Case Report

Traumatic Ulcerative Granuloma with Stromal Eosinophilia

Sunira Chandra BDS MDS•[1], Srinivasa Raju BDS MDS[1], Kunal Sah BDS MDS[2], Prachi Anand BDS[1]

Abstract

Chronic ulcers of the oral mucosa are the lesions which a physician comes across frequently. "Eosinophilic Ulcer" is a rare variety of that. Eosinophilic ulcer or traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) is a chronic benign lesion of the oral mucosa and is a relatively recent delineated entity. Its etiopathogenesis is still uncertain but trauma seems to play a fundamental role. Clinically the lesion manifests as an isolated ulcer, showing a raised and indurated border in addition to a white or yellowish bed. Microscopically, it is characterized by diffuse polymorphic inflammatory infiltrate, rich in eosinophils, involving the superficial mucosa and the deeper muscle layer with epitheliod cells. Hereby, reporting a case of a 60-year-old female patient who presented with a chief complaint of non-healing painful ulcer on the tongue.

Keywords: Eosinophilic granuloma, eosinophilic ulcer, stromal eosinophilia, tongue, trauma, traumatic ulcer, traumatic ulcerative granuloma

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Introduction

Eosinophilic ulcer (EU) or traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) is a rare chronic benign lesion of the oral mucosa, which is self limiting.[1–3] It's etiopathogenesis is not obvious but trauma plays an important role in its development. Viral or toxic agent hypothesis is also been included in its development.[4–7] It is most frequently diagnosed in patients aged between 30 – 50 years. It can also occur in infants as well as in elderly people. Male to Female ratio is 1:1 or slightly more elevated in females. Most frequent location for EU is on the tongue but can occur in other locations as well (lips, buccal mucosa, palate, gingival and floor of the mouth).[8–9] Clinically, the lesion presents as an ulceration with mild indurated borders and yellow fibrinous base.[7] Microscopically, there is a polymorphic inflammatory infiltrate predominately of eosinophils and histiocytes, extending deep into the submucosal (muscle and even salivary glands). Mitosis is frequent, and in some instances shows a pseudolymphomatous aspect.[7,8] Many different therapeutic approaches for TUGSE have been reported in the literature but most frequently performed therapy is simple surgical excision and its recurrence is rare. [1,5] Topical steroids or mouthwashes can be also prescribed. Other therapeutic modalities include intralesional or oral corticosteroids, topical antibiotics, curettage and cryotherapy.[5,7]

Case Report

A 60-year-old female patient presented with a chief complaint of ulcer on the left side of the postero-lateral aspect of tongue since 30 days. She had mild pain due to which she had difficulty in eating. Also she injured her tongue by her left lower posterior tooth. No lymphadenopathy was appreciated and the patient was in good health. The patient gave history of tobacco consumption in crude form, 4 to 5 times daily, since she was 22 years old. Her past medical history was noncontributory. Intra-oral examination revealed an ulcerated lesion on the left postero-lateral surface of the tongue, measuring about 1.5 cm in diameter, with pale surrounding area. Its margins were indurated with yellow fibrinous base (Figure 1). It was firm in consistency and tender on palpation. Intra-oral hygiene was fair with generalized stains, calculus and attrition. 26 and 36 showed marked attrition with sharp edges. Diagnosis of traumatic ulcer was made and coronoplasty of sharp offending tooth was done.

Symptomatic treatment was planned and topical local anesthetic gel was prescribed to the patient for its application on the lesional area, twice daily with multivitamin supplements once daily. The patient was recalled after 2 weeks. No response to the treatment was observed even after 2 weeks. It was suspicious for malignancy and an excisional biopsy was performed. Histopathological analysis revealed epithelium ulceration with fibrinopurulent exudates overlying inflamed stroma chiefly composed of mixed infiltrate predominately eosinophils and epitheliod cells extending into submucosa. These cells exhibited pleomorphism, voluminous cytoplasm and nucleus with prominent nucleolus (Figures 2 and 3). Based on the histopathological features a definite diagnosis of an TUGSE or EUOM was established. Symptomatic treatment was again prescribed and the patient was again recalled after 2 weeks. Complete healing was observed after 2 weeks (Figure 4).

