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Case Report

Traumatic ulcerative granuloma with stromal eosinophilia, an unusual clinical manifestation in the oral mucosa. Case report.

Granuloma ulcerativo traumático con eosinofilia estromal, una manifestación clínica inusual en la mucosa oral. Reporte de un caso.

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Abstract: Introduction: Traumatic ulcerative granuloma with stromal eosinophilia is an uncommon condition of the oral mucosa with a chronic course, usually affecting the tongue. **Case Report:** Clinically it presents as a chronic ulcer, with raised and indurated borders, rarely presented as a tumor. Histologically it shows a diffuse mixed inflammatory infiltrate, rich in eosinophils. The etiology of this lesion is still unclear; however, chronic irritation from traumatic agents is considered a major initiating factor. In some cases, the presence of CD30⁺ mononuclear cells within the lesions suggest the possibility of a CD30⁺ lymphoproliferative disorder. This article presents a case of a traumatic ulcerative granuloma with stromal eosinophilia manifested in a 56-year-old female with a solitary ulcerated tumor inside the right cheek. **Conclusion:** It was diagnosed based on clinical data and histopathological features. In a brief literature review, the entity has been characterized, analyzing its etiology and nature.

Keywords: *ki-1 antigen; ulcer; mouth mucosa; eosinophils; eosinophilic granuloma; eosinophilia.*

Resumen: Introducción: El granuloma ulcerativo traumático con eosinofilia estromal es una afección infrecuente de la mucosa oral de curso crónico, que suele afectar a la lengua. **Reporte del Caso:** Clínicamente se presenta como una úlcera crónica, con bordes elevados e indurados, rara vez se presenta como un tumor. Histológicamente muestra un infiltrado inflamatorio mixto difuso, rico en eosinófilos. La etiología de esta lesión aún no está clara; sin embargo, la irritación crónica por agentes traumáticos se considera un factor de iniciación importante. En algunos casos, la presencia de células mononucleares CD30⁺ dentro de las lesiones sugiere la posibilidad de un trastorno linfoproliferativo CD30⁺. En este artículo se presenta el caso de un granuloma ulcerativo traumático con eosinofilia estromal que se manifiesta en una mujer de 56 años con un tumor ulcerado solitario en el interior de la mejilla derecha. **Conclusión:** Se diagnosticó con base en datos clínicos y características histopatológicas. En una breve revisión de la literatura se ha caracterizado la entidad, analizando su etiología y naturaleza.

Palabra Clave: *antígeno ki-1; úlcera; mucosa bucal; eosinófilos; granuloma eosinófilo; eosinofilia.*

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INTRODUCTION.

Traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) is an uncommon, chronic and benign lesion of the oral mucosa.[1] This lesion has been known by different names, Riga-Fede disease in infants and neonates, sublingual granuloma, traumatic granuloma, eosinophilic granuloma, eosinophilic ulcer, and ulcerative eosinophilic granuloma.[2] The term TUGSE was coined by Elzay in 1983.[3] TUGSE is most commonly found in the 5th decade of life[4] and exhibits a slight female predominance.[5] The tongue is the most common location involved[1] and clinically it presents as a chronic ulcer, with raised and indurated borders, being rarely presented as a tumor.[6]

Histologically, it is characterized as a lesion with superficial ulceration and underlying granulation tissue showing a chronic inflammatory infiltrate, rich in eosinophils. Atypical large mononuclear cells scattered within the inflammatory infiltrate have been described in some cases.[7] The Etiology of TUGSE is controversial. However, trauma is considered to have a major role in its pathogenesis. CD30^{+} cells have been reported in some cases, suggesting that it could be a CD30+ lymphoproliferative disease.[1]

CASE REPORT.

A 56-year-old woman was referred to the oral medicine service, with a 4-month history of oral lesion, located inside her right cheek. She reported having had this lesion before, which was removed (without anesthesia) and reappearing later with the same features. Intra oral exam revealed a 1.9cm in diameter ovoid pedunculated tumor, with smooth surface areas of heterogeneous coloration, painless with a tendency to bleed. It was firm in consistency and tender to palpation. The lesion was adjacent to an edentulous alveolar bone area and the patient was a non-prosthesis wearer. (Figure 1)

Her past medical history was noncontributory. A provisional diagnosis of irritative fibroma was made and an excisional biopsy was performed under local anesthesia. Microscopic examination showed parakeratinized pluristratified squamous epithelium that becomes atrophic and it is interrupted by fibrin and polymorphonuclear neutrophils.

