Case Report

# Eosinophilic ulcer of the tongue masquerading as malignant ulcer: An unexplored distinct pathology

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**Abstract**

Eosinophilic ulcer (EU) is a rare self-limiting chronic benign ulcerative lesion of the oral mucosa often misdiagnosed as oral malignancy. Its etiopathogenesis is ambiguous, but trauma plays an important role in the development. Microscopically, it is characterized by a polymorphic inflammatory infiltrate with a prominent eosinophilic component and large mononuclear cells extending deep into the submucosa, underlying muscle and salivary glands. We discuss a case of EU in a 55-year-old male, which presented with a symptomatic nonhealing ulcer on the right lateral border of the tongue and was further clinically misdiagnosed as malignant ulcer.

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

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## INTRODUCTION

Eosinophilic ulcer (EU) of the oral mucosa (EUOM) is considered to be a reactive and a self-limiting disorder with a benign clinical course.[1] EUOM has been known by different terms including EU, eosinophilic granuloma of tissue, traumatic granuloma, atypical histiocytic granuloma and traumatic ulcerative granuloma with stromal eosinophilia. In infants, it has been called as Riga–Fede disease.[2,3] We report a rare case of EU which was misdiagnosed as malignant ulcer. Its clinicopathological characteristic which is crucial for its accurate diagnosis and appropriate treatment is also been discussed.

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## CASE REPORT

A 55-year-old male patient presented with a chief complaint of painful nonhealing ulcer on the right lateral border of the tongue since 2 months. He has twice visited the local dentist for its treatment but was not relieved. He denied any other physical or chemical injuries. He also gave a history of tobacco intake in crude form with lime, 4–5 times a day regularly for 23 years. His medical history was noncontributory.

No extraoral abnormality was detected. Intraoral examination revealed a solitary ulcer measuring about 1.2 cm × 1 cm in diameter, roughly oval in shape with elevated and indurated borders on the right posterolateral



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border of tongue. The ulcer showed slightly elevated and indurated borders with yellowish fibrinous base [Figure 1]. His oral hygiene was poor with generalized attrition, stains, calculus and carious/grossly carious teeth. Sharp cuspal edges were appreciated in 45 and 47 and coronoplasty of sharp offending tooth was performed. As the patient also falls into the high-risk group category, a clinical differential diagnosis of traumatic ulcer and malignant ulcer, and a provisional diagnosis of malignant ulcer was made. Routine hemogram was within normal limits. An excisional biopsy was performed under local anesthesia. The biopsy tissue was routinely processed and was stained with Hematoxylin and Eosin.

Histopathological analysis revealed an ulcerated stratified squamous epithelium overlying dense mixed inflammatory cell infiltrate predominantly consisting of eosinophils, followed by lymphocytes and epithelioid cells extending deep into submucosa [Figures 2 and 3]. These cells exhibited pleomorphism with voluminous cytoplasm [Figure 4]. Based on these classical features, a diagnosis of EU was made. Wait-and-see approach was followed and the ulcer itself resolved spontaneously within 2 weeks.

## DISCUSSION

Popoff (1956) first described the EUOM in adults. First reported in the 1960s and some authors also proposed the term ulcerated granuloma eosinophilicum diutinum of the tongue.[1] In 1970, Shapiro and Juhlin proposed this as a distinct entity. Since then, different names have been used to define this process, leading to further confusion.[1,4] The pathogenesis of EU is poorly understood may be because of limited data available to elucidate its origin. Epidemiological data suggests following factors may play a vital role in its development:[4-7]

1. Trauma
    a. A traumatic event is recorded in a variable proportion of EU cases

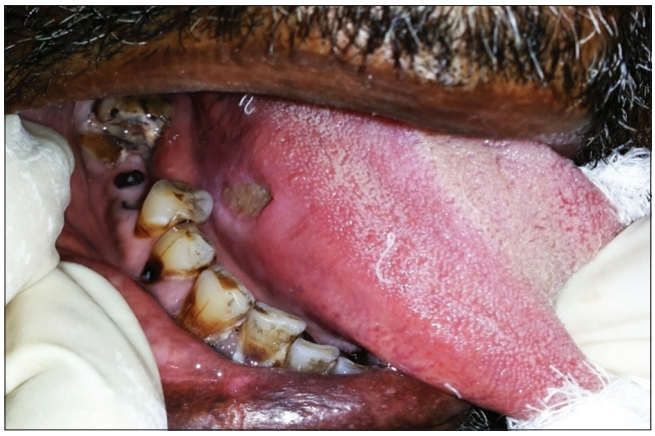

**Figure 1:** Solitary ulcer showing elevated and indurated borders on right posterior-lateral border of tongue with yellowish base

