#### **ORIGINAL ARTICLE**

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Radicular cyst in primary dentition showing angiolymphoid hyperplasia with eosinophilia (ALHE)-like features: An immunohistochemical study

# Abstract:

The microscopical diagnosis of radicular cyst (RC) is straightforward; nonetheless, in some cases with unusual histopathological features, strict clinicopathological correlation is necessary to achieve the correct diagnosis. We report a case of a 5-year-old girl was referred presenting extensive carious lesion in the tooth #55, associated with vestibular sinus tract. Medical history revealed allergic asthma diagnosis. After clinical and imaginological exams, the deciduous tooth was extracted. Microscopically, the soft tissue lesion attached to the root showed typical RC features; however, in the cystic capsule, lymphoid follicles and vascular networks (lined by epithelioid endothelial cells) surrounded by numerous eosinophils, were observed. Immunohistochemistry, through CD3, CD20, CD34 and alpha-smooth muscle actin antibodies, highlighted these findings. Moreover, CD1a and CD207 were negative. To the best of our knowledge, this is the first report of RC showing angiolymphoid hyperplasia with eosinophilia (ALHE)-like features.

**Keywords:** Radicular cyst; periapical periodontitis; immunohistochemistry; angiolymphoid hyperplasia with eosinophilia; epithelioid hemangioma; jaws.

### **INTRODUCTION**

Radicular cysts (RCs) are the most common odontogenic cystic lesions that occur in the jaws. However, in the primary dentition, RCs are rarely reported, comprising between 0.5-3.3% of all RCs. These lesions originate from epithelial remnants located in the periodontal ligament space as a result of inflammation, consequence of pulp necrosis. Microscopically, the RC shows a cystic cavity lined by non-keratinized epithelium, with variable elongated interconnecting rete ridges, and a cystic capsule consisting of fibrous connective tissue containing numerous chronic inflammatory cells, variably associated with cholesterol clefts, dystrophic calcifications and odontogenic epithelial rests<sup>1,2</sup>.

On the other hand, epithelioid hemangioma (EH) is a benign vascular neoplasm lined by endothelial cells with ample eosinophilic cytoplasm and distinct epithelioid appearance. EH often affects adults, with predilection for the skin of the head and neck region. To date, three histopathological variants of EH are recognized: conventional, cellular and angiolymphoid hyperplasia with eosinophilia (ALHE)<sup>3</sup>. ALHE was firstly described in 1969, typically as solitary or multiple skin papules or nodules in the head and neck region. Posteriorly, extracutaneous cases, affecting the oral mucosa, bone, parotid gland and colon, were also described. To date, approximately 908 ALHE cases have been reported<sup>4</sup>. Rarely, ALHE can show association with other lesions, such as squamous cell carcinoma or vascular malformation<sup>4</sup>. Noteworthy, several relevant studies agree that ALHE should be better considered an EH variant<sup>4</sup>. Here, we present a typical RC case affecting a deciduous molar in a patient with allergic asthma diagnosis. However, on the microscopical analysis exhibited ALHE-like features, which are unusual findings.

# **CASE REPORT**

A 5-year-old female patient with a previous diagnosis of allergic asthma, receiving inhaled oral corticosteroids twice daily, was referred presenting extensive dental caries in the tooth #55, associated with vestibular sinus tract. The patient was asymptomatic, afebrile, and presented mild discomfort on palpation at the site lesion. The radiograph exam showed an extensive coronal destruction in close continuity with a small, ill-defined osseous radiolucent furcation lesion, with preservation of the pericoronal space of the tooth germ #15 (Figure 1). All other adjacent teeth were healthy. Moreover, lymphadenopathy and cutaneous lesions were absent.



Figure 1. A- Clinical view of the right deciduous maxillary second molar with extensive dental caries associated with vestibular sinus tract. B- Radiographic exam showing large coronal destruction and radiolucent osseous interradicular lesion.

The deciduous tooth was extracted, due to extensive carious lesion and mobility, the soft tissue lesion attached to the root was submitted to histotechnical processing and the sections was stained with hematoxylin and eosin (HE). The histopathological analysis showed typical features of RC; however, in the cystic capsule, well-formed tertiary lymphoid follicles supported by connective tissue containing vascular networks lined by endothelial cells with epithelioid appearance and surrounded by numerous eosinophils were observed (Figure 2).



**Figure 2.** Histopathological analysis on H&E stain slides. A- Panoramic view showing irregular tissue fragments associated with prominent inflammatory cellular infiltrate. Notice the typical cystic epithelium (arrows) and cystic capsule (stars) (x2.5). B- Details of well-formed tertiary lymphoid follicles (x10). C- Endothelial cells with epithelioid appearance (red arrowheads) admixed with plasma cells, eosinophils (black arrowheads) and neutrophils in the cystic capsule (x40). D- The typical radicular cyst is observed; note the presence of cystic epithelium (arrows) (x20). E and F- In high-power view, the cystic capsule showed numerous plasma cells, eosinophils (black arrowhead), endothelial cells (red arrowhead) and foci of blood vessels with florid neutrophil and eosinophil diapedesis (x40). Rectangles or squares are shown at higher magnification in adjacent images.