Discussion

Eosinophilic ulcer of oral mucosa (EUOM) is a unique and relatively recently delineated entity of the oral mucosa which is a lesion with uncertain nature, etiology, pathogenesis and treatment.[3,4] Other terms have been used to describe it such as traumatic granuloma of the tongue or traumatic ulcerative granulo-

Authors' affiliations: [1]Department of Oral Medicine & Radiology, Saraswati Dental College and Hospital, Faizabad Road, Lucknow, India, [2]Department of Oral Pathology & Microbiology, Saraswati Dental College and Hospital, Faizabad Road, Lucknow, India.

•Corresponding author and reprints: Dr. Sunira Chandra BDS MDS, Department of Oral Medicine & Radiology, Saraswati Dental College and Hospital, Faizabad Road, 233 Tiwari Ganj, Lucknow- 227105, Uttar Pradesh, India. Tel.: +91 9720168332, E-mail.: sunira_chandra1@yahoo.co.in.

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Table 1. Difference Between Eosinophilic, Traumatic and Malignant Ulcer

	Eosinophilic ulcer	Malignant ulcer	Traumatic Ulcer
Etiology	Obscure, reactive, inflammatory	Genetics	Traumatic
Clinical features	Usually solitary ulcer	Ulcer	Ulcer
	Induration, elevated and indurated borders	Deep ulcer with indurated raised borders ,exophytic or verrucous growth	No elevated borders
	Benign, self–limiting growth	Malignant, no self-limitation of growth	Benign
	Often asymptomatic	Asymptomatic in early stages	Symptomatic
	Fast healing after treatment	Ulceroproliferative growth and non-spontaneous healing	Fast healing after removal of traumatic agent
	Frequently on tongue	Tongue /oral mucosa	Oral mucosa
	Non–involvement of lymph nodes	Non–involvement of lymph nodes in early stages	Frequent involvement of lymph nodes
Histopathological findings	Intact, well differentiated epithelium through slightly hyperplasic, intense inflammatory cell infiltrate and pronounced eosinoiphilia	Loss of basement membrane and disturbed architecture of the basal layers of epithelium, replacement of basal cells by large irregular cell with cytoplasmic processes extending into connective tissue	Stratified squamous epithelium, hyperplastic or not, hyperkeratosis, consisting of granumolatous tissue and intense mixed inflammatory cell infiltrate
Treatment	Incisional biopsy, corticosteroids	Surgery, radiotherapy, quimiotherapy	Removal of traumatic agent

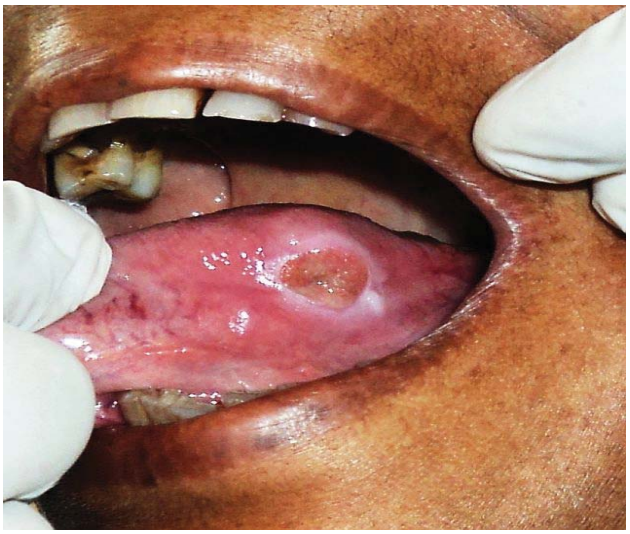

Figure 1. Clinical photograph of an ulcer located on the left postero-lateral surface of the tongue

