CASE REPORT

Traumatic ulcerative granuloma with stromal eosinophilia of the soft palate: An unusual clinical presentation

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INTRODUCTION

Traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) is a rare, self-limiting, benign lesion of the oral mucosa that is underreported in the dermatologic literature. TUGSE most commonly arises on the tongue and often clinically presents as an ulcer with indurated and raised borders with a yellow-gray fibrinous base. The lesion can be painless or present with mild-to-severe pain. TUGSE has a rapid onset, clinically mimicking more concerning malignant or infectious processes.

In this report, we present an unusual case of TUGSE, which developed on the soft palate, arising after a punch biopsy of a preexisting major aphthous ulcer.

CASE REPORT

A 51-year-old woman presented with a nonhealing soft palate ulcer that was clinically suspicious of malignancy. The ulcer was causing significant pain, making eating and swallowing difficult. She was unable to recall the duration of the lesion. Oral inspection revealed a 2- to 3-cm ulcer located on the left anterior pillar of the soft palate (Fig 1, A).

She had no tobacco use history, no history of trauma, no human papillomavirus infection risk factors, or negative chemotherapy and radiation history. Her medical history was noncontributory. There was no prior history of oral aphthous stomatitis and she denied any trauma in her mouth. The ulcer was extremely painful and was accompanied by difficulty in swallowing. Clinical differential included squamous cell carcinoma, infection (deep fungal, syphilis, viral, and tuberculosis), lymphoma, and a major aphthous ulcer. A punch biopsy showed mucosal spongiosis and ulceration with a mixed inflammatory infiltrate consisting of abundant neutrophils and lymphocytes (Fig 1, B-D). No pathogenic fungal organisms were identified on a periodic acid–Schiff with diastase stain. A diagnosis of a major aphthous ulcer was made. She was closely monitored over the following 3 weeks and the lesion persisted with central necrosis and raised rolled border immediately adjacent to the area of ulceration (Fig 2). A repeat punch biopsy was performed at the edge of the lesion, which showed a polymorphous inflammatory infiltrate composed of small lymphocytes, histiocytes, neutrophils, abundant eosinophils, and occasional plasma cells (Fig 3, A and C).

Additional immunohistochemical (IHC) workups included CD3, CD20, CD21, CD30, and CD56; ultimately, there were no signs of lymphoma. Periodic acid–Schiff with diastase, acid-fast bacilli, and Fite special stains were negative for microorganisms. IgG/IgG4 immunohistochemistry was negative for IgG4.
related pathology. Epstein-Barr encoded RNA in situ hybridization, spirochete-IHC, and herpes simplex virus-IHC provided no evidence of Epstein-Barr virus infection, treponemal infection, or herpes infection. S100 and CD1a immunostains were negative and suggested no evidence of Langerhans cell histiocytosis. Her ulcer slowly healed over the next 3 months (Fig 4).

The final diagnosis of TUGSE was made on the basis of clinicopathologic correlation and the histopathologic exclusion of more serious conditions.

**DISCUSSION**

TUGSE is most commonly present on the dorsal or lateral aspect of the tongue.\(^2\) It has also been identified on the lip, gingiva, vestibular mucosa, buccal mucosa, retromolar area, the floor of the mouth, and hard palate.\(^3\)\(^,\)\(^5\) In the case of our patient, TUGSE was identified on the soft palate. The etiology of TUGSE is not completely understood; however, the consensus is that trauma could play a contributory role. Although TUGSE has often been associated with trauma, >50% of cases present no evidence of such.\(^3\)\(^,\)\(^5\) In the case of our patient, the initial punch biopsy conducted on the major aphthous ulcer may have acted as a source of trauma, suggesting a potential etiology for the TUGSE lesion.

Microscopically, TUGSE lesions are characterized by polymorphic inflammatory infiltrates, including lymphocytes, histiocytes, plasma cells, large atypical mononuclear cells, and eosinophils that extend into the submucosa and muscle layers and infiltrate the salivary glands.\(^3\)\(^,\)\(^6\) The presence of eosinophils is antithetical to other forms of traumatic ulcers, which are devoid of this cell type.\(^3\) It is not fully understood why eosinophils are present, although some have
proposed that mucosal breakdown following trauma could lead to the introduction of an unknown antigen, leading to the subsequent production of eosinophils by the affected tissue.6,7 Numerous antigens have been suggested, including those with a viral, microorganismal, toxin, foreign protein, or degraded endogenous origin.1,4 Past literature proposed that atypical mononuclear cells had a macrophage, dendritic cell, histiocyte, or myofibroblast origin.3,4,5 Newer reports suggest T lymphocyte functionality, depicted via positive IHC against T cell markers; the majority of the mononuclear cells show CD30, CD3, and T cell intracytoplasmic antigen 1 positivity.3,4 The CD30+ cells identified in TUGSE lesions have been a matter of discussion. Some authors have suggested that TUGSE is a benign oral counterpart of cutaneous CD30+ lymphoproliferative disorders, whereas others have suggested that the CD30+ may be because of nonspecific T or B lymphocyte activation.3,4

