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Crystal-storing histiocytosis: a rare lesion in periapical pathology☆,☆☆

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Abstract Crystal-storing histiocytosis is a rare manifestation of plasma cell dyscrasia/monoclonal gammopathies and lymphoproliferative disorders, characterized by cytoplasmic accumulation of crystallized immunoglobulins in histiocytes. Nevertheless, some reported cases of crystal-storing histiocytosis raise the possibility that this lesion may also be reactive. Crystal-storing histiocytosis in the oral cavity is extremely rare; only one case affecting the tongue has been reported in the English-language literature. In this report, we discuss the case of a 38-year-old man who presented a persistent periapical lesion affecting the maxillary left lateral incisor. Histopathological analysis showed numerous crystal-laden histiocytes associated with a mild plasma cell infiltrate within a fibrous stroma. The plasma cells failed to show clonal light-chain restriction, and the patient had no associated hematologic disorder or systemic disease. Thus, this lesion was probably the result of hypersecretion of immunoglobulins by polyclonal plasma cells found in the periapical lesion. Crystal-storing histiocytosis should be considered in the differential diagnosis of periapical lesions.

Keywords: Crystal-storing histiocytosis; Periapical lesion; Oral; Immunohistochemistry

1. Introduction

Crystal-storing histiocytosis (CSH) is a pathological condition characterized by accumulation of histiocytes containing paraprotein-related crystallized immunoglobulins. The disease may be systemic, usually associated with a poor prognosis, or may even be limited to a single organ. It is commonly related to underlying plasma cell dyscrasia/monoclonal gammopathies, multiple myeloma, or malignant lymphoma. Interestingly, some cases of CSH have presented as an early manifestation of multiple myeloma or malignant lymphoma at the subclinical stage. Because of this common association, an extensive clinical workup, including radiologic studies, laboratory investigations, and bone marrow biopsy, should always be performed to rule out this possibility [1-3]. In the head and neck region, several cases of CSH have been described, the majority of these being associated with either multiple myeloma or malignant lymphoma [4-8]. In the oral cavity, only a single case of CSH affecting the tongue in a patient with rheumatoid arthritis and polyclonal hypergammaglobulinemia has been reported [3]. Here, we report an extremely rare case of CSH in a periapical location.

2. Case report

The patient, a 38-year-old man, was referred to the Oral Diagnosis Center of School of Dentistry, University of

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Ribeirão Preto, complaining of slight pain in the left anterior maxillary region with duration of 6 months. The medical history was noncontributory, and the extraoral examination showed no alterations. On intraoral examination, a purulent discharge draining in the vestibular mucosa apical to the maxillary left lateral incisor was visualized, which also showed sensitivity on palpation and to the percussion test. Radiographically, a well-circumscribed, unilocular, radiolucent lesion located in the periapical region of the maxillary left lateral incisor, measuring approximately 1.0 cm in diameter, was observed. The root canal had been endodontically treated 2 years previously, followed by a metal post restoration (Fig. 1). The maxillary left canine and first premolar responded positively to a cold pulp test. According to the clinical and radiographic features, a chronic periapical lesion, such as periapical granuloma or radicular cyst, was the main differential diagnosis. Thus, under local anesthesia, the lesion was fully excised, followed by apical surgery, without complications.