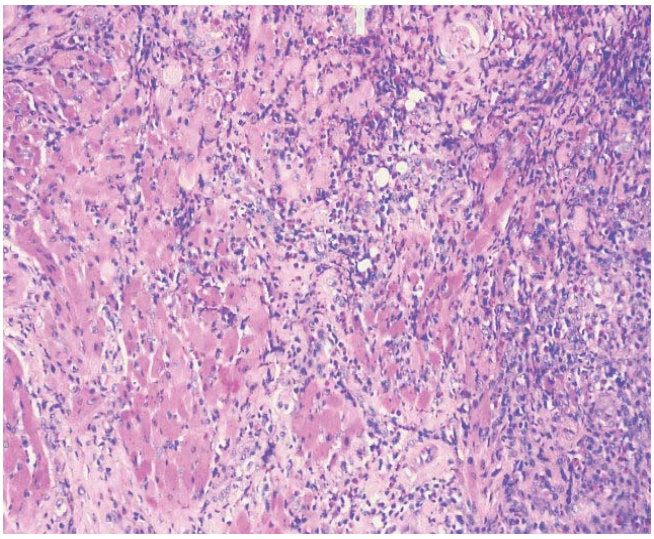

Figure 2. Photomicrograph showing diffuse polymorphic inflammatory infiltrate, rich in eosinophils, involving the superficial mucosa and the deeper muscle layer with epitheliod cells (H & E x10)

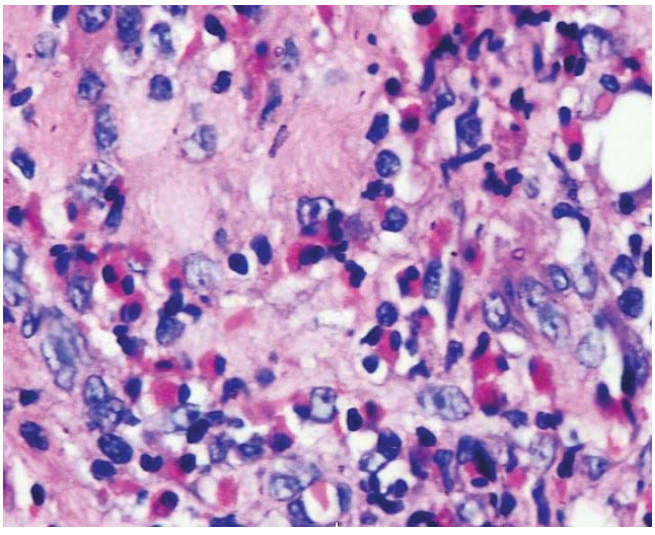

Figure 3. Photomicrograph showing presence of abundant eosinophils in lesional area (H & E x100)

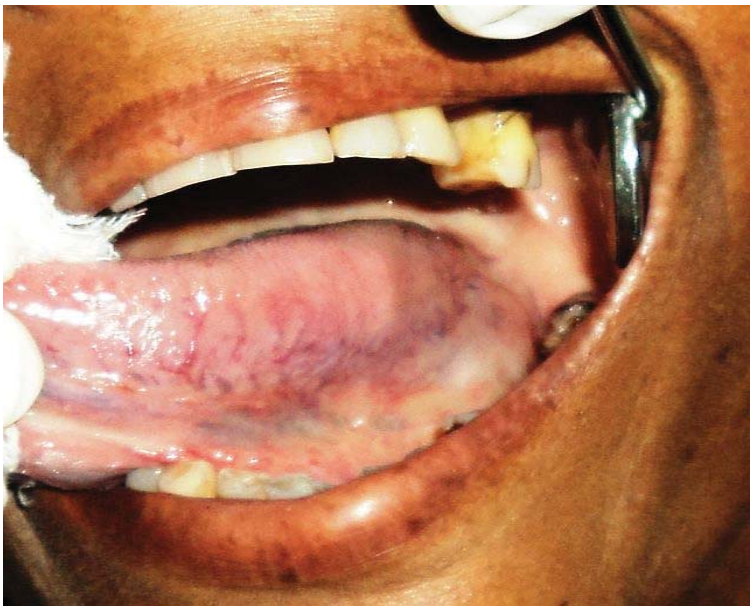

Figure 4. Clinical photograph showing healed ulcer (2 week follow-up)

ma with stromal eosinophilia, eosinophilic granuloma of tissue and atypical histiocytic granuloma. In infants it is called Riga-Fed disease.[4,7,9] The condition was first described in adults by Popoff in 1956. In 1970, this lesion was proposed as a distinct entity by Shapiro and Juhlin.[11] Since then, different names have been used to define it.[7,9]

