Eosinophilic Ulcer of the Tongue – Clinico-Pathological Analysis

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ABSTRACT

Eosinophilic ulcer is an uncommon self limiting lesion, clinically manifest as a solitary ulceration with elevated indurated border affecting the tongue. The etiology remains obscure, although trauma plays a major role. Clinically it closely mimics malignant ulcer and traumatic ulcer cause difficulty in diagnosis and can lead to over diagnosis. Aim to study & discuss a series of cases of eosinophilic ulcer of tongue with a clinicopathological analysis. Ten cases of eosinophilic ulcers were analyzed clinically with a detailed history. H & E stained sections were obtained to 3-4 µm thickness were obtained to study the detailed histopathology. Patients reported with a pain (8/10) & non healing ulcer (2/10) with a mean age of 52 years & an equal distribution among both the sexes. Solitary ulcers varying in size from 1-3 cms in diameter were seen on the posteriolateral border of tongue with indurated, erythematosus margins & existed with the duration from few days to several months. Patient had history of tobacco usage (2/10) & an adjacent sharp cusp tooth (4/10). The provisional diagnosis was either traumatic ulcer or malignancy. Incisional biopsy was performed & histopathological examination revealed an ulcerated epithelium and inflammatory infiltrate comprised of lymphocytes, histiocytes and predominantly eosinophils in the stoma. The inflammatory cells extended deep into the muscle fibers. Eosinophilic ulcer was confirmed. None of the patients reported & uneventful healing was seen within 1-2 months. Eosinophilic ulcer is a histopathological diagnosis; biopsy helps to confirm and also aids in differentiate it from other lesions ranging from reactive, granulomatous to malignancy.

KEYWORDS: Eosinophils, eosinophilic ulcer, histiocytes, malignancy, tongue, trauma

INTRODUCTION

Eosinophilic ulcer is a rare benign, chronic self limiting lesion of tongue. The exact etiopathogenesis is unknown, but trauma is an important factor inducing the ulcer development, rarely viral or toxic agents are also considered in the etiology. The common age group affected is 30 to 50 years with the male to female ration 1:1 or slightly more common in females [1, 2]. Buccal mucosa is the commonest site affected followed by tongue, lips, palate, gingival and floor of the mouth. Clinically, the lesion presents as a non healing ulcer, leading to discomfort with difficulty in chewing and talking. Usually ulcer has indurated border and the base is covered with fibrin [3] Microscopically, the epithelium is discontinuous with pseudo epitheliomatous hyperplasia and polymorphous neutrophils in the ulcerated region. Also lymphocytes, histiocytes and predominantly eosinophils are seen the stroma. These inflammatory cells are infiltrating deep into the submucosal layer leading to delay in the healing process [1-3].

Clinically EU mimics from traumatic ulcer to malignant ulcer especially when associated with the tobacco habit history. Biopsy is mandatory to rule out the suspicion of malignancy. Here we report an institutional review of ten cases of EU of tongue with the brief review of literature and the addition ten new cases of EU to the literature.

CASE REPORT

Diagnosed cases of EU were retrieved from department of Oral Pathology, SDM College of Dental Sciences, Dharwad. Ten cases having characteristic histopathological features were included in the study. Table 1 describes the details of ten cases. 3-4 µ thickness hematoxylin and eosin stained sections were obtained to study the detailed histopathology.
### Table 1. Demographic and clinical findings in cases of Eosinophilic ulcer of Tongue