Beneath it, there was a proliferation of fibroblastic tissue with abundant dilated vessels and neoformation with foci of hemorrhage and mixed inflammatory infiltrate with histiocytes, lymphocytes, plasmocytes and abundant eosinophils throughout the sample. (Figure 2)

Figure 1. Intraoral clinical photograph of the pedunculated lesion.

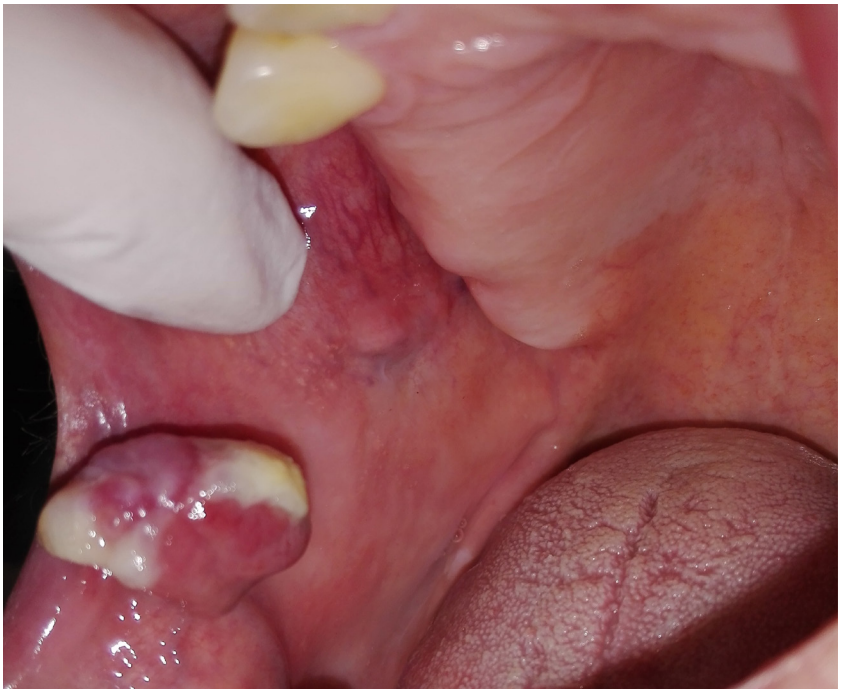
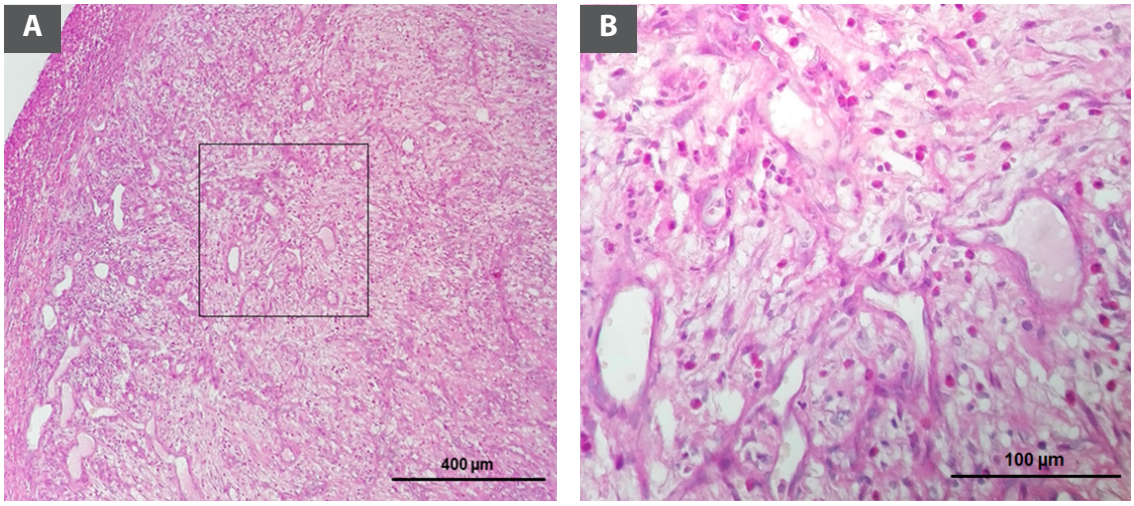


Figure 2. Histological findings.