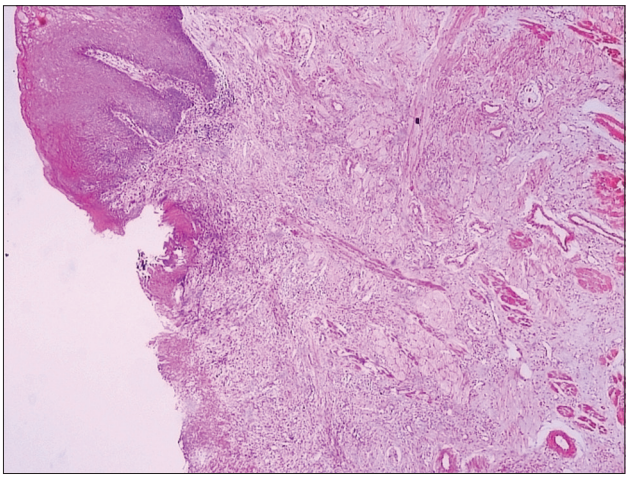

**Figure 2:** Ulcerated stratified squamous epithelium overlying dense polyinflammatory infiltrate (H & E, ×10)

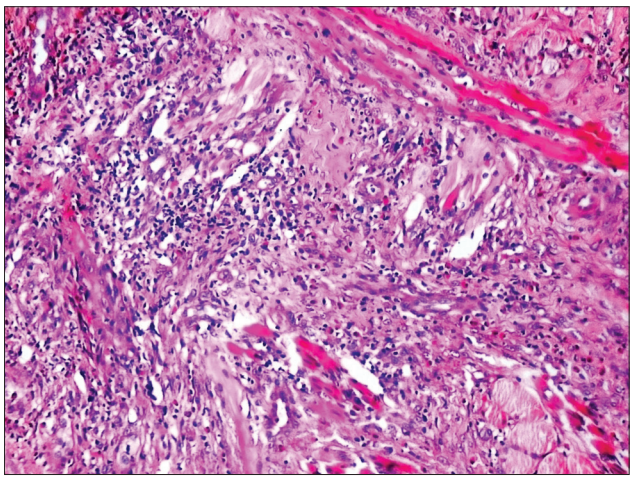

**Figure 3:** Polyinflammatory infiltrate predominantly encomprising eosinophils, lymphocytes and mast cells extending to the underlying deeper stroma (H & E, ×20)