<table>
<thead>
<tr>
<th>Sl. no</th>
<th>Age (in yrs)</th>
<th>Sex</th>
<th>Sign &amp; symptom</th>
<th>History of Habit &amp; sharp cusp</th>
<th>Site</th>
<th>Duration</th>
<th>Clinical presentation</th>
<th>Size of ulcer</th>
<th>Provisional diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>M</td>
<td>Pain</td>
<td>Tobacco chewing, 3times/day, since 10 yrs</td>
<td>Left Posterior lateral border</td>
<td>15 days</td>
<td>Solitary with indurated margin</td>
<td>1x1 cm</td>
<td>Traumatic ulcer/ Carcinoma of tongue</td>
</tr>
<tr>
<td>2</td>
<td>55</td>
<td>F</td>
<td>Pain</td>
<td>None Sharp cusp 48</td>
<td>Right, Posterior lateral border</td>
<td>8 days</td>
<td>Solitary with indurated margin</td>
<td>3x3 cm</td>
<td>Traumatic ulcer</td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>F</td>
<td>Pain</td>
<td>None Decayed 48</td>
<td>Right, Posterior lateral border</td>
<td>1 month</td>
<td>Solitary, with erythematous border</td>
<td>2x2 cm</td>
<td>Traumatic ulcer</td>
</tr>
<tr>
<td>4</td>
<td>73</td>
<td>M</td>
<td>Non healing ulcer</td>
<td>None</td>
<td>Right, Posterior lateral border</td>
<td>6 months</td>
<td>Solitary with indurated &amp; evereted margin</td>
<td>2x2 cm</td>
<td>Traumatic ulcer/ Carcinoma of tongue</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>F</td>
<td>Pain</td>
<td>None</td>
<td>Right, Posterior lateral border</td>
<td>2 months</td>
<td>Solitary with raised border</td>
<td>2x2 cm</td>
<td>Traumatic ulcer</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>F</td>
<td>Non healing ulcer</td>
<td>None Decayed 37</td>
<td>Left Posterior lateral border</td>
<td>15 days</td>
<td>Solitary with indurated margin</td>
<td>1x 2.5 cm</td>
<td>Traumatic ulcer/ Carcinoma of tongue</td>
</tr>
<tr>
<td>7</td>
<td>55</td>
<td>F</td>
<td>Pain</td>
<td>None</td>
<td>Left Posterior lateral border</td>
<td>20 days</td>
<td>Solitary, with irregular erythematous margin</td>
<td>2x 1 cm</td>
<td>Carcinoma of tongue</td>
</tr>
<tr>
<td>8</td>
<td>53</td>
<td>M</td>
<td>Pain</td>
<td>Sharp cusp 18</td>
<td>Right, Posterior lateral border</td>
<td>20 days</td>
<td>Solitary, everted &amp; indurted margin</td>
<td>3x1cm</td>
<td>Traumatic ulcer/ Carcinoma of tongue</td>
</tr>
<tr>
<td>9</td>
<td>34</td>
<td>M</td>
<td>Pain</td>
<td>None</td>
<td>Left Posterior lateral border</td>
<td>2 months</td>
<td>Solitary, oval with regular margin</td>
<td>2x 1 cm</td>
<td>Traumatic ulcer</td>
</tr>
<tr>
<td>10</td>
<td>58</td>
<td>M</td>
<td>Pain</td>
<td>Pan &amp; betel quid chewing 4-5 times/day- 15yrs</td>
<td>Right, Posterior lateral border</td>
<td>3 months</td>
<td>Solitary, with irregular erythematous margin</td>
<td>1x1 cm</td>
<td>Traumatic ulcer/ Carcinoma of tongue</td>
</tr>
</tbody>
</table>

All the patients reported to the hospital with complain of pain (8/10) and non-healing ulcer (2/10). Patient’s age ranged from 34 years to 73 years (mean age - 52 years) with the male and females equal distribution. All the lesions were restricted to posterior lateral border of tongue. Ulcer presented as a solitary lesion with indurated, erythematous margin. Duration of the ulcer ranged from few days to several months and size varied from 1x1cm to 3x3cms. Two patients had a history of tobacco usage and four reported with adjacent sharp tooth.

At the time clinical examination the provisional diagnosis was either traumatic ulcer or malignant ulcer. Systemic and medical history was noncontributory. All the patients had submandibular lymph nodes enlarged and three had tenderness on palpation. Incisional biopsy was performed to arrive at a confirmative diagnosis.

Histopathological examination revealed ulcerated area covered with fibrinous exudates and mixed inflammatory cell infiltrate (Fig.1). The stroma chiefly composed of eosinophils, lymphocytes and occasional histiocyte. The inflammatory infiltrate extended deep into muscle fibers and adipose tissue (Fig.2). Degeneration of muscle fiber, degranulation of eosinophils, increased capillaries lined by plump endothelial cells was also seen. None of the patients reported with recurrence and uneventful healing was seen within one to two months.
DISCUSSION

To our knowledge, this is the first large series of cases of EU of tongue in the English language literature and PubMed search. The largest report is five cases by Movassaghi K et al [3]. EU is self limiting ulcerative lesion, with the peak incidence between 5th and 6th decade. This lesion also shows a bimodal age distribution with first peak (referred as Riga–Fede disease) occurrence at the first peak occurring at childhood and second during the 5th decade of life. In the present review the age distribution was 34yrs to 73yrs with a mean age of 52years. In the current series there was an equal distribution were observed among male and female, Elzay et al also reported slight female predominance in contrast to an equal distribution reported by El-Mofty [1, 2] Clinically EU manifested as a solitary ulcer, with diameter 1cm to larger size of 3cms in diameter. With elevated borders arising mainly in the tongue (posterior lateral and dorsal surface) followed by buccal mucosa. Similar clinical findings have been noted by various authors [1,4,5].

