Russell body apical periodontitis: an unusual case report

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Russell bodies (RBs) changes in chronic apical lesions have rarely been reported in the literature. We describe a case of a periapical lesion abundantly and extensively composed of RB. Microscopic examination showed accumulation of plasma cells containing globular, spherical, polygonal, and eosinophilic structures against fibrous connective tissue. Initial diagnostic considerations based on a smaller magnification included hypersecretory plasmocytoma, although there was no evidence of infiltrative growth, mitotic activity, nuclear atypia, or cellular pleomorphism. Then, a panel of immunohistochemical markers was applied and the cells showed positivity with both kappa and lambda chains demonstrating their polyclonal origin. The extensive accumulation of RBs involving the periapical region represents an unreported and significant histologic change, as it was mimicking a malignant neoplasm. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;106:903-908)

Russell bodies (RBs) represent aggregates of immunoglobulins that occur because of the hyperproduction of normal secretory protein by plasma cells.1,2 They were first described by William Russell in 1890 as organisms involved in the etiology of some cancers.3-6 RBs are found in different organs and in different lymphoproliferative diseases such as myelodysplastic syndrome, monoclonal gammopathy of unknown cause, multiple myeloma,7,8 and cutaneous leishmaniasis,9 as well as in chronic inflammatory periapical lesions.10-12

Histopathologically, RBs are characterized as small, spherical, and eosinophilic structures that are present intra- and/or extracellularly or are arranged in groups.2,3 According to Paik,2 Maldonado et al.,8 Fujiyoshi et al.,13 and Erbersdobler et al.,14 when this aberrant accumulation occurs inside plasma cells, these cells are called Mott cells.

Although the distribution of RBs in oral tissues might be the same as that found throughout the human organism,15 to our knowledge there are no studies in the literature describing the abundant accumulation of these structures arising as a periapical lesion. Therefore, the objective of the present study was to report the case of a periapical lesion rich in RBs and to describe its clinical, histological, and immunohistochemical features and differential diagnosis in an attempt to call the attention of pathologists to this new entity that might be misinterpreted.

CASE REPORT

A 36-year-old woman sought an endodontist with complaints of numbness and pressure in the region of the upper incisors. Intraoral examination revealed discrete enlargement in this region, as well as the presence of a single fixed prosthesis corresponding to the upper lateral incisor. On the x-ray, this tooth presented a crown with a metal nucleus and had been treated endodontically, in addition to exhibiting a radiolucent image in the periapex of the right lateral incisor (Fig. 1, A). Taking into account a possible fracture and under the clinical suspicion of a periapical scar, the endodontist decided not to re-treat the root canal and referred the patient to an oromaxillofacial surgeon. At that time, detailed examination of the x-rays revealed that the periapical image was intense, circumscribed, oval, and distally inclined, measuring approximately 1.5 cm in its major extension, and was associated with the apical third. Thus, on the basis of the features described, the lesion was surgically excised and the material was sent for histopathological analysis at the Surgical Pathology Service, Faculty of Dentistry, Federal University of Bahia. Immunohistochemistry ruled out the possibility of a
tumor and the diagnosis of chronic apical periodontitis rich in RB and plasma cells was established. The present patient is under clinical and radiographic follow-up and shows bone healing in the affected region (Fig. 1, B).

MATERIAL AND METHODS

The material was fixed in 10% neutral formalin and embedded in paraffin, and 5-μm sections were cut and stained with hematoxylin and eosin and Brown and Brenn.

For immunohistochemistry, 3-μm sections were deparaffinized and the primary antibodies (Table I) were applied using the EnVision HRP System (Dako Corporation, Glostrup, Denmark). The reactions were developed with diaminobenzidine as chromogen solution. Finally, the slides were counterstained with Harris hematoxylin and examined under a light microscope. Positive and negative controls were included.

RESULTS

Gross pathology

The lesion presented as a brown friable mass with an irregular surface and shape, measuring 1.5 × 0.5 × 0.5 cm.

Light microscopy

The sections presented vascular fibrous connective tissue rich in plasma cells that contained RB in their
cytoplasm (Mott cells). These bodies were globular, spherical, polygonal and eosinophilic and were often arranged in plaques (Fig. 1, C, D, E and F). Eventually, polygonal eosinophilic structures, as well as sparse lymphocytes and neutrophils and focal accumulation of xanthomatous cells, were noted. In addition, microorganisms were not detected.

**Immunohistochemistry**

The cells containing RB were positive for CD45LCA, CD79alpha, CD138, plasm cells, kappa (KLC) and lambda (LLC) light chains, and CD20, indicating the polyclonality of the lesion (Fig. 2). CD68-positive cells were present in small groups of xanthomatous cells. The diagnosis was chronic apical periodontitis rich in plasma cells and RBs.

**DISCUSSION**

In the present case, the lesion involved the periapex of the right lateral incisor of a 36-year-old woman. The presence of RBs in pulp and periapical inflammatory lesions and in other lesions containing an inflammatory infiltrate is not a surprising finding, since these structures can affect oral tissues and dental pulp. However, there is no report in the literature of a periapical lesion abundantly and extensively composed of RBs.

RB are dilated cisternae of the endoplasmic reticulum that contain large amounts of condensed immunoglobulins. This accumulation is because the aggregate of formed proteins exceeds the elimination capacity of the organelles, impairing cellular digestion. However, there is no report in the literature of a periapical lesion abundantly and extensively composed of RBs.