A: Proliferation of fibroblastic tissue with abundant dilated vessels (total original magnification 100x, hematoxylin and eosin stain).
B: Mixed inflammatory infiltrate with abundant eosinophils (total original magnification 400x, hematoxylin and eosin stain).

Based on the clinicopathological features, a diagnosis of Traumatic Ulcerative Granuloma with Stromal Eosinophilia (TUGSE) was established. No other treatment was needed in addition to clinical follow-up after surgery. Complete healing was noted after one year.

DISCUSSION.

Although the etiology for oral TUGSE lesions is controversial, traumatic irritation of mucosa is considered to be the most likely cause. However obvious trauma could be demonstrated only in 50% of cases.[4] Suggestions have been made that some patients could have a predisposition to develop an eosinophilic ulcer related to immune dysfunction condition.[8]

In 1964 Bhaskar and Lilly's experimental studies with rats, demonstrated similar lesions to TUGSE, after repeated injury to the tongue. They concluded that the appropriate term was "traumatic granuloma", as the injury is essentially reactive and the result of trauma.[9]

The presence of eosinophils is not completely understood because most traumatic oral ulcers are devoid of eosinophils. Nevertheless, Sharma *et al.*,[2] proposed a flowchart depicting the pathogenesis of TUGSE, where recurrent trauma leads to alteration of tissue antigens or introduces toxins, micro-organisms, endogenous degradation products or foreign proteins into the tissues; either events could trigger a local immune reaction, mediated by T-cells. This reaction activates T lymphocytes and the production of some cytokines (IL-1, IL-5 y TNFα). Some authors have even reported a possible interaction among mast cells, release of eosinophil chemotactic factors and tissue eosinophilia. A previous study showed a lack of TGF-α and TGF-ß production by eosinophils infiltrating oral TUGSE lesions, and this may be why oral TUGSE lesions have a prolonged healing process and are often suspected as malignant lesions.[10]

Also the eosinophilic cells release aryl sulfates and histamines which inhibit slow-reacting substance of anaphylaxis and consequently prevent the basophils and mast cells degranulation. This ultimately leads to inhibition in the release of other mediators of inflammation by the mast cells. In addition, major basic protein which causes tissue destruction is also released by the eosinophils.[8]

In this case report, the traumatic agent identified is produced due to the fact the patient is edentulous in the molars zone, therefore as she is not a denture wearer, during mastication, a constant trauma inside the cheek is caused.

It has been suggested that TUGSE may be a CD30+ lymphoproliferative disorder.[11] CD30 is a transmembrane protein of the tumor necrosis factor (TNF) family. CD30 positivity is found in various lesions ranging from reactive conditions to T- or B-cell lymphomas.[1]

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CD30⁺ cells are observed in 42%–70% of TUGSE cases, while the number of cells has been variable. However, strong and homogeneous CD30 expression in most neoplastic cells is restricted to classic Hodgkin lymphoma, anaplastic large cell lymphomas, and primary cutaneous CD30 T-cell lymphoproliferative disorders.[1]

Ficarra *et al*.,[12] were the first to report a case in which CD30⁺ cells were found in an ulcerated lesion histologically resembling TUGSE. They suggested that TUGSE of the oral mucosa may represent the oral counterpart of cutaneous CD30+ lymphoproliferative disorder. However in 2003 Cepeda et al suggested that CD30⁺ cells are a component of a reactive rather than a neoplastic process.[13] Also in 2004 Alobeid *et al*,[14] described 3 cases, demonstrating by PCR the clonal expansion of CD30⁺ cells. They believed that the lesions they reported represented a subset of cases of TUGSE that share common features with primary cutaneous CD30+ lymphoproliferative disorders.