Patients reported to the hospital either due to the pain (8/10) or non healing ulcer (2/10). Pain is the persistent features of any oral ulcer, also approximately one third of cases of EU presents with pain or tenderness. All the ulcers were painful, solitary with indurated or erythematous margin with regular to irregular border [5]. In addition rarely multiple lesions are also been reported [5,6].

Clinically these lesions mimic traumatic ulcer due to the history of trauma, as tongue being the common site or has resemblance malignant ulcer due to delay in the healing process, indurated margin and presence of history of habit. Here indurated margin is because of proliferating epithelium at the margin of the ulcer. Tongue carcinoma is reported even without the history habitual use of tobacco, in such cases HPV is the factor; trauma would be the etiological factors [5,7].

EU is a histopathological diagnosis rather clinical and the histopathological features would help to distinguish between the reactive lesions from a malignant. Microscopically, an ulcerated mucosa with a polymorphic inflammatory infiltrate including lymphocytes and abundant eosinophils and are seen extending into deeper tissues like muscle fibers and salivary glands. Other inflammatory cells like plasma cells and histiocyte are also seen [8,9]. Usually oral traumatic ulcers are devoid of eosinophils, but EU is considered as hypersensitive host tissue response to tissue injury or reaction to unknown antigen. Etiology of EU remains obscure but trauma is considered as a contributing factor, 51% of the reported cases have shown coexistence. Only four cases had a history of sharp tooth or irritation from the adjacent tooth. Previously documented cases of eosinophilic ulcers are seen to be associated with trauma [10,7,6,11,12].

Recently Elvoc et al demonstrated the lack of expression transforming growth factor in eosinophils of EU may play a crucial role in the impaired healing, in contrast normal healing process. The eosinophils in lesions also generate many inflammatory and regulatory cytokines like tumor necrosis factor which can further enhance the tissue damage [11]. Also the possible interaction of mast cells, release of eosinophilic chemotactic factors and tissue eosinophilia has also been postulated. Abraham et al has demonstrated the cytotoxic T cell activity in all his cases, suggesting the role of cytotoxic T cells and cell mediated immunity in the pathogenesis of EU [9].

We did not carry out the immunohistochemistry as there is no precise marker. Various studies shows immunohistochemically these cells are positive for macrophage marker CD 68, dendritic cell marker, factor XIIIa, myofibroblastic marker such as vimentin, CD30, CD3, CD4 and CD8 [4]. CD30 positive expression in EU represents a spectrum of lymphoproliferative disorder, angiolymphoid hyperplasia with eosinophilia and atypical histiocytic granuloma [13]. Regezi et al demonstrated large mononuclear cells were positive for macrophage marker.
CD68 or dendrocyte marker factor XIII, with a few submucosal S100 positive cells [8]. Ficarra et al and Alobeid et al described CD30 positive atypical large mononuclear cells leading to the conclusion of EU could be included in the spectrum of CD30 lymphoproliferative disorders [14, 15]. El--Mofty et al reported the atypical large cells were positive for vimentin and lacked expression of lymphoid and histiocytic marker suggesting these may represent myofibroblast [2].

Exact treatment protocol unknown varies from antibiotic to surgical excision. Spontaneous healing occurs usually within one month, but may rarely take as long as eight months. Conservative surgical excision with clean margin or sometimes an incisional biopsy may lead to complete recovery and also will useful in diagnosis. Topical as well as systemic prednisone is an effective in the treatment [5,16]. Etiological identification followed by correction of the sharp or restored teeth & prosthesis is mandatory. As EU shows very rarely recurrence, similarly none of our cases showed recurrence and healed within one to two months.

CONCLUSION

We conclude that, EU is a self healing reactive lesion of the oral cavity which is of unknown etiology although trauma is etiological factor. But it is important to identify or diagnose histopathologically as clinically it mimics malignant lesion. Biopsy is the important investigation to confirm the diagnosis and also it initiates the healing process in eosinophilic ulcer. It is easy to establish the diagnosis when the clinical and histopathological features are correlated to avoid an unnecessary and a more radical surgery.

REFERENCES


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