases of ameloblastoma from a period of 17 years in a Brazilian center and to explore potential differences in children and adolescents in relation to adults. Seventy-five patients diagnosed with ameloblastoma from 2001 to 2018 were included. Data from each patient including gender, age, histologic type, location, and radiographic characteristics were reviewed and analyzed retrospectively. The association between the clinical, radiographic, and histologic findings was investigated. No differences regarding the histological pattern of the lesions were observed between groups. Children and adolescents presented well-defined lesions associated with an unerupted tooth compared to adults ($p<0.05$). The presence of an unerupted tooth was associated with cortical erosion and expansion and MC displacement ($p<0.05$). Despite similar histologic characteristics, differential radiographic appearance was observed between young patients and adults.

KEY WORDS: ameloblastoma; dental radiography; histology; odontogenic tumors; jaws; adolescent.

INTRODUCTION

Ameloblastoma is a benign tumor of the jaws originated from odontogenic epithelium (El-Naggar *et al*., 2017). Clinically, it appears as a slow growing, locally invasive, asymptomatic lesion. Facial asymmetry, tooth displacement and mobility can also be present (Hendra *et al*., 2020). The majority of the lesions are located in the posterior region of the mandible (Agbaje *et al*., 2018; Hendra *et al*.). According to the current 2017 World Health Organization (WHO) classification of odontogenic tumors, four categories of ameloblastoma are considered: (a) classic intraosseous ameloblastoma presenting the follicular, plexiform, acanthomatous, granular, basaloid and/or desmoplastic histological types; (b) unicystic, which occurs as a single cystic cavity; (c) peripheral, occurring in the oral mucosa (extraosseous); and (d) metastasizing, which can present metastasis despite its benign histological appearance (El-Naggar *et al*.).

Incidence rate, sex predilection and patients' mean age varies among different study populations (Kim & Jang, 2001; Krishnapillai & Angadi, 2010; Saghravanian *et al*., 2016; Ruslin *et al*., 2018; Siriwardena *et al*., 2018). The pooled global incidence rate has been estimated to be 0.92 per million population per year. Male predominance has been reported in Africa, North America, and Asia. The majority of affected patients are adults with a peak of incidence in their fifth and the sixth decades in Europe and North America, between their third and sixth decades in Asia and in their third decade in South America (Hendra *et al*.). Occurrence in children and adolescents is considered uncommon (Avelar *et al*., 2011).

Radiographically, a unilocular or multilocular

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radiolucent lesion is observed. Cortical bone thinning, expansion and disruption and tooth resorption are often detected. Occasionally the lesion can also be associated with unerupted teeth (Kim & Jang; Krishnapillai & Angadi; Ariji *et al*., 2011). Previous research has shown that ameloblastoma differential radiographic appearance is related to differential biologic behavior and prognosis (Ueno *et al*.,1989; Li *et al*., 2012). Accurate radiographic examination of the lesion is indispensable for the treatment planning (Alves *et al*., 2018). Several studies have described clinical, histological, and radiographic data of ameloblastoma in different populations. However, few have analyzed those features in children and adolescents (Arotiba *et al*., 2005; Zhang *et al*., 2010). The purpose of this study was to investigate radiographic, clinical, and histological features of cases of ameloblastoma from a period of 17 years in a Brazilian center and to explore potential differences in children and adolescents compared to adults.

MATERIAL AND METHOD

This retrospective study was approved by the Human Research Ethics Committee of São Leopoldo Mandic Dental School and Research Center (protocol CAAE nº 61425116.4.0000.5374). All cases diagnosed from 2001 to 2018 at the department of Oral Pathology at same institution were screened and cases diagnosed as ameloblastoma with incisional or excisional biopsy were selected. Cases with incomplete clinical data, in which the radiographic image was not available, or image quality was not sufficient for analysis, and cases of lesion relapse were excluded from the sample.

In order to confirm the diagnosis, haematoxylin-eosin slides included in this research were revised by a pathologist. Samples were classified in accordance with the current 2017 World Health Organization (WHO) classification of odontogenic tumors as follicular, plexiform, acanthomatous, granular, basaloid, desmoplastic or unicystic (El-Naggar *et al*.). In cases where two or more histologic patterns were present, the predominant pattern was identified and considered for analysis. Clinical data including age at time of diagnosis, sex and symptomatology were collected.