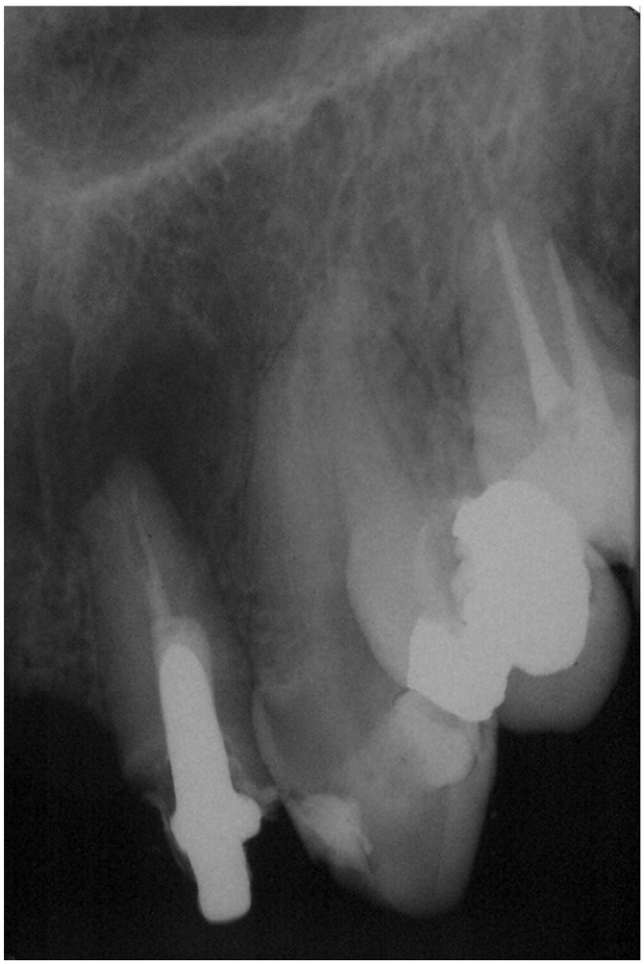

Fig. 1. Radiographic view of a well-circumscribed, unilocular, radiolucent lesion in periapical region of the maxillary left lateral incisor diagnosed as crystal-storing histiocytosis.

3. Pathologic findings

3.1. Morphologic findings and histochemical analysis

The specimen measuring 1.0 × 0.9 cm was fixed in 10% formalin and routinely processed for histological examination. Histological sections stained with hematoxylin and eosin (H&E) showed a nodular lesion containing numerous large epithelioid eosinophilic cells within a fibrous stroma intermingled with a mild plasmacytic infiltrate and scattered lymphocytes distributed around slitlike vascular structures (Fig. 2A, B). At higher magnification, the bright eosinophilic cytoplasm of the epithelioid-shaped cells seemed to be filled with numerous needlelike crystals and exhibited focal areas of birefringence under polarized light microscopy (Fig. 2C, D). The nuclei were small and bland, and there were no mitoses. Other sections stained for periodic acid–Schiff, with and without diastase digestion, were negative. Moreover, stains for acid-fast bacilli and fungi failed to reveal infectious microorganisms.

3.2. Immunohistochemistry and in situ hybridization

Tissue sections 3-μm thick were placed on silanized slides and were stained using the avidin-biotin peroxidase complex technique and heat-induced epitope retrieval buffer. The antibodies used included CD3, CD20, CD34, CD43, CD45, CD68 (PG-M1 and KP1), CD79a, CD117, CD138, myeloperoxidase, epithelial membrane antigen, plasma cell marker (VS38c), S100, heavy chain for immunoglobulin (Ig) G, and κ and λ light-chain immunoglobulins (DAKO, Carpinteria, CA). The crystal-laden epithelioid-shaped cells showed positivity for both CD68 (KP1) (Fig. 3A) and CD68 (PG-M1), confirming their histiocytic origin. CD68 (KP1) immunostained stronger than CD68 (PG-M1). The surrounding typical plasma cells were positive for CD138 (Fig. 3B), CD79a, epithelial membrane antigen, VS38c, IgG (Fig. 3C), and κ and λ light-chain immunoglobulins (Fig. 3D, E). The intracytoplasmic crystal-like inclusions showed weak immunoreactivity for IgG and κ and λ light-chain immunoglobulins (Fig. 3C-3E). CD45, CD3, and CD43 showed scarce T-cell lymphocytes, whereas CD20 was negative. The slitlike vessels were evidenced with CD34, whereas CD117, myeloperoxidase, and S100 showed scarce mast cells, neutrophils, and dendriticlike cells, respectively. In situ hybridization for Epstein-Barr virus–encoded small nuclear RNA (EBER) complementary to Epstein-Barr virus EBER1 and EBER2 loci (EBER, PNA probes, DAKO, Glostrup, Denmark) was negative.

3.3. Scanning electron microscopy

Scanning electron microscopy (Jeol JSM 5600 LV, Dental School of Piracicaba-UNICAMP, Piracicaba, Brazil) using a 5-μm paraffin section for tissue morphology evaluation revealed numerous histiocytes showing several cytoplasmic prolongations blending with each other.

