Traumatic ulcerative eosinophillic granuloma with stromal eosinophilia of tongue

Dear Editor,

Traumatic ulcerative eosinophilic granuloma with stromal eosinophilia is a unique benign lesion, which possibly represents a CD30-positive lymphoproliferative disorder, occurring anywhere in the oral cavity. It characteristically presents as a self-healing solitary ulcer of weeks or months duration following trauma, although in most cases the history of trauma cannot be elicited. Because it has indurated margins combined with rapid development and delayed healing, it is likely to be confused for oral malignancy such as squamous cell carcinoma. Histologically, because of the presence of large histiocyte-like cells, the lesion is confused for atypical histiocytic granulomas, angiolymphoid hyperplasia with eosinophilia and Langerhans cell histiocytosis. Most cases heal without any intervention. Because a subset of these cases, particularly the recurrent ones, shows monoclonality for T cell marker or CD 30, all the recurrent cases need immunohistochemical analysis for CD30 marker clonality and long-term follow-up.

A 48-year-old female presented with non-healing ulcer over the ventral surface of her tongue of 3 weeks duration. Her general physical examination was unremarkable. On local examination, a tender ulcer was noted on the right side of the tongue on the ventral surface measuring 1 cm × 1 cm; the margins were indurated with necrotic material at the base [Figure 1]. There was no history of trauma, dental implants or other significant trauma.

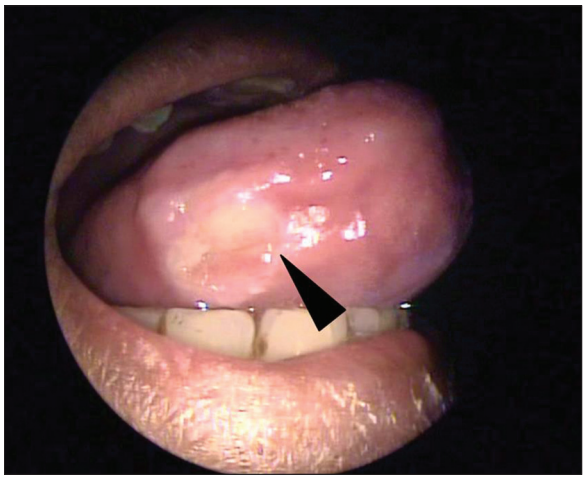

Figure 1: Ulcer with indurated margin and slough in the base (black arrow head)

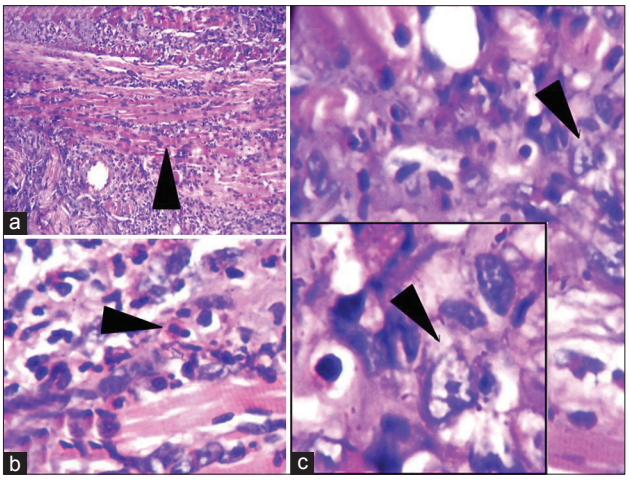

Figure 2: Microscopy showing (a) polymorphic inflammatory infiltrate separating the muscle fascicles (black arrow head) [×10, hematoxylin and eosin (H and E)], (b) rich in eosinophils (black arrow head) [×40, H and E] and (c) large atypical looking histiocytes with prominent large eosinophilic nucleoli (black arrow head) [×100, H and E]. Inset: characteristic large cell with large nucleoli (black arrow head)

Biopsy from the ulcer showed ulcerated stratified squamous epithelium. There was dense polymorphic inflammatory infiltrate comprised of lymphocytes, abundant eosinophils and neutrophils. These infiltrates were seen extending from the subepithelial stroma into the skeletal muscle bundles and separating them [Figure 2a and b]. Interestingly, among these, there were scattered large atypical-looking histiocytes. They were large with variable amount of cytoplasm, large nucleus with irregular nuclear contour, with single prominent nucleoli and mitotic figures [Figure 2c and inset]. There were also endothelial cells' proliferation with granulation tissue in the stroma. Histologically, the lesion was diagnosed as "Traumatic ulcerative granuloma with stromal eosinophilia" (TUGSE).

The lesion healed following biopsy in about 5 weeks and there was no recurrence in the follow-up period of 3 years. We did not subject the lesion for immunohistochemistry as there was no recurrence.

TUGSE is also called by other names including eosinophilic granuloma, eosinophilic ulcer, Riga Fede disease (in infants and children) and atypical histiocytic granuloma. TUGSE can occur anywhere in the oral cavity, and the most common sites include the ventral surface of the tongue, buccal mucosa, vestibule and floor of the mouth.[1] Although it usually follows some form of trauma, most patients do not have a history of trauma. Most commonly, the lesion presents as a self-healing solitary ulcer with rolled up or indurated margins of weeks to months duration. The lesion can also present as multiple recurrent self-healing ulcers.