Bidimensional radiographic images were analyzed by a radiologist unaware of clinical and histological data. Lesions' location (anterior or posterior maxilla or mandibulae), locularity (unilocular or multilocular), radiodensity (radiolucent or mixed), margins (well or ill defined), effect on adjacent cortical bone (resorption and expansion), effect on involved teeth (impaction, displacement or resorption) and involvement of mandibular condyle were evaluated.

Statistical Analysis. Statistical data were analyzed using SPSS 20.0 (SPSS, Chicago, IL, USA). Clinical, histopathological, and radiographic data are presented using descriptive statistics. Counts and percentages were used to summarize categorical data. Mean and standard deviation were calculated for patients' age. Cases were grouped according to patient's age: Group 1: age $\leq$ 18 years; and Group 2: age > 18 years. Clinical, histopathological, and radiographic variables were compared between both age groups using chi-square test (a=0.05). For data with less than five expected observations, associations between variables were tested using Fisher's exact test.

RESULTS

Clinical and Histopathologic Features. A total of 23,238 cases were diagnosed at the laboratory of Oral Pathology at São Leopoldo Mandic Dental School. One hundred and seventy-five cases of ameloblastoma were identified. After exclusion criteria consideration, 76 cases were included for radiographic evaluation.

Mean age at presentation was 31.37 $\pm$ 15.8. The male/female ratio was 1.1:1. A large number of the lesions (77.6 %) corresponded to conventional (solid) ameloblastoma. The unicystic subtype was present in 22.4 % of the cases. In cases of conventional ameloblastoma, more than one histologic type was present in 32 (54 %) cases and one single type in 27 (45 %). The predominant histologic pattern was considered for analyses (Fig. 1). Descriptive clinical and histopathologic data are presented in Table I.

Radiographic Features. Radiographically, the lesion's appearance was predominantly radiolucent, multilocular, well-defined images located in the posterior region of the mandible (Table II). Scalloping margins were present in 42.1 % of the lesions. Tooth displacement was observed in 43.4 % and resorption

Table I. Clinical and histopathologic characteristics.

		n (%)
Sex	Male	41 (53.2)
	Female	36 (46.8)
Age	≤18 years	17 (22.4)
	>18 years	59 (77.5)
Symptoms	Symptomatic	21 (27.6)
	Asymptomatic	43 (56.6)
	Not informed	12 (15.8)
Subtype	Conventional (solid)	59 (77.6)
	Unicystic	17 (22.4)
Histologic type	Follicular	16 (21.1)
	Acanthomatous	40 (52.6)
	Granular	2 (2.6)
	Basaloid	1 (1.3)
	Unicystic	17 (22.4)

in 53.9 % of the cases. In 31.6 % of the cases the lesion was associated with an unerupted tooth. In such cases, the inferior third molar was the most involved tooth (71.4 %).

Mandibular cortical (MC) narrowing and discontinuation were observed in 65.3 % and 23.6 % of the cases, respectively. In lesions located in the posterior mandible, MC canal displacement was present in 54.1 %, while MC discontinuation was present in 59 %. Radiographic features description is summarized in Table II.

No significant association was found between the lesion subtype (solid or unicystic) and clinical or