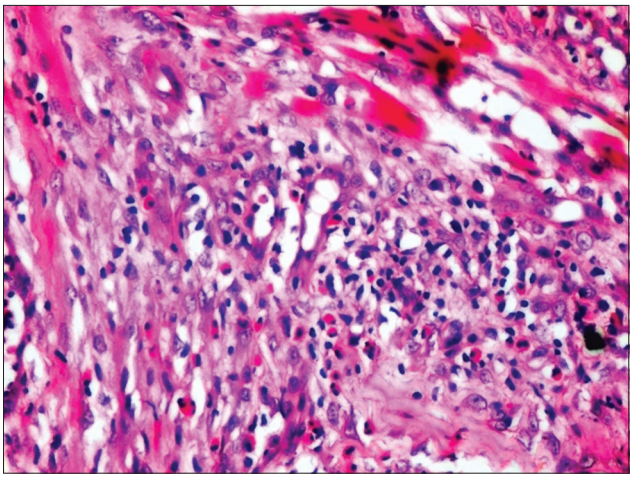

**Figure 4:** Epithelioid cells exhibiting pleomorphism with voluminous cytoplasm (H & E, ×40)

   b. The lesions are frequently located on the tongue where traumatisms are frequent
   c. Two peaks of age incidence have been identified, one peak during the first 2 years of life, in the context of nursing and teething, and another among the sixth decade, when missing and malposed teeth, as well as dental appliances and dentures may be more common.
2. Viral or toxic agents could be implicated. However, different attempts have failed to demonstrate viral particles and/or ultrastructural dense immune deposits in clear-cut cases of EU
3. Role of cytokine and chemotactic factors released by eosinophils in the development of EU has been hypothesized
4. An increase in mast cells (intact and degranulating) and a possible interaction between mast cell, a release eosinophil chemotactic factors and tissue eosinophilia has also been postulated
5. T-lymphocytes infiltrate suggests cell-mediated immunity may play a significant role in its pathogenesis
6. Lack of significant synthesis of transforming growth factor by eosinophils, which explains the delayed healing trait of EU.

EUOM seems to be an umbrella term covering a spectrum of disorders with diverse cells of origin. Nevertheless, the histogenesis of EUOM remains controversial.[8] In the present case, we also consider that the trauma plays an important role in its pathogenesis, due to injury to the tongue by 45 and 47.

It shows a bimodal age distribution, with the first peak occurring in early childhood and the second during the sixth decade of life. Clinically, it usually manifests as a rapidly developing solitary ulcer, white to yellowish base, from few millimeters to several centimeters in diameter, with elevated and hard borders. Any mucosal surface can be affected; however, the tongue is the most common location, accounting for more than half the patients, followed by buccal mucosa, mucobuccal fold, lips, gingiva, palate, floor of the mouth and retromolar area.[1,4]

The differential diagnosis of EUOM includes major apthous ulcers, Wegener's granulomatosis, syphilis, histiocytosis X, histoplasmosis, tuberculosis, discoid lupus erythematosus, lymphoma, salivary gland tumors and squamous cell carcinoma.[1,4] Major trait to distinguish eosinophilic, traumatic and malignant ulcer is highlighted in Table 1.[1]

Histologically, EUOM shows polyinflammatory cell infiltrate predominantly encomprising eosinophils, followed by lymphocytes and mast cells with a large mononuclear cells with round to ovoid pale nuclei, showing occasional nuclear atypia, extending deeper to underlying soft tissue, muscle fibers and salivary gland.[1] These epithelioid cells showed variable positive for Macrophage marker, Dendritic cell marker, Factor XIIIa and Myofibroblast markers.[9,10]

Spontaneous healing usually occurs within a month, but may rarely take as long as few months. Most cases of EU heal without any complications or recurrence. Recurrence is rarely reported and these cases should be subjected to immunohistochemical analysis for CD30 marker clonality because monoclonal cases need long-term follow-up.[9,10] Beside surgical excision other cited treatment/therapies are summarized in Table 2.[4,6]

EUOM is a rare self-limiting chronic benign ulcerative lesion often misdiagnosed as oral malignancy. Its histogenesis remains controversial, but trauma plays an important role

**Table 1: Difference between eosinophilic, traumatic and malignant ulcer**

| | EUOM | 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 nonspontaneous healing | Fast healing after removal of traumatic agent |
| | Frequently on tongue | Tongue/oral mucosa | Oral mucosa |
| | Noninvolvement of lymph nodes | Noninvolvement 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, intense mixed inflammatory cell infiltrate |
| Treatment | Incisional biopsy, corticosteroids | Surgery, radiotherapy, chemotherapy | Removal of traumatic agent |

EUOM: Eosinophilic ulcer of the oral mucosa

**Table 2: Therapeutic options for eosinophilic ulcer of the oral mucosa**

| |
|---|
| Wait-and-see approach |
| Surgical excision |
| Topical/intralesional/systemic corticosteroids |
| Curettage |
| Antibiotics |
| Cryosurgery |

in its pathogenesis. It is generally a self-limiting disorder, and surgical excision or incision resolves it spontaneously with in few weeks. Histopathological evaluation is essential for its definite diagnosis.

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## Conflicts of interest

There are no conflicts of interest.

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