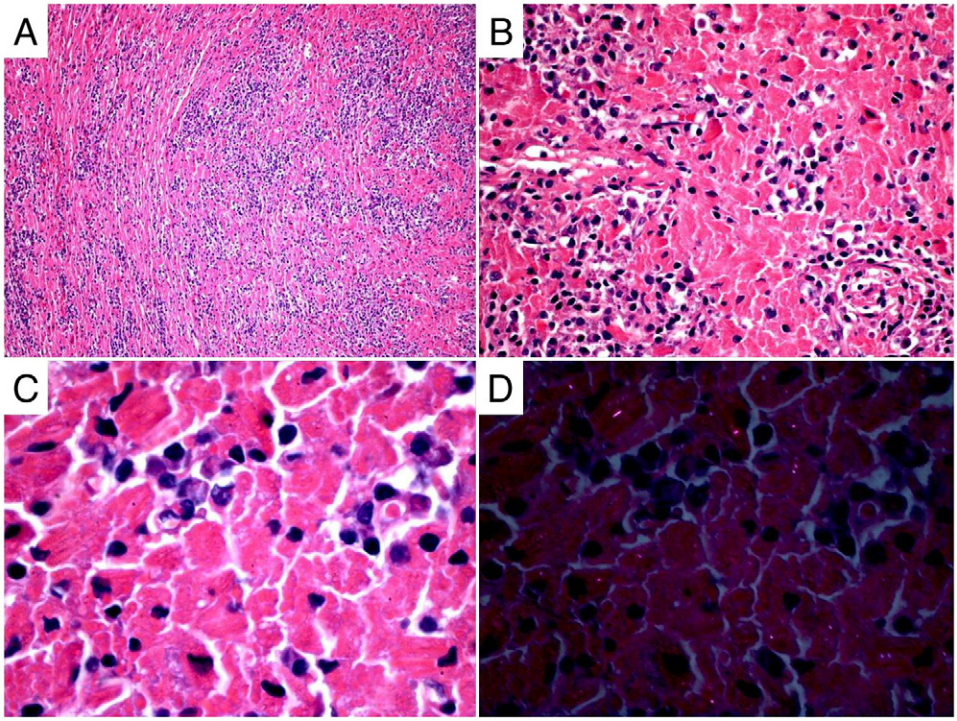

Fig. 2. Microscopical aspects of crystal-storing histiocytosis (H&E stain). Numerous large epithelioid eosinophilic cells intermingled with a mild plasmacytic infiltrate within a fibrous stroma (A, original magnification [OM] ×10; B, OM ×40). At higher magnification, notice the bright eosinophilic cytoplasm of epithelioid-shaped cells containing numerous needlelike crystals (C, OM ×100). The same area showing birefringence under a polarized light microscopy (D, OM ×100).

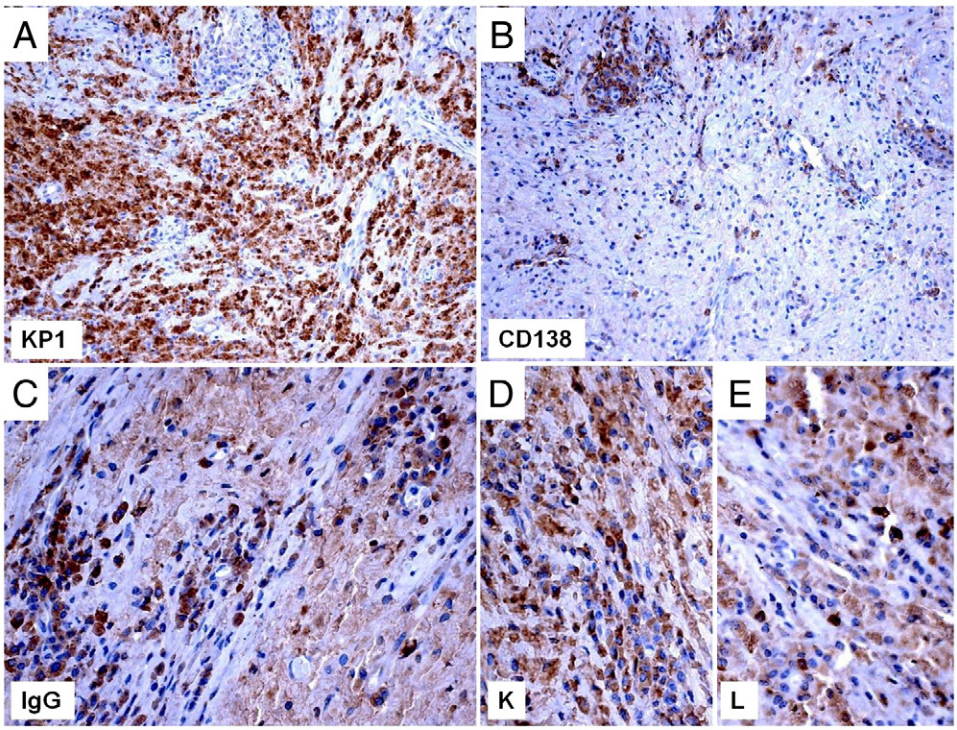

Fig. 3. Immunohistochemical findings of crystal-storing histiocytosis. The mononuclear epithelioid-shaped cells were strongly positive for CD68 (KP1) (A, OM ×20) and CD68 (PG-M1), supporting a histiocytic lineage. The same area of panel A showing plasma cells positive for CD138 in perivascular distribution (B, OM ×20). Notice the weak cytoplasmic positivity in histiocytes and stronger cytoplasmic positivity in plasma cells for IgG (C), κ light chain (D), and λ light chain (E) (OM ×40).