The immunohistochemical analysis highlighted the lymphoid follicles through CD3 and CD20 antibodies, which evidenced T-cell and B-cell populations, respectively, while that CD34 and alpha-smooth muscle actin exhibited a wide microvascular network (Figure 3).



**Figure 3.** Immunohistochemical findings. A- CD20 evidenced the B-cell central component of the lymphoid follicles (x2.5, inset shows cellular details). B- CD3 highlighted the T-cell population at the periphery of the lymphoid follicles (x2.5, inset shows cellular details). C- Alpha-SMA showed an ample microvascular network (x10). E- The same area of C, exhibiting CD34-positive endothelial cells delimiting microvascular network (x10).

Moreover, CD1a and CD207 were negative, whereas S100 evidenced scarce cells. Thus, a diagnosis of primary tooth-associated RC exhibiting ALHE-like features was rendered. A detailed laboratory tests, including complete blood count, electrolytes, blood glucose, blood urea nitrogen, creatinine and urine analysis, did not show alterations.

After 2-year follow-up, the patient is well, without alteration of the eruption path of the permanent tooth successor.

#### DISCUSSION

To the best of our knowledge, we report here the first RC case showing ALHE-like features in primary dentition. These histopathological findings are unusual, and probably a relationship of allergic asthma on its pathogenesis should be considered. Noteworthy, these findings have not been reported in RCs of permanent dentition, the most common inflammatory cystic lesion in the jaws. Furthermore, considering that the structural components of the RC have been maintained, especially the cystic capsule retaining its morphology with ALHElike features, it is unlikely that the current case could represent a collision lesion.

Atopic or allergic asthma is a chronic inflammatory pulmonary disease presenting recurrent episodes of wheezy and labored breathing. This disease affects mainly childhood or young adulthood, being caused by common allergens, including pollens, house dust, animal dander, foods and drugs. Atopic asthma presents detectable allergen-specific IgE and skin test positive upon allergen provocation. It is controlled, depending on severity, with bronchodilators, long-acting muscarinic antagonists, anti-inflammatory drugs such as corticosteroids (inhaled or oral), leukotriene modifiers and anti-IgE therapy<sup>5</sup>. Notably, because the constant detection of eosinophilic inflammation in the airways, the eosinophils appear to be involved in the asthma pathogenesis. The current had an allergic asthma diagnosis, and on the previously commented, at least in part, the florid eosinophilic infiltration observed in the RC may be due to asthma.

Remarkably, ALHE represents about half of the EH cases, affecting often the skin of the head and neck region, whereas the conventional and cellular EH variants are more often located in bone and soft tissue<sup>6</sup>. A relationship between ALHE with asthma is not clear. Moran et al. (2005)<sup>7</sup> reported two ALHE (EH) cases affecting the lung; of them, only one patient had a long-standing history of asthma<sup>7</sup>. Differently, Galindo-Ferreiro et al. (2016)<sup>8</sup> assessed ALHE cases with orbital and adnexal involvement, and none of them had asthma<sup>8</sup>. On the other hand, approximately 20% of the ALHE patients present blood eosinophilia and lymphadenopathy. Differently, in the current case, the laboratory tests did not show alterations and lymphadenopathy was not evident<sup>8</sup>.

The ALHE with oral involvement affects mainly young adults, without gender preference. The most frequent sites are lips, followed by buccal mucosa and tongue<sup>9</sup>. Microscopically, ALHE presents vascular structures of varying sizes, lined by endothelial cells with epithelioid appearance, a mixed inflammatory cell infiltrate containing numerous eosinophils and variable presence of lymphoid follicles.

Uncommonly, Langerhans cell histiocytosis (LCH) can mimic a periapical pathology<sup>10</sup>, and such as it should be included in the differential diagnosis. LCH is a clonal neoplastic proliferation of Langerhans-type dendritic cells, frequently affecting children younger than 15 years of age. Approximately 20% of the cases affect the jaws, with strong predilection for the mandible. Oral manifestations include gingival pain, ulceration, swelling, and tooth mobility due to expansion of alveolar bone. Dental radiographs may show destructive bone lesions. LCH in association with periapical granulomas and cysts is unusual<sup>11</sup>. In fact, aggregates of LCH cells can be found in chronic periapical lesions and it seem to represent a chronic localized LCH. Relevantly, clinical follow-up suggests that curettage is the adequate treatment, with excellent prognosis<sup>11</sup>. In the current case, typical LCH cells were not found, and by immunohistochemistry, CD1a and CD207 were negative.

### CONCLUSION

In summary, when assessing chronic periapical lesions, ALHE (or EH with ALHE morphology)-like features should be included on its histopathological spectrum, especially in pediatric patient with allergic asthma diagnosis. However, further studies are necessary to better define a relationship between allergic asthma and ALHE pathogenesis.

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