Traumatic ulcerative granuloma with stromal eosinophilia: Comparative analysis of institutional cases

RUNNING TITLE: TUGSE: A comprehensive review with institutional insights

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ABSTRACT

Background: Traumatic Ulcerative Granuloma with Stromal Eosinophilia (TUGSE) is an uncommon oral ulceration that can resemble malignancy. Literature consists largely of case reports and small case series, often with limited clinical context. This review compiles published cases and compares them with eleven institutional TUGSE cases. **Methods:** A literature search was performed in PubMed, Scopus and Google Scholar (1997 to 2024). Case reports and case series describing clinical and histopathological features of TUGSE were included. Institutional cases were identified from retrospective clinical and histopathology records. Data were extracted for demographics, etiology, clinical appearance, histopathology and management. **Results:** Trauma was identified in 63.6 percent of institutional cases and in more than half of published cases. Tongue and buccal mucosa were the most common sites. All institutional cases underwent biopsy with eosinophil-predominant inflammatory infiltrate. No cases showed malignant progression after removal of irritants or excision. **Conclusion:** Clinical morphology and histopathology varied across both literature and institutional cases. The comparison confirms that TUGSE is reactive, resolves after eliminating traumatic factors and requires biopsy for exclusion of malignancy.

Keywords: oral eosinophilia; reactive ulcer; stromal eosinophilia; traumatic ulcerative granuloma

CDHA Research Agenda category: oral health frameworks

INTRODUCTION

Traumatic Ulcerative Granuloma with Stromal Eosinophilia (TUGSE) is a rare, reactive oral lesion that often presents with deep, chronic and painful ulceration, raising clinical suspicion for malignancies such as squamous cell carcinoma [1]. The condition was initially described by Riga and Fede in 1881 as traumatic ulcerations on the ventral tongue of infants, later termed Riga-Fede disease [2]. In 1956, Popoff identified TUGSE as an eosinophilic ulcer and Shapiro later introduced the term "eosinophilic ulcer of the tongue" for similar lesions in adults [3]. By the 1970s, clinical reports highlighted occurrences beyond the tongue and in 1983, Wright formally coined the term Traumatic Ulcerative Granuloma with Stromal Eosinophilia to emphasize its benign, reactive nature [4]. TUGSE is histopathologically characterized by an inflammatory infiltrate rich in eosinophils, atypical histiocytes and macrophages, often mimicking more aggressive pathologies [4]. Shapiro and Juhlin described it as a distinct entity due to its self-limiting yet potentially recurrent nature [3]. While the lateral and dorsal surfaces of the tongue are the most commonly affected sites, lesions have also been reported in the buccal mucosa, vestibular mucosa, gingiva, retromolar region, palatal mucosa and the floor of the mouth

[1]. Trauma is implicated in at least 50% of cases, though the exact pathogenic mechanism remains incompletely understood [2][1].

Despite extensive documentation in literature, the clinical presentation and progression of TUGSE remain variable, making accurate diagnosis and differentiation from malignant and infectious ulcerations crucial. In our institutional cohort, we observed variations in lesion duration, response to treatment and recurrence patterns, offering valuable insights into the diagnostic and therapeutic approach to TUGSE. This narrative review consolidates the current literature on TUGSE while integrating our institutional experience to highlight its clinical characteristics, histopathological findings, diagnostic challenges and management strategies. By comparing our cases with existing reports, we aim to refine diagnostic criteria and provide a more comprehensive perspective on this unique entity.

MATERIALS AND METHODOLOGY

Review framework

The literature search was conducted using the scoping review methodological framework proposed by Arksey and O'Malley, with guidance from the PRISMA-ScR reporting recommendations. This structured approach was adopted to comprehensively chart the characteristics of TUGSE in published cases and to compare them with findings from an institutional case series.

Research question

What are the reported demographic, etiological, clinical, histopathological, investigational and management characteristics of TUGSE in the literature and how do they compare with institutional cases?

Search strategy

A structured search was performed in PubMed, Scopus and Google Scholar using the terms "TUGSE," "traumatic ulcerative granuloma" and "eosinophilic ulcer." "traumatic ulcerative granuloma" OR "traumatic ulcerative granuloma with stromal eosinophilia" OR "TUGSE" OR "eosinophilic ulcer" OR "eosinophilic ulcer of the oral mucosa" OR "traumatic eosinophilic granuloma" "oral mucosa" OR "tongue" OR "buccal mucosa" OR "lip" OR "gingiva" OR "palate". The search included published clinical case reports and case series in English with extractable patient information.

Eligibility criteria

Inclusion criteria

• Human clinical cases with confirmed diagnosis of TUGSE
• Articles with extractable data on demographics, clinical profile, histopathology, treatment or

outcomes

• English language publications

Exclusion criteria

• Review papers

• Non-clinical studies

• Reports without sufficient clinical or diagnostic details

Study selection

Two reviewers independently screened titles and abstracts, followed by full-text assessment. Disagreements were resolved through discussion until agreement was reached.

Data charting and variables extracted

A standardized extraction template was used to collect the following variables:

• Age and gender

• Anatomical location

• Trauma history

• Clinical appearance and symptoms

• Histopathological features

• Investigations

• Treatment and healing outcome

Institutional case series

Eleven cases were identified retrospectively from clinical and histopathology records with confirmed diagnosis of TUGSE. Inclusion required sufficient clinical description and biopsy confirmation. Cases without diagnostic confirmation or adequate documentation were excluded.

Ethics consideration

Institutional ethics approval was waived because data were anonymized and collected from archived records without patient identifiers, as per institutional policy.

RESULTS

Data from literature and institutional cases were grouped under key clinical domains for side-by-side comparison. Quantitative pooling was not conducted due to variability in reporting formats.

Age and gender

Published cases include patients from 13 to 86 years. Most occur in middle age and later life, especially between 51 and 81 years [1–35]. The institutional cohort showed a similar pattern, with 51 to 60 years

being the most common decade (45.45 percent), followed by 61 to 70 years (36.36 percent). Only two institutional cases occurred below 50 years and none below 30 years. Both literature and institutional findings show a near-balanced gender distribution, with slight variation between studies. This suggests no strong sex-based predisposition, though demographic factors may vary across populations.

Etiology of TUGSE: Comparison of institutional cases with literature

Trauma contributed to more than half of the published cases (58.6 percent), arising from sharp teeth, dentures, cheek biting, dental calculus, tobacco chewing and dental procedures [3–6,9,13,15,16,19,20,23–25]. Idiopathic cases were also reported, including patients with lymphoma or chemotherapy-related mucosal injury [1,10,13