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Clinically, the lesion only showed discrete enlargement in the region of the right lateral incisor. Upon radiography, the lesion seemed to be a common lesion such as a periapical cyst, whose involved tooth presented root and crown fillings, although the oval appearance, intense radiolucency in this region, and its size are not common for radicular cysts. According to Kirkevang et al., although the quality of root filling is not associated with the incidence of apical periodontitis, the presence of root and crown fillings, crowns, and caries lesions indicates a high risk for the development of periodontitis.

Histopathological analysis at a smaller magnification first pointed to a neoplastic alteration suggestive of a plasmacytoma. However, numerous spherical eosinophilic structures were identified in the lesion at subsequent magnifications and in view of its marked density, we concluded that a hypersecretory plasmacytoma should be part of the differential diagnosis despite the periapical nature of the lesion. According to several investigators, in addition to odontogenic tumors arising as a periapical lesion, primary malignant tumors, such as lymphomas and sarcomas, and even metastatic tumors may also be found at this site.

Over the past few years, a special type of chronic gastritis associated with *Helicobacter pylori* infection has emerged, which was first described by Tazawa and Tsutsumi in 1998 and which is characterized by the marked predominance of RBs that displace the nucleus of plasma cells to the periphery. The term RB (Russell Body) gastritis has been applied to these cases. *H. pylori* has been associated with this type of lesion, but it is unknown whether its presence is a casual finding or whether the microscopic alterations are caused by this microorganism.

In the present study, gross inspection showed that the lesion was friable. This is a common feature of chronic human periapical lesions analyzed in our laboratory. In the present case, the microscopic features observed were similar to those reported for RB gastritis. The lesion consisted of numerous spherical eosinophilic globular, sometimes polygonal, structures of variable diameters that were found inside or outside cells containing eccentric nuclei (Mott cells), permeating fibrous connective tissue. With respect to microorganisms, we were not able to show evidence of them in the periapical tissue sample available. This finding might be because conventional paraffin techniques cannot detect infections in apical biopsies owing to a lower number of bacterial organisms in the periapical region.

<table>
<thead>
<tr>
<th>Antibodies</th>
<th>Clone</th>
<th>Dilution</th>
<th>Incubation period, min</th>
<th>Retrieval</th>
<th>Source</th>
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<td>CD45LCA</td>
<td>2B11 PD26</td>
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<td>CD79alpha</td>
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<tr>
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</table>
All cases presenting marked formation of RBs have been identified on the basis of their immunohistochemical profile. Cases of RB gastritis have been shown to be immunoreactive against CD79a, CD138, kappa light chain, lambda light chain, and VS38c.\textsuperscript{2,29,30} The present case was positive for all of these markers and showed focal aggregates of CD68-positive cells. Thus, positive immunohistochemistry for kappa and lambda light chains indicated the polyclonality of the lesion, confirming that the plasma cells were apparently not neoplastic. In addition, characteristic features of malignant tumors such as infiltrative growth, mitotic activity, nuclear atypia, or cellular pleomorphism were not observed in the material examined. Eventually, some cells mimicked signet-ring cells. In the past, we diagnosed a case of signet-ring lymphoma, but no Mott cells or any characteristic eosinophilic structure were detected.\textsuperscript{33} In addition, some investigators include extramedullary plasmacytoma, multiple myeloma, and signet-ring carcinoma in the differential diagnosis\textsuperscript{14,34,35}; however, in the case of the last condition the formation of clear vacuoles is observed.\textsuperscript{29}

The diameter of a RB does not always indicate its true size and its shape varies according to the angle of the blade used during microtome cutting\textsuperscript{15}; in fact, although spherical eosinophilic inclusions predominated in the present case, the surface of some of these structures was polygonal. According to Yam et al.,\textsuperscript{36} depending on the molecules that interact with the host cell, the aggregation of these proteins may occur in 2
different subcellular regions involved in the secretory mechanism, indicating the existence of different shapes of RBs: if immunoglobulin light chains are present, ΔμCH1-light aggregates are found on structures covered with ribosomes, called rough RB, conferring a circular shape. In contrast, in the absence of these light chains, aggregation occurs on smooth tubular vesicles controlled by ER-GIC-53 (ER-golgi intermediate compartment), conferring an irregular shape. RBs may also be formed by other types of misfolded proteins, as well as by nonlymphoid cells.19,36

As described for RB gastritis3 and chronic pulp inflammation,12 it is possible that bacteria originating from the root canal provoke hyperactivation of plasma cells in the periapical region, with subsequent hyperproduction of immunoglobulins and formation of RBs due to the difficulty in cellular digestion as described previously.6,7,14 Furthermore, type I proinflammatory cytokines may also play an important role in the elevated production of immunoglobulins in dentinal tubules and pulp tissues37 and, consequently, in the tooth periapex with the progression of caries. However, other immunological aspects and those related to the host should be further investigated.

Finally, considering that the microscopic features of the case reported here resemble a condition called RB gastritis and may mimic other conditions such as those of a neoplastic nature described in the literature, we believe that the recognition of this periapical lesion is important to prevent misinterpretations. Thus, oral pathologists should be aware of this new chronic periapical condition, which should be included in the differential diagnosis of chronic human periapical lesions. The present patient is under clinical and radiographic follow-up and shows bone healing in the affected region.

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REFERENCES


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