3.4. Follow-up

After the diagnosis of CSH had been rendered, extensive clinicoradiological investigations were indicated. The results of laboratory investigations, especially with reference to blood cell counts, hemoglobin, glucose, erythrocyte sedimentation rate, immunoglobulins, lactate dehydrogenase, urea, creatinine, sodium, potassium, calcium, phosphate, total protein, and albumin, were within normal limits. Both serum and urine protein electrophoresis tests showed no abnormal monoclonal band. Skull and chest radiographs showed no abnormalities. The postsurgical follow-up did not reveal any abnormality; but unfortunately, the patient was lost to follow-up at that time.

4. Discussion

In the head and neck region, several cases of CSH have been described, the majority of them associated with either multiple myeloma or malignant lymphoma. Yamamoto et al [8] and Pock et al [4] described a case of CSH associated with multiple myeloma affecting the cornea and the skin of the neck region, respectively. Crystal-storing histiocytosis associated with extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue type affecting the lachrymal gland [5] and parotid gland [6] and CSH associated with lymphoplasmacytic lymphoma affecting the larynx [7] have also been described. In the oral cavity, only a single case of CSH affecting the tongue of a patient with rheumatoid arthritis and polyclonal hypergammaglobulinemia has been reported [3]. To the best of our knowledge, the current case is the second report in the oral cavity and the first report in periapical pathology. Differently to the case reported by Bosman et al [3], the present case was not related to paraproteinemia or systemic disease. Interestingly, a few cases of CSH not associated with clonal lymphoproliferative disorder, usually affecting the lung, have also been reported [2,9-12]. These findings show that some cases of CSH are not restricted to clonal lymphoid or plasma cell neoplasms. Thus, in these cases, detailed clinical, immunohistochemical, and genotypic studies are mandatory to confirm its polyclonal nature.

As previously mentioned, CSH is usually associated with intracytoplasmic accumulation of crystallized immunoglobulins in patients with lymphoproliferative disorders or plasma cell dyscrasias. However, another 2 conditions have also been described, such as CSH due to histiocytic accumulations of phagocytosed clofazimine, a drug used to treat lepromatous leprosy [13], and CSH due to massive accumulation of Charcot-Leyden crystals in a case of eosinophilic colitis [14]. Moreover, Chantranuwat [15] reported a noncrystallized form of CSH as a cause of chronic lung infiltration in multiple myeloma. These reports expand the spectrum of the nature and morphology of intracytoplasmic immunoglobulin accumulation in cases of CSH. Although no electron microscopic examination was made in the present case, it probably represents a crystallized form of CSH, as shown in the higher-magnification analysis of the H&E stain slide under a polarized light microscopy. Moreover, for the first time, we show the scanning electron microscopy image that revealed histiocytes with cytoplasmic prolongations blending with each other.

The differential diagnosis of a periradicular radiolucency associated with a tooth with pulp necrosis or one that has been endodontically treated includes mainly periapical granuloma and radicular cyst; nevertheless, other lesions such as odontogenic cysts and tumors, nonodontogenic tumors, and mesenchymal reactive lesions should also be considered [16].

Periapical granulomas and radicular cysts are very common inflammatory lesions of the jaws. It is likely that a prolonged presence of microbial irritants and the local humoral immune response are involved in the pathogenesis of these lesions. It is generally accepted that B-cell lymphocytes and plasma cells are prominent in periapical lesions; and these cells locally produce IgG, IgA, and IgM to a lesser extent [17]. We think that these polyclonal plasma cells were the source of the secretion of immunoglobulins in the present case.

The extensive documentation of periapical pathoses with different treatment and prognostic implications has prompted several authors to recommend that periapical lesions that do not respond to conservative endodontic therapy should be examined histopathologically. The histopathological study of periapical pathosis can occasionally reveal nonendodontic lesions. Odontogenic tumors constitute the largest group; but rare cases of Langerhans cell histiocytosis, leukemic infiltrated, malignant lymphoma, and multiple myeloma have also been described [16,18]. In the current case, a periapical lesion with distinctive diffuse proliferation of crystal-laden histiocytic cells was observed after endodontic treatment; and the delay in healing of this lesion is probably due to their distinctive morphological pattern. Nevertheless, after the surgical procedure, an adequate healing process was observed. Thus, the lesion appears to have a good prognosis, although a long follow-up time and reports of further cases are necessary to know and clarify the true nature of these lesions.

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