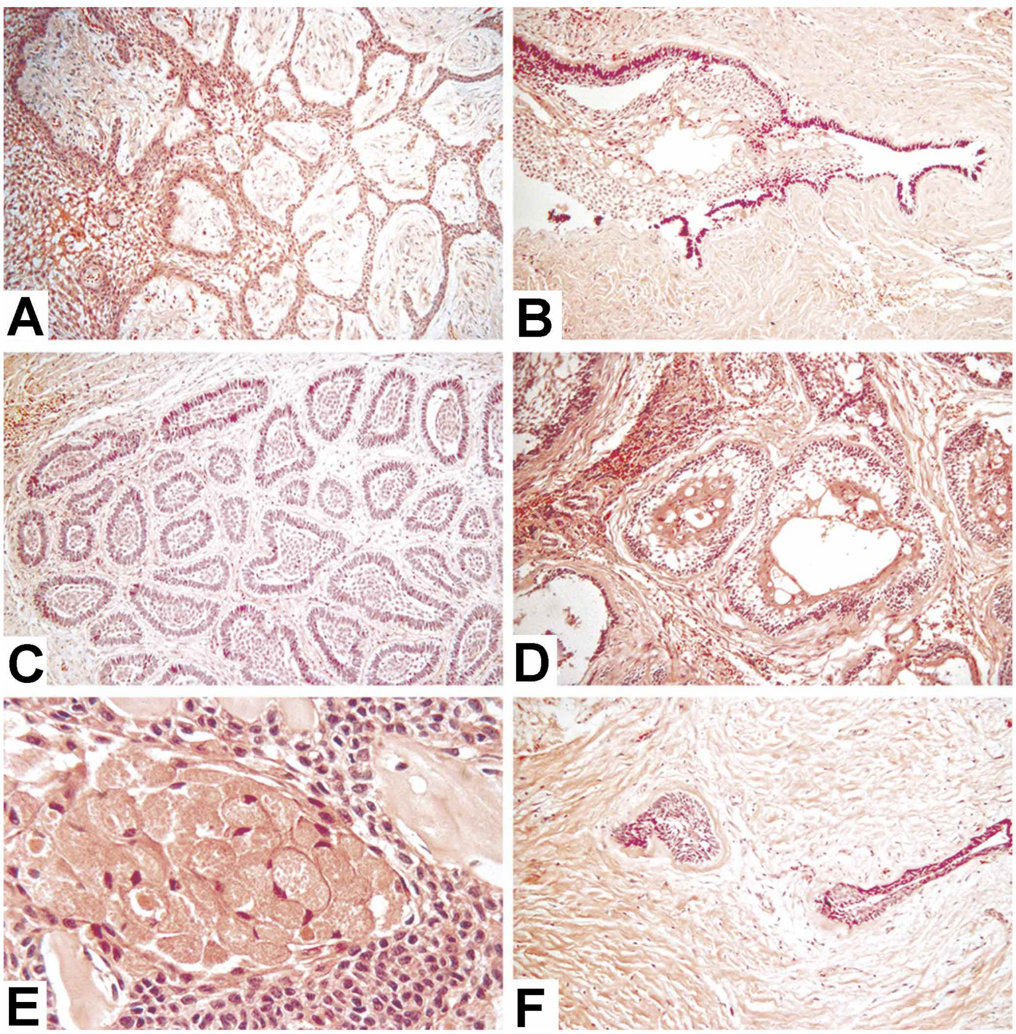

Fig. 1. Histological types of ameloblastoma tumor: A) plexiform; B) cystic; C) follicular; D) acanthomatous; E) granular cells; and F) desmoplastic. In all patterns, neoplasm is characterized by the proliferation of epithelial cells of odontogenic origin, which exhibit cylindrical morphology, arranged in a palisade and reverse polarization of the nucleus. HE (100x)

Table II. Lesion s radiographic appearance.

	Radiographic appearance	N (%)
Lesion density	Radiolucent	67(88.2)
	Mixed	9 (11.8)
	Radiopaque	0 (0.0)
Radiographic loculation	Unilocular	27 (35.5)
	Multilocular	48 (63.2)
Margins	Well-defined	60 (78.9)
	ill-defined	16 (21.1)
Surrounding sclerotic halo	Absent	41 (53.9)
	Present	35 (43.4)
Scalloping	Absent	44 (57.9)
	Present	32 (42.1)
Location	Maxillae	4 (5.2)
	Mandible	72 (94.8)
Relationship with adjacent teeth	No changes	21 (27.6)
	Displacement	15 (19.7)
	Resorption	26 (34.2)
	Displacement and Resorption	14 (18.4)
Unerupted tooth	Absent	54 (71.1)
	Present	22 (28.9)
Cortical bone expansion	Absent	41 (53.9)
	Present	35 (46.1)
Cortical bone discontinuation	Absent	56 (73.7)
	Present	20 (26.3)
Cortical narrowing	Absent	28 (36.8)
	Present	48 (63.2)
Mandibular cortical displacement*	Absent	35 (48.6)
	Present	37 (51.4)

*Considering cases involving the mandible n=72.

radiographical characteristics. In 12 (70.6 %) unicystic lesions, radiographic findings were consistent with a multilocular radiolucency. Unilocular radiolucency was observed in 22 (37.3 %) solid lesions.

Association between patients' age group, radiographic and histopathological features. Fifty-nine patients (77.6 %) were older than 18-years. Seventeen (22.4 %) patients were aged between 10 and 18 years. Clinical, histopathological, and radiographic data were compared between young patients (≤18 years old) and adults (>18 years old) (Table III).