Hirshberg *et al*.,[7] reported that most cases of TUGSE are reactive; some, however, may harbor a dominant clonal T-cell population. Atypical histologic findings in addition to the presence of monoclonality can serve as a warning sign for a malignant lymphoid proliferation. The question of whether monoclonality indicates a true T-cell lymphoma of low-grade malignancy or a variant of a reactive lymphoproliferative process to some unknown stimulus has not been resolved. It has to be considered that CD30⁺ cells are also found in many non-neoplastic cutaneous disorders such as atopic dermatitis, adverse drug reaction, scabies and insect bites.[11]

Different therapeutic approaches have been tried for TUGSE and the most common is simple surgical excision with very low recurrence.[8] The use of antibiotics, topical, intralesional and/or systemic corticosteroids, curettage and cryosurgery have also been reported.[15] In the case presented above, a simple surgical excision was performed, no recurrence was observed after one year, suggesting that it is a reactive process instead of a neoplastic one.

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REFERENCES.

1. Shen WR, Chang JY, Wu YC, Cheng SJ, Chen HM, Wang YP. Oral traumatic ulcerative granuloma with stromal eosinophilia: A clinicopathological study of 34 cases. J Formos Med Assoc. 2015;114(9):881-5.

2. Sharma B, Koshy G, Kapoor S. Traumatic Ulcerative Granuloma with Stromal Eosinophila: A Case Report and Review of Pathogenesis. J Clin Diagn Res. 2016;10(10):ZD07-ZD09.

3. Elzay RP, Richmond V. Traumatic ulcerative granuloma with stromal eosinophilia (Riga-Fede's disease and traumatic eosinophilic granuloma). Oral Surg Oral Med Oral Pathol. 1983;55: 497–506.

4. Marszalek A, Neska-Dlugosz I. Traumatic ulcerative granuloma with stromal eosinophilia. A case report and short literature review. Pol J Pathol. 2011;62:172-5.

5. Salisbury CL,Budnick SD, Li S. T-cell receptor gene rearrangement and CD30 immunoreactivity in traumatic ulcerative granuloma with stromal eosinophilia of the oral cavity. Am J Clin Pathol. 2009; 132(5):722–7.

6. 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.

7. Hirshberg A, Amariglio N, Akrish S, 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(4):522-9.

8. Soyele O, Adesina O, Ladeji A, Kuye K, Owotade F. Traumatic ulcerative granuloma with stromal eosinophilia: Review of the literature and case report. Afr J Med Health Sci. 2017;16 (2):115-9.

9. Bhaskar, SN, Lilly GE. Traumatic granuloma of the tongue (human and experimental). Oral Surg Oral Med Oral Pathol. 1964; 18(2): 206–18.

10. Elovic AE, Gallagher GT, Kabani S, Galli SJ, Weller PF, Wong DT. Lack of TGF-alpha and TGF-beta 1 synthesis by human eosinophils in chronic oral ulcers. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996;81(6):672-81.

11. Kuriyama Y, Shimizu A, Toki S, Endo Y, Yasuda M, Motegi SI, Ishikawa O. Two cases of chronic oral ulcers effectively treated with systemic corticosteroid therapy: Circumorificial plasmacytosis and traumatic ulcerative granuloma with stromal eosinophilia. J Dermatol. 2019;46(1):48-51.

12. Ficarra G, Prignano F, Romagnoli P. Traumatic eosinophilic granuloma of the oral mucosa: a CD30+(Ki-1) lymphoproliferative disorder? Oral Oncol. 1997;33(5), 375–9.

13. Cepeda LT, Pieretti M, Chapman SF, Horenstein MG. CD30-positive atypical cells in common non-neoplastic cutaneous infiltrates rich in neutrophils and eosinophils. Am J Surg Pathol. 2003; 27(7): 912-918.

14. Alobeid B, Pan LX, Milligan L, Budel L, Frizzera G. Eosinophil-rich CD30+ lymphoproliferative disorder of the oral mucosa. Am J Clin Pathol. 2004;121:43-50

15. Chandra S, Raju S, Sah K, Anand P. Traumatic ulcerative granuloma with stromal eosinophilia. Arch Iran Med. 2014;17(1):91-94.

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