

Eosinophilic ulcer of oral mucosa: a case report

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Summary

Eosinophilic Ulcer (EU) is a rare self-limiting chronic benign lesion of the oral mucosa with pathogenesis still unclear, however it may resemble malignancies, traumatic ulcerations and some infections such as deep fungal infections, tuberculosis and primary syphilis. This is a case report of a patient with EU in the lateral border of the tongue with no history of associated trauma and refractory to treatment with drugs. The ulcer rapidly healed after an incisional biopsy and the definite diagnosis was achieved only combining histologic findings and the clinical follow-up.

Key words: eosinophilic ulcer, oral mucosa, ulcerative eosinophilic granuloma.

Introduction

Eosinophilic ulcer (EU) is a rare self-limiting chronic benign lesion of the oral mucosa. Clinically, the ulceration has been most frequently found in tongue and it is characterized by the presence of mildly indurated borders which may resemble malignancies, traumatic ulcerations and some infections such as deep fungal infections, tuberculosis and primary syphilis (1-8). EU also has been referred as traumatic ulcerative granuloma with stromal eosinophilia, traumatic eosinophilic granuloma, traumatic granuloma and ulcerative eosinophilic granuloma. In infants, usually on the ventral surface of the anterior tongue secondary to trauma from newly erupted primary teeth, EU is referred as Riga-Fede disease (1-8).

The pathogenesis of the EU is still unclear, however the lesion is thought to be reactive since trauma has been implicated as initiating factor, nevertheless trauma cannot be demonstrated in many cases. Histopathological findings consist of eosinophil-rich mixed infiltrates involving the superficial mucosa and the deeper muscle layer, accompanied by a population of large mononuclear cells that may correspond either to histiocytic cells, myofibroblastic cells or activated lymphoid cells. Immunohistochemical studies showed the expression of CD3, CD4, CD8, CD20, CD43, cytotoxic granules (TIA-1) and for the large cells expression of CD30, vimentin and CD68. Lymphocytes may also express the proliferation marker Ki-67 in small and large cells. The markers ALK (anaplastic lymphoma kinase), CD5, Beta-F1 and CD56 were all described as negative. The differential histopathologic diagnosis may include Langerhans cell histiocytosis, Kimura disease, angiolymphoid hyperplasia with eosinophilia, atypical histiocytic granuloma, CD30+ lymphoproliferative disorder of the oral mucosa, lymphoma, allergic reactions and parasitic diseases. Definite diagnosis can be achieved only by combining histologic findings with clinical follow-up (1-10).

Case report

A 33 year-old male patient searched treatment due a solitary and painful ulcerative lesion in his right lateral border of the tongue with two months of evolution and with no history of associated trauma (Fig. 1). Examination revealed a painful ulcer with relative firmness but not indurated, containing borders bringing two aspects, erythematous or nodular, with a central ulcer reaching 4-5 cm in diameter that had a white-yellow fibrinous base. There were no significant regional lymphadenopathies. The patient was non smoker and had a past of alcoholism (has stopped for more than a year) with no actual alcohol abuse. The patient reported a previous clinical treatment with his physician with no improvement or healing of the lesion. He was admitted to Santa Terezinha University



Fig. 1. Initial clinical aspect of the eosinophilic ulcer.



Fig. 2. Clinical aspect of the lesion following the incisional biopsy.

Hospital due to his clinical debilitating condition and due to the complaint of severe pain with significant impairment of food intake. He was medicated empirically with intravenous Cephazolin 500 mg (three times a day), topical Tetracycline (three times a day, mouthwash), topical corticoid (Dexamethazone, three times a day, mouthwash), non steroidal antiinflammatory and opioid analgesics for five days with no signs of healing. Preparing for a biopsy, blood tests were taken with none alterations found in complete blood count, hemosedimentation velocity, HIV test, rheumatoid factor, antinuclear antibody and fluorescent treponemal antibody-absorption test (FTA-ABS) though, C-reactive protein showed to be very high (51.61 mg/L while the normal parameter is below than 6.5 mg/L). Chest radiographs were normal. An incisional biopsy was performed and the patient was delivered from the hospital. Ten days postbiopsy the ulcer was markedly diminished in size (Fig. 2).

The histopathological findings showed an ulcerated area covered with fibrinoid material. A dense polymorphous inflammatory infiltrate was seen and with numerous eosinophils (Fig. 3). The infiltrate extends from the ulcer base deep into subjacent skeletal muscle. There were no mitotic figures or nuclear atypia in the infiltrate. Immu-

nohistochemistry for CD68 antibody revealed a diffuse pattern of stain mostly in large cells localized from the surface of the ulcerated area until the skeletal muscle. Positive stain for CD34 antibody was observed only in blood vessels present within the lesion. Periodic acid-Schiff (PAS) and Ziehl-Nielsen stains were negative for microorganisms. At this point the histopathological diagnosis was inconclusive, however it was possible to reach the diagnosis of EU by combining histologic findings with the clinical follow-up.