Diagnosis of TUGSE is based on clinical and histologic features that include the presence of an ulcer with a polymorphic inflammatory infiltrate including lymphocytes and abundant eosinophils, extending into deeper tissues, admixed with scattered large atypical histiocyte-like cells with large vesicular nuclei and prominent nucleoli and

often with mitotic figures.

Usually, oral ulcers are devoid of eosinophils. But, TUGSE shows abundant eosinophils, which could probably be due to tissue reaction to some unknown antigen introduced via mucosal breakdown following trauma.

Characteristic ulcer with rolled margins is attributable to mucosal degeneration with a possible role of cytotoxic T cells and toxic products of degranulating eosinophils. Abraham *et al*.[1] found in his study a positivity for marker of cytotoxic T cell activity in all his cases, supporting the role of cytotoxic T cells in the pathogenesis of TUGSE.

Why delayed healing?

Elovic *et al*.[2] observed a lack of significant synthesis of transforming growth factor beta by eosinophils, which explains the delayed healing characteristic of TUGSE. The eosinophils elsewhere in the lesions generate many inflammatory and regulatory cytokines; some of these, such as tumor necrosis factor, can enhance tissue damage.

Nature of large atypical mononuclear cells

We did not perform immunohistochemistry as none of the markers are specific for large atypical cells. Studies reveal that, immunohistochemically, these cells are variably positive for macrophage marker CD68, dendritic cell marker, factor XIIIa, myofibroblast marker such as vimentin, CD30, CD3, CD4 and CD8.[3,4]

Some authors postulated that TUGSE represents a spectrum that includes CD30-positive lymphoproliferative disorders, atypical histiocytic granuloma and angiolymphoid hyperplasia with eosinophilia. Most cases of TUGSE heal without any complications or recurrence. Only those cases that show recurrence should be subjected to immunohistochemical analysis for CD 30 marker clonality and, if monoclonality is found, these cases need long-term follow-up.

CD30 is an activation marker and also an early differentiation antigen. It is a transmembrane glycoprotein with extracellular domain homologous to tumor necrosis factor/nerve growth factor receptor superfamily.[5,6]

CD30 (a marker originally described in Reed Sternberg cells using Ki 1 monoclonal antibody) is commonly expressed on activated B and T cells, in certain lymphoproliferative disorders including lymphomatoid papulosis, primary cutaneous anaplastic large cell lymphoma and borderline CD30 + lesions.[1] It is also expressed in non-neoplastic lesions such as atopic dermatitis, drug reactions, scabies and molluscum contagiosum.[1,7]

However, oral involvement of lymphoproliferative disorders is rare and only few cases are reported.[1,8,9] Ficarra *et al*. were the first to report a case in which CD30 + cells were found in an ulcerated lesion histologically resembling TUGSE that presented with multiple episodes of recurrent self-healing eosinophilic ulcers in the oral mucosa.[5]

Alobeid *et al*. in his study of TUGSE cases found three cases showing T cell clonality and concluded that a subset of TUGSE cases share common features with primary cutaneous CD30 + lymphoproliferative disorders.[6]

Treatment

Simple surgical excision is the treatment of choice. Rapid healing has been achieved in many cases following the biopsy. Some administer intralesional steroids.

TUGSE is a benign lesion of the oral cavity and may represent a CD30-positive lymphoproliferative disorder, commonly presenting as a self-healing solitary ulcer of short duration. Because some of these cases show monoclonality, particularly the recurrent ones, they need immunohistochemical evaluation and long-term follow-up.

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References

1. Abraham H, Ninette A, Sharon A, Yahalom R, Rosenbaum H, Okon E, *et al*. Traumatic ulcerative granuloma with stromal eosinophilia: A reactive lesion of the oral mucosa. Am J Clin Pathol 2006;126:522-9.
2. Elovic AE, Gallagher GT, Kabani S, Galli SJ, Weller PF, Wong DT. Lack of TGF-α and TGF-β synthesis by human eosinophils in chronic oral ulcers. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996;81:672-81.
3. Regezi JA, Zarbo RJ, Daniels TE, Greenspan JS. Oral traumatic granuloma: Characterization of the cellular infiltrate. Oral Surg Oral Med Oral Pathol 1993;75:723-7.
4. El-Mofty SK, Swanson PE, Wick MR, Miller AS. Eosinophilic ulcer of the oral mucosa: Report of 38 new cases with immunohistochemical observations. Oral Surg Oral Med Oral Pathol 1993;75:716-22.
5. Ficarra G, Prignano F, Romagnoli P. Traumatic eosinophilic granuloma of oral mucosa: A CD30+(Ki-1) lymphoproliferative disorder? Oral Oncol 1997;33:375-9.
6. Alobeid B, Pan LX, Milligan L, Budel L, Frizzera G. Eosinophil-rich CD30+lymphoproliferative disorder of oral mucosa. Am J Clin Pathol 2004;121:43-50.
7. Guitart J, Hurt MA. Pleomorphic T cell infiltrate associated with molloscum contagiosum. Am J Dermatopathol 1999;21:178-80.
8. Wright JM, Dunsworth AR. Follicular lymphoid hyperplasia of hard palate: A benign Lymphoproliferative process. Oral Surg Oral Med Oral Pathol 1983;55:162-8.
9. Eversole LR, Leider AS, Jacobson PL, Kidd PM. Atypical histiocytic granuloma: Light microscopic, ultrastructural and histochemical findings in an unusual pseudomalignant reactive lesion of the oral cavity. Cancer 1985;55:1722-9.

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