The male/female radio was 0.88:1 in the young patients' group and 1.18:1 between adults. Symptomatology was reported in 35.6 % cases in the adult group and in none of the youngest group (p=0.01). Ill-defined margins were only observed in the adults' group (p=0.01), while in younger patients all lesions had well-defined appearance. Tooth displacement and lesion's association with unerupted teeth were more frequent in young patients (p<0.05; Fig. 2).

Differential radiographic pattern in lesions associated with unerupted teeth. Different radiographic characteristics were observed in lesions associated with an unerupted tooth (Table IV). Overall, these lesions were more frequently surrounded by a sclerotic halo and associated with tooth displacement and cortical expansion and narrowing. Condyle involvement was observed in two cases involving unerupted teeth. Considering the histologic pattern, no significant differences were observed between lesions associated or not with unerupted teeth (p>0.05). The samples were classified as conventional (solid) in 17 (77.3 %) of the lesions associated with unerupted teeth and in 42 (77.8 %) of the lesions not associated.

Displacement of the unerupted tooth associated with the lesion was present in 20 (90.9 %) cases. Super-inferior dislocation was more frequently observed (10; 50 %) followed by mesio-distal displacement (8; 40 %). In two cases (10 %) both supero-inferior and mesio-distal dislocation were observed.

Table III. Clinical, radiographic, and histopathological characteristics in young and adult patients.

		n (%)		*p*
		Age ≤18 y	Age >18 y	
Symptoms	Absent	14 (82.4)	29 (49.2)	0.01[a]
	Present	0	21 (35.6)	
	Not reported	3 (17.6)	9 (15.3)	
Subtype	Ameloblastoma (solid)	11 (64.7)	48 (81.4)	0.13[b]
	Unicystic	6 (35.3)	11 (18.6)	
Lesion density	Radiolucent	17 (100)	50 (84.7)	0.08[b]
	Mixed	0	9 (15.3)	
Radiographic loculation	Unilocular	9 (52.9)	18 (30.5)	0.08[a]
	Multilocular	8 (47.1)	41 (69.5)	
Margins	Well defined	17 (100)	43 (72.9)	0.01[b]
	ill defined	0	16 (27.1)	
Surrounding sclerotic halo	Absent	7 (41.2)	36 (61)	0.14[a]
	Present	10 (58.8)	23 (39)	
Scalloping	Absent	12 (70.6)	32 (54.2)	0.22[a]
	Present	5 (29.4)	27 (45.8)	
Tooth displacement	Absent	5 (29.4)	39 (66.1)	0.007[a]
	Present	12 (70.6)	20 (33.9)	
Tooth resorption	Absent	5 (29.4)	30 (79.7)	0.11[a]
	Present	12 (70.6)	29 (20.3)	
Unerupted tooth	Absent	6 (35.3)	48 (81.4)	<0.001[a]
	Present	11 (64.7)	11 (18.6)	
Cortical bone expansion	Absent	7 (41.2)	34 (57.6)	0.23[a]
	Present	10 (58.8)	25 (42.4)	
Cortical bone discontinuation	Absent	13 (76.5)	43 (72.9)	0.51[b]
	Present	4 (23.5)	16 (27.1)	
Cortical narrowing	Absent	4 (23.5)	24 (40.7)	0.19[a]
	Present	13 (76.5)	35 (59.3)	
Mandibular cortical displacement*	Absent	5 (29.4)	31 (52.5)	0.18[a]
	Present	12 (70.6)	27 (45.8)	

a chi-square; b Fisher's exact test. *Considering cases involving the mandible (n=72).

