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EOSINOPHILIC ULCER OF THE TONGUE MIMICKING A MALIGNANT ULCER- A DIAGNOSTIC CONUNDRUM

Surgery

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ABSTRACT

Eosinophilic ulcer of the oral mucosa (EUOM) is a non malignant, rare ulcerative lesion with unknown pathogenesis that affects the oral mucosa, predominantly the tongue. In this study, we describe a case of a 76 year-old female with a one month history of a painful ulcer on the left lateral side of her tongue. The ulcer had everted margins with induration and there was no evidence of regional lymph node involvement. Radiological evaluation showed features suggestive of a malignant lesion with bilateral cervical nodes involvement. Histopathological examination showed basal cell hyperplasia with inflammatory cells,lymphoid follicles with an abundance of eosinophils. No evidence of malignancy was noted. Based on the patient's history and biopsy findings, a final diagnosis of eosinophilic ulcer of the oral mucosa was made.

KEYWORDS

carcinoma, eosinophilic ulcer, tongue, eosinophils

INTRODUCTION:

In clinical practice, eosinophilic ulcer of the oral mucosa (EUOM) is an uncommon and benign lesion encountered, that usually affects the tongue. The etiopathogenesis of eosinophilic ulcers is still unknown, and they might be challenging to diagnose clinically since they resemble malignancy. EUOM is also known as traumatic ulcerative granuloma with stromal eosinophilia (TUGSE), atypical histiocytic granuloma, traumatic granuloma, and eosinophilic granuloma of the tongue. Often, it gets resolved by itself.[1] It's also referred to as infantile Riga-Fede sickness in children.[2] Not all traumatic ulcers show the same histological presence of lymphocytes and eosinophils as EUOM, despite the fact that trauma is estimated to be a contributory factor in about 33% of cases. As a result, it has been suggested that trauma may offer a channel through which viruses or toxic proteins could enter into the tissue and trigger the inflammatory response that is characteristic of the vulnerable population.[3] Additionally, this could also mimic a lymphoma variant known as CD30+ lympho-proliferative illness.[4] This case report describes a situation in which an eosinophilic ulcer was misdiagnosed as a malignant ulcer and how histo-pathological confirmation assisted in making the correct diagnosis.

CASE REPORT:

A 76 year old female, presented to the General Surgery OPD with a non healing ulcer over the lateral border of tongue for 1 month. She had occasional pain aggravated on eating food. She denied history of trauma or sharp tooth. Oral cavity examination revealed fair oral hygiene, with a few dental caries and missing tooth. A 2x1 cm non tender ulcerative lesion over left lateral border of tongue approximately 5cm from tip of tongue, with induration and everted margins was noted.(Figure1) The ulcer did not cross the midline. There were no palpable cervical lymph nodes.

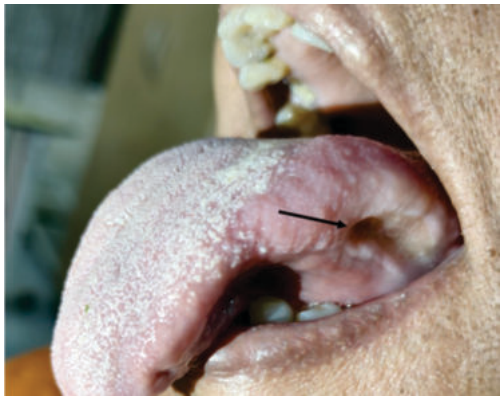


Figure 1: Showing ulcer in the lateral aspect of tongue

With a clinical diagnosis of malignant ulcer of tongue, we proceeded with an MRI Head & Neck which showed an ulcerative lesion measuring 3.5 cm x2.8cm lesion with depth of invasion measuring up to 12 mm in the left middle ⅓ and posterior ⅓ of tongue and extended up to left glosso tonsillar sulcus. Lesion involved intrinsic muscles of tongue. The lateral margin of tumor was approximately 13mm from midline. Prominent nodes in bilateral level 2,3 and 5 regions largest measuring 6.5mm in short axis.(Figure 2)