According to Segura and Pujo the etiology of EUOM remains obscure, although most authors suggest that the lesions are of traumatic origin, caused by accidental bites or by repeated thrusting against sharp, misplaced or fractured teeth.[9] Vélez, et al. have suggested that trauma is only a contributing factor in the development of EUOM and could lead to viral or toxic agents entering the underlying tissue and cause an inflammatory response.[10] The increased incidence of this lesion on the tongue, which is easily exposed to trauma through mastication, and the definitive history of traumatic injury in one-third to one-half of reported cases agree with this hypothesis.[1,4,10]

Most of traumatic oral ulcers are devoid of eosinophils and contain polymorphous infiltrate. Several hypotheses have been proposed to explain the prominent eosinophilic infiltrates observed in EUOM. Role of cytokine and chemotactic factors released by eosinophils has been hypothesized in its development. A possible interaction among mast cells, release of eosinophil chemotactic factors and tissue eosinophilia has also been postulated. [9] Cell-mediated immunity may play an important role in its pathogenesis as it also contains T lymphocytic infiltrate.[3] However, its etiopathogenesis is still uncertain and its histogenesis remains controversial. Large atypical cells in TUGSE infiltrate showed immunophenotypic towards myofibroblastic or histiocytic origin.[1,4,8] Elovic, et al. showed lack of significant synthesis of transforming growth factor by eosinophils, which can explain the delayed healing characteristic of TUGSE.[11]

It is reported that EUOM exhibits a slight female predominance in most of the cases with a peak incidence between the sixth and seventh decades of life.[5,9] This lesion also shows a bimodal age distribution, with the first peak occurring at early childhood and the second during the fiftieth decade of life. Lymphadeonapathy can be observed in extremely rare cases.[3] In our case EUOM occurred in almost same decade of life but in a male patient, without lymphadeonapathy.

Clinically tongue is the most commonly affected site, which seems reasonable since movement makes it more vulnerable to trauma.[4,9,12] However, an absolute linkage between trauma and the development of such lesions wasn't found in all studies.[9,10] Other oral sites such as buccal mucosa, lip, floor of the mouth or the palate have been previously reported to be involved in this condition.[1,14] Clinically, it manifests as a rapidly developing solitary ulcer with elevated or indurated borders. It can range from few millimeters to several centimeters in its diameter.[1,8,9] In infants, it is usually observed on the ventral surface of the anterior tongue secondary to trauma from newly erupted primary teeth, and is referred as Riga-Fede disease.[4,7,9] According to Vélez, et al.[10] and Alobeid, et al.[14] it is symptomatic (17 % – 100 %). 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 and because of its rapid growth and indurated borders it can mimic squamous cell carcinoma[13,14] and that is where this condition became important.

In our case, a solitary ulcerated lesion was present on the left postero-lateral surface of the tongue, measuring about 1.5 cm in diameter, with pale surrounding area. Its margins were indurated with yellow fibrinous base. It was firm in consistency and tender on palpation.

The differential diagnosis of ulcerative lesions of the tongue should also include traumatic ulcers, specific infections such as primary syphilis, lymphoma, metastasis, and reactionary proliferative processes such as atypical histiocytic granuloma and proliferative myositis, squamous cell carcinoma. The mainstay feature to distinguish eosinophilic, traumatic and malignant ulcer is highlighted by Goncales et al.[15], Table 1.

Microscopically, under an ulcerated mucosa, a poorly formed granulation tissue showing an increased number of capillaries with prominent endothelial cells is usually observed. A dense diffuse submucosal polymorphous inflammatory infiltrate involving occasionally the overlying epithelium is usually noted.