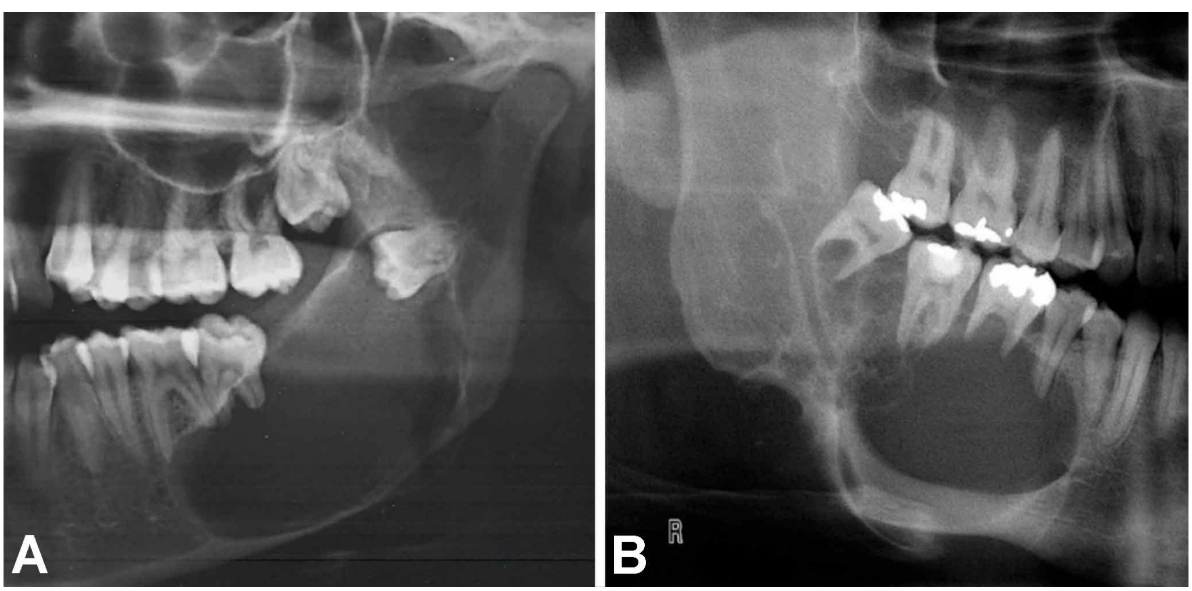

Fig. 2. A. Well-defined radiolucency associated with unerupted third molar in a 15-year-old female patient. Mesio-distal displacement of the involved tooth is observed. B. Multilocular radiolucency with ill-defined boundaries in the posterior region of the jaw in a 27-year-old male patient.

Table IV. Differential radiographic patterns between lesions associated or not with unerupted teeth.

		Unerupted tooth n (%)		*p*
		Absent	Present	
Surrounding sclerotic halo	Absent	35 (64.8)	8 (36.4)	0.02[a]
	Present	19 (35.2)	14 (63.6)	
Cortical bone expansion	Absent	34 (63.0)	7 (31.8)	0.01[a]
	Present	20 (37.0)	15 (68.2)	
Cortical narrowing	Absent	25 (46.3)	3 (13.6)	0.007[a]
	Present	29 (53.7)	19 (86.4)	
Mandibular cortical displacement *	Absent	29 (58.0)	5 (25.0)	0.01[a]
	Present	21 (42.0)	15 (75.0)	

a chi-square. * n= 70 (in one case located in the mandible it was not possible to evaluate the MC path).

DISCUSSION

Ameloblastoma mostly affects young adults and is rare in childhood and uncommon in adolescents (Agbaje *et al*.). However, considering patients in the first and second age of life it is the most common odontogenic tumor excluding odontoma (Servato *et al*., 2012; da Silva Barros *et al*., 2019). The aim of this study was to describe clinical, histological, and radiographic features of cases of ameloblastoma diagnosed during a period of 17 years in a Brazilian center and to analyze lesions' characteristics in children and adolescents in comparison to adults. In young patients, ameloblastoma presented mainly as an asymptomatic well-defined radiolucent image associated with an unerupted molar. Lesions associated with unerupted teeth both in young and adult patients were more frequently surrounded by a sclerotic halo and were associated with cortical narrowing and cortical and MC displacement. However, no significant differences were observed in histological features between groups.

Lesion radiographic appearance may be related both to lesion biological behavior and host particularities. Children present different jawbone architecture, with a greater percentage of bone marrow, increased cellularity, and active bone remodeling related to growth and tooth eruption. During adulthood, significative changes occur in bone marrow composition, with progressive increase in fat content and qualitative changes in cells (Ogawa *et al*., 2000; Prabhakar *et al*., 2009). Additionally, bone metabolism and physiology are also influenced by aging and hormonal changes during life (Hoffman *et al*., 2019). It is possible that the active process of bone remodeling in children contributes to the formation of a bone barrier around the lesion and to the erosion and expansion of mandibular cortical bone visualized in this research.