Clinically, TUGSE may mimic, and thus must be differentiated from, malignant processes, such as squamous cell carcinoma and CD30+ lymphoproliferative disorder, or infectious processes, such as syphilis, tuberculosis, and Epstein-Barr virus mucocutaneous ulcer.1,3,5 As seen in this case, a clinical inspection of the lesion is often not sufficient to exclude malignancy, thus biopsy is indicated. It is also recommended to screen for the aforementioned infectious diseases.3

Management of TUGSE varies because variability in the length of healing ranges from days to months. Some authors have suggested that the slowed self-healing process that is occasionally seen in TUGSE is

Fig 3. A, A punch biopsy on the edge of the lesion shows a polymorphous inflammatory infiltrate containing lymphocytes, histiocytes, neutrophils, and eosinophils. B, Higher power view showing polymorphous inflammatory infiltrate containing lymphocytes, histiocytes, neutrophils, and eosinophils. C, Occasional plasma cells were present in the superficial connective tissue stroma. (A, B, and C, Hematoxylin-eosin stain; original magnifications: A, ×20; B, ×40; and C, ×20.)

Fig 4. Traumatic ulcerative granuloma with stromal eosinophilia lesion with significant healing 3 months after the initial consultation.
because of the production of cytokines, such as tumor necrosis factors that prolong the inflammatory response and perpetuate further tissue damage. It has also been suggested that eosinophils’ lack of significant production of TGF α and TGF β could explain the delayed healing properties seen with some TUGSE lesions. In many cases, TUGSE spontaneously resolves without the need for treatment. If traumatic agents are identified, they should be removed or avoided. The literature has shown that an incisional biopsy of a TUGSE lesion on the tongue and buccal mucosa can initiate the lesion’s complete resolution. Other treatments, such as corticosteroids (topical, systemic, or intralesional injection), antibiotics, 0.1% triamcinolone acetonide mouthwash, irradiation, electrocoagulation, and liquid nitrogen have been reported. If the ulcer does not resolve, it may require total excision. Because TUGSE is often a diagnosis of exclusion, clinical follow-up should take place after the lesion has resolved.

Conflicts of interest
None disclosed.

REFERENCES
1. Lakkam BD, Astekar M, Alam S, Saleem A. Traumatic ulcerative granuloma with stromal eosinophilia: a puzzle. J Oral Maxillofac Pathol. 2021;25(suppl 1):S42-S45. https://doi.org/10.4103/jomfp.JOMFP_321_20
2. Marszałek A, Neska-Długosz I. Traumatic ulcerative granuloma with stromal eosinophilia. A case report and short literature review. Pol J Pathol. 2011;62(3):172-175.
3. Benitez B, Müll J, Tzankov A, Kunz C. Traumatic ulcerative granuloma with stromal eosinophilia—clinical case report, literature review, and differential diagnosis. World J Surg Oncol. 2019;17(1):184. https://doi.org/10.1186/s12957-019-1736-z
4. Sarangarajan R, Vaishnavi Vedam VK, Sivadas G, Sarangarajan A, Meera S. Traumatic ulcerative granuloma with stromal eosinophilia—mystery of pathogenesis revisited. J Pharm Bioallied Sci. 2015;7(2):5420-5423. https://doi.org/10.4103/0975-7406.163474
5. Segura S, Romero D, Mascaro JM Jr, Colomo L, Ferrando J, Estrach T. Eosinophilic ulcer of the oral mucosa: another histological simulator of CD30 lymphoproliferative disorders. Br J Dermatol. 2006;155(2):460-463. https://doi.org/10.1111/j.1365-2133.2006.07331.x
6. 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):722-727. https://doi.org/10.1309/AJCPX35MSOVVLOP
7. Hirshberg A, Amanioglou N, Akrish S, et al. Traumatic ulcerative granuloma with stromal eosinophilia: a reactive lesion of the oral mucosa. Am J Clin Pathol. 2006;126(4):522-529. https://doi.org/10.1309/AFC0A406GB70N2Y64
8. 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):672-681. https://doi.org/10.1016/s1079-2104(96)80073-4