This infiltrate tends to extend to the deeper underlying soft tissue, muscle fibers and salivary gland. The inflammatory infiltrate is composed of small round lymphocytes, abundant polymorphonuclear eosinophils and other inflammatory cells [neutrophils, plasma cells and histiocytes]. Large mononuclear cells with round to avoid pale nuclei, showing occasional nuclear atypia, intermingled in the inflammatory infiltrate are also frequently observed.[5,8,9] Same histopathological features were observed in the present case. These epithelioid cells were anti-CD68 positive.[3,4,13]

Many different therapeutic approaches for EUOM have been reported in literature. Several therapeutic options for EU of oral mucosa in adults has been described e.g. wait-and-see approach, antibiotics, topical, intralesional and/or systemic corticosteroids, curettage, cryosurgery and surgical excision. The most frequently performed therapy is simple surgical incision/excision. This approach seems to be especially recommended in cases with persistent lesions. No further local recurrences are usually noted after excision. [15–17] In our case simple excision was preformed and a rapid improvement of the ulcer was seen similarly to what was described by other authors.[6,7,9] Elovic et al.[11] observed a lack of significant synthesis of transforming growth factor beta by eosinophils, which explains the delayed healing observed in EUOM.

In conclusion, diagnosis of EUOM is made by the combination of clinical and histopathological features. The pathogenesis of this condition remains uncertain and its histogenesis still remains controversial. Eosinophilic ulcer of the oral mucosa is characterized by rapidly growing ulcers with indurated borders that outline a wide clinical differential diagnosis. This condition is characteristically self-healing with a benign course.

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References

1. Regezi JA, Zarbo RJ, Daniels TE, Greenspan JS. Oral traumatic granuloma. Characterization of the cellular infiltrate. *Oral Surg Oral Med Oral Pathol*. 1993; **75(6):** 723 – 727.
2. Alobeid B, Pan LX, Milligan L, Budel L, Frizzera G. Eosinophil-rich CD30+ lymphoproliferative disorder of the oral mucosa. A form of "traumatic eosinophilic granuloma". *Am J Clin Pathol*. 2004; **121(1):** 43 – 50.
3. 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(6):** 716 – 722.
4. 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 – 379.
5. Gao S, Wang Y, Liu N, Li S, Du J. Eosinophilic ulcer of the oral mucosa: a clinicopathological analysis. *Chin I Dent Res*. 2000; **3(1):** 47 – 50.
6. Mezei MM, Tron VA, Stewart WD, Rivers JK. Eosinophilic ulcer of the oral mucosa. *J Am Acad Dermatol*. 1995; **33:** 734 – 740.
7. Boffano P, Gallesio C, Campisi P, Roccia F. Traumatic ulcerative granuloma with stromal eosinophilia of the retromolar region. *J Craniofac Surg*. 2009; **20(6):** 2150 – 2152.
8. Eleni G, Panagiotis S, Andreas K, Georgia A. Traumatic ulcerative granuloma with stromal eosinophilia: a lesion with alarming histopathologic presentation and benign clinical course. *Am J Dermatopathol*. 2011; **33(2):** 192 – 194
9. Segura S, Pujol RM. Eosinophilic ulcer of the oral mucosa: a distinct entity or a non-specific reactive pattern? *Oral Dis*. 2008; **14(4):** 287 – 295.
10. Vélez A, Alamillos FJ, Dean A, Rodas J, Acosta A. Eosinophilic ulcer of the oral mucosa: report of a recurrent case on the tongue. *Clin Exp Dermatol*. 1997; **22(3):** 154 – 156.
11. 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 – 681.
12. Shapiro L, Juhlin EA. Eosinophilic ulcer of the tongue report of two cases and review of the literature. *Dermatologica*. 1970; **140(4):** 242 – 250.
13. Ficarra G, Prigano F, Romagnoli P. Traumatic eosinophilic granuloma of the oral mucosa: a CD30 (Ki-1) lymphoprolifeative disorder. *Oral Oncology*.1997; **33:** 375 – 379.
14. Bouquot JE, Muller S and Nikai H. Lesions of the oral cavity In: GNEP DR, eds. Diagnostic Surgical Pathology of the Head and Neck. Philadelphia: Saunders, 2009; 267 – 277.
15. Gonçales ES, Rubira-Bullen IF, Rubira CM, Miyazawa M, Chinellato LE, Consolaro A. Eosinophilic ulcer of the oral mucosa versus squamous cell carcinoma. *Quintessence Int*. 2007; **38(8):** 677 – 680.
16. Ada S, Seckin D, Tarhan E, Buyuklu F, Cakmak O, Arikan U. Eosinophilic ulcer of the tongue. *Australas J Dermatol*. 2007; **48(4):** 248 – 250.
17. 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 – 529.