Ill-defined images were only observed in adults, contradicting Ogunsalu *et al*. (2006) that reported ill-defined lesions as the most common pattern in patients under the age of 20 years. Ameloblastoma boundaries may predict neoplastic biological behavior and patient prognosis. Li *et al*., (2011) have demonstrated that ill-defined boundaries are associated with higher cell proliferation and higher recurrence. Lesion boundaries in ill-delimited images probably lie beyond the apparent macroscopic surface and radiographic boundaries of the tumor, invading the intertrabecular space (Agbaje *et al*.). Conversely, the presence of surrounding cortical margins shows a host osteoblastic reaction to form an edge, meaning that the bone adjacent to the lesion may be normal and hence a less aggressive treatment is needed (Ogunsalu *et al*.). Individual careful radiographic evaluation is especially important while considering treatment options in young patients because of concerns for facial growth and potential deformity (Arotiba *et al*.).

It is not simple to explore ameloblastoma demographic similarities in children and adolescents since previous literature has defined the upper age limit differently, e.g., 16 years (Zhang *et al*.), 18 years (Olaitan & Adekeye, 1996) and less than 20 years (Ord *et al*., 2002; Ogunsalu *et al*.). In this research, equal gender distribution was observed, and all cases occurred in patients aged 10 years or older. Since many of the lesions were associated mainly with the third and second unerupted molars, peak incidence isexpected to coincide with the development of these teeth. Indeed, previous literature shows that only 10 % of the tumors in a pediatric population occurs in patients younger than 10 years old (Zhang *et al*.). However, it is important to point out that ameloblastoma is predominantly an asymptomatic lesion, which may delay diagnosis. Hence it is very likely that the age of a patient at tumor onset is younger than is clinically reported (Agbaje *et al*.).

Solid ameloblastoma was the most frequent subtype in both age groups. Similarly, to previous evidence (Zhang *et al*.; Bansal *et al*., 2015), it was not possible to differentiate histological unicystic and conventional (solid) types based only on the radiographic appearance. The majority of the unicystic lesions (70.6 %) presented a multilocular radiographic pattern and in 37.3 % of solid lesions a unilocular pattern was present. Conventional radiography remains the first choice for the initial evaluation of jawbone tumors. However, bidimensional images have limitations inherent to the technique, such as the image overlapping and distortion. Computed tomography may be indicated to provide more information for the diagnosis and treatment planning in cases of large lesions and in cases where the complexity of surrounding anatomical structures demands tridimensional evaluation (Oenning *et al*., 2018).

The limitations of this work should be pointed out. This investigation was based on a retrospective analysis of data acquired from our center's archives. Therefore, data of the treatment and follow-up could not be obtained. It was not possible to establish the relationship between patients' age, lesions' radiographic appearance and prognosis or recurrence. Further prospective investigations on this topic are encouraged.

In conclusion, in children and adolescents ameloblastoma presented a well-defined pattern and was most associated with an unerupted third molar, while ill-defined lesions were only observed in adults. These radiographic differences were not associated with the histological patterns. The role of host bone response in the radiographic presentation of odontogenic lesions should be further investigated.

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RESUMEN: El objetivo de este trabajo fue investigar las características radiográficas, clínicas e histológicas de casos de ameloblastoma en un período de 17 años, en un centro brasileño y explorar las posibles diferencias en niños y adolescentes en relación con los adultos. Se incluyeron 75 pacientes diagnosticados con ameloblastoma desde 2001 hasta 2018. Los datos de cada paciente, incluyendo el sexo, la edad, el tipo histológico, la ubicación y las características radiográficas, se revisaron y analizaron retrospectivamente. Se investigó la asociación entre los hallazgos clínicos, radiográficos e histológicos. No se observaron diferencias en cuanto al patrón histológico de las lesiones entre los grupos. Los niños y adolescentes presentaron lesiones bien definidas asociadas a un diente no erupcionado en comparación con los adultos (p<0,05). La presencia de un diente no erupcionado se asoció con erosión y expansión cortical y desplazamiento de MC (p<0,05). A pesar de las características histológicas similares, se observó una apariencia radiográfica diferente entre pacientes jóvenes y adultos.

PALABRAS CLAVE: ameloblastoma; radiografía dental; histología; tumores odontogénicos; mandíbulas; adolescente.

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