Forty-five days later the patient went through a corrective surgery due to the permanence of the exophytic growths in the tongue and the histopathological analysis of this removed tissue brought none additional or interesting information. After an additional period of 30 days the tongue showed a complete healing (Fig. 4).

Discussion

Eosinophilic ulcer of the oral mucosa may be best regarded as a reactive pattern of unclear etiology (5) and is characterized as rare benign entity which occurs as

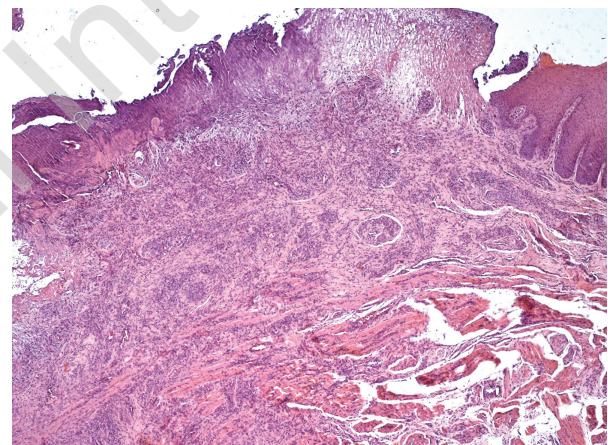


Fig. 3. Histopathological aspect of the tongue lesion. Notice that the infiltrate extends from the ulcer base deep into subjacent skeletal muscle (H&E; 100x).



Fig. 4. Final aspect of the tongue.

an ulcerated and sometimes with nodular-ulcerated lesion which is most frequently located on the tongue. The entity brings several clinical differential diagnoses which include mainly malignancies, infectious diseases, autoimmune diseases or others (2,3,5-8,10).

In our case the immunohistochemical study showed positivity for CD68 similarly to what was found by others (1,4,7), and this is a routine macrophage marker, which may present immunohistochemical expression for monocytes, macrophages, neutrophils, basophils, large lymphocytes, myeloid precursors, osteoclasts, mast cell, synovial cells, Langerhans' cell histiocytosis, interdigitating reticulum cell sarcomas and melanomas. CD68 has been described as having diagnostic utility for true histiocytic lymphomas and granulocytic sarcoma (11). In the present case, the CD34 immunohistochemical reaction was expressed in normal endothelial cells. The main diagnostic utility for CD34 is the identification of endothelial differentiation. It is sensitive regardless of tumor grade, recognizing greater than 85% of angiosarcomas and Kaposi's sarcomas (11).

In our case a rapid improvement of the ulcer occurred after the incisional biopsy similarly to what was described by other authors (4,6,7,8) and the reason for that behavior is unknown. Accordingly to Eleni et al. (8) this behavior may be indicative that the healing response is reactivated to the surgical intervention.

Several therapeutic options for EU of the oral mucosa in adults has been described like wait-and-see approach, antibiotics, topical, intralesional and/or systemic corticosteroids, curettage, cryosurgery and surgical excision (10). In this presented case topical or intravenous antibiotics as well as topical corticosteroids showed no results with none signs of healing of the ulcer. Intralesional and systemic corticosteroids where not an option since deep fungal infection where considered as clinical hypothesis. Accordingly to el-Mofty et al. (9) in a review of 38 cases, suggest that cell-mediated immunity might play an important role in the pathogenesis of EU, since that topical, as well as systemic prednisone, is effective in the treatment of this disorder. None response with that medicine was obtained in this case as described above and this is in accordance with Segura and Pujol (5) which stated that the use of topical steroids does not have conclusive evidence of efficacy in treating EU.

Surgical excision is the most commonly cited treatment procedure among the different therapies used and this approach showed to be a reliable method with an excellent end result in this case report. Considering the benign and self-limiting behavior of EU, achieving a correct

diagnosis and monitoring these patients are important to avoid possible complications or overtreatment due to the difficulties that arise in the histopathological exam, since there is no specific hallmark of the disease and, therefore, the histopathological diagnosis of EU is by exclusion (5). Monitoring is also important because low-grade lymphoma in routine microscopic exam, for example, may only be recognized retrospectively, when lesions recur several times, spread to other areas, or develop more pronounced malignant features microscopically (4).

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