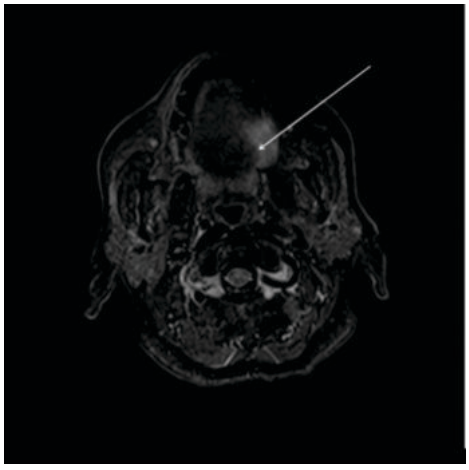
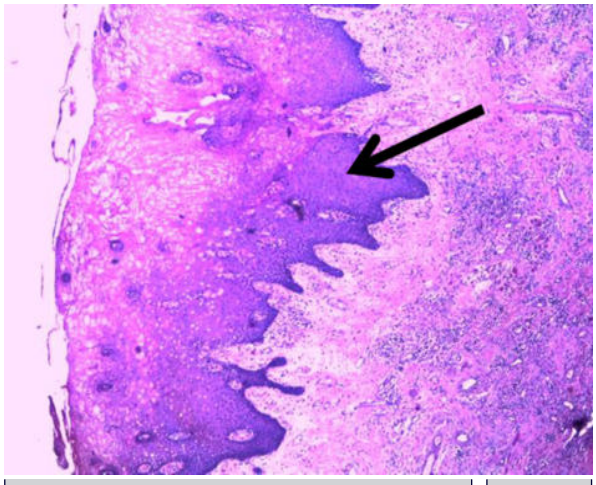


Figure 2: MRI showing the lesion involving intrinsic muscles



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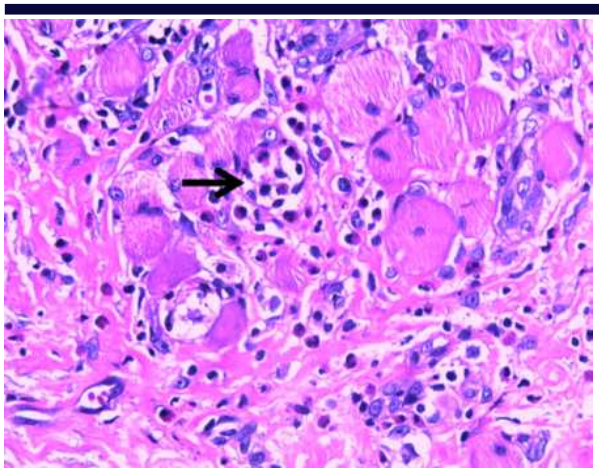

Figures 3 & 4: HPE slide showing eosinophilic infiltration

A diagnosis of Carcinoma Tongue (cT3) was thus made and incision biopsy of the lesion was carried out. Histopathological analysis revealed mucosa lined by stratified squamous epithelium exhibiting basal cell hyperplasia. The subepithelium showed many proliferating capillaries surrounded by lymphoid follicles with secondary germinal centres, sheets of eosinophilia (> 50 /HPF) with occasional plasma cells, inflammatory infiltrate seen surrounding the deep skeletal muscle of tongue. (Figure3,4) There was no evidence of malignancy. Differential diagnosis of Eosinophilic ulcer of oral mucosa / Angiolymphoid hyperplasia with eosinophilia was made. On follow-up, after 1 month, the ulcer seemed to have regressed spontaneously without requiring further intervention.

DISCUSSION:

Riga, in 1881, gave the first clinical description of Eosinophilic Ulcer of the Oral Mucosa(EUOM) and the histological description was given by Fede in 1890.[5] Eosinophilic ulcers have a bimodal distribution. Equal distribution in both genders, a slightly more female preponderance.[6] More than half of the EUOM lesions involve the tongue; other less common sites are lips, oral mucosa, gingiva, palate and the floor of the mouth. Lesions are painful in 30% of the cases. They can present as round to oval ulcers with elevated and indurated borders(as seen in our case); sometimes they could also appear as a nodular-ulcerated lesion or simply as an induration.[7] As discussed earlier, the etiology of this disease remains a mystery. While trauma has been showed to have an important role, other possible influencing factors could be viral/toxic agents, T-cell mediated immune response, lack of synthesis of transforming growth factors by eosinophils, which explains the delayed healing that is characteristic of an eosinophilic ulcer.[3,7,8,9]The etiological factor in our case still remains unidentified.

Histologically, EUOM shows a background of inflammatory cells predominantly consisting of eosinophils, followed by lymphocytes and mast cells with large mononuclear cells having round to ovoid pale nuclei, showing occasional nuclear atypia, extending deeper into the underlying structures - soft tissue, muscle fibers and salivary glands. These epitheloid cells are positive for Macrophage marker, Dendritic cell marker, Factor XIIIa and Myofibroblast markers.[10]

An incisional biopsy is usually required for a confirmatory diagnosis. In similarity with other studies, in our case also, the ulcer healed rapidly following the incision biopsy. This behaviour could probably be indicative of a healing response reactivation after the surgical intervention, but the exact mechanism still remains unclear. Majority of them heal without any complications or recurrence. Recurrence is rarely reported and if so, should be subjected to immunohistochemical analysis for CD30 marker clonality because monoclonal cases will need long-term follow-up.[10,11]

The similarity of clinical features of EOM leads to multiple other differential diagnoses namely squamous cell carcinoma, major aphthous ulcers, Angiolymphoid Hyperplasia with Eosinophilia of Tongue (ALHE), Kimura's disease, Wegener's granulomatosis, tuberculosis and lymphoma. A simplified table discussing differentiating features of EUOM from Malignant and traumatic ulcer is shown below. (Table 1)[8,10]

Table 1 : Showing Differentiating Features Of EUOM With Classical Malignant Ulcer And Traumatic Ulcer

DISEASE	EUOM	MALIGNANT ULCER	TRAUMATIC ULCR
ETIOLOGY	Obscure, reactive inflammatory	Genetics	Trauma
CLINICAL FEATURES	Solitary ulcer, benign, self limiting, indurated and elevated borders Asymtomatic, heals fast Frequently involves tongue, no lymph node involvement	Deep ulcers with indurated, raised borders, exophytic/ verrucous growths Malignant, not self limiting Asymptomatic in early stages Ulceroproliferat ive growth, non spontaneous healing Involves tongue/oral mucosa Lymph node involvement present	No elevated borders Benign Symptomatic Fast healing after removal of traumatic agent Involves tongue/oral mucosa
HISTOPATHO LOGICAL FEATURES	Intact, well differentiated epithelium, hyperplastic intense inflammatory cell infiltrates with intense eosinophilia	Loss of basement membrane Disturbed architecture of basal layers of epithelium Replacement of basal cells with large irregular cells with cytoplasmic processes extending into connective tissue	Stratified squamous epithelium, hyperplastic, hyperkeratotic with mixed inflammatory cell infiltrates
TREATMENT	Incisional biopsy, corticosteroids	Surgery, chemotherapy, radiotherapy	Removal of traumatic agent

While the other rare differentials include ALHE and Kimura's Disease. ALHE tends to present with more prominent vascular changes, while Kimura's disease is characterized by marked lymphoid involvement on histopathology. ALHE lesions are usually more localized and discrete nodules, red papules, macules, associated with pruritus. Endothelial cells have a cobblestone appearance, with perivascular lymphocytic and eosinophilic infiltrates in the interstitium. Kimura's disease may involve deeper structures and is often characterized by Lymphoid hyperplasia which has a well-maintained architecture. Presence of eosinophilic micro-abscesses is the key feature consistent with Kimura's disease. Demographically, ALHE is more common in females and Kimura disease has a higher prevalence in males of Asian descent.

In summary, although ALHE and Kimura disease share some similarities with EUOM, careful consideration of clinical, histopathological, and demographic factors can help differentiate between these entities. A definitive diagnosis often relies on a combination of clinical findings and histopathological features.[12,13]

CONCLUSION:

EUOM is an infrequently encountered, benign ulcerative lesion and is often misdiagnosed as oral malignancy. The etiological factors precipitating the disease still remain controversial, but trauma plays an important role in its etiopathogenesis. Histopathological analysis plays a key role in arriving at a diagnosis. It generally has an indolent course, and surgical excision or incision resolves it spontaneously within few weeks. Even though it is self limiting, regular monitoring is essential, because a low grade lymphoma also has a very similar clinical presentation.[14] Apart from surgical excision/incision, topical corticosteroids, curettage, antibiotics and cryosurgery are the other

modalities that can be used in treating EUOM. However, surgical excision is the most commonly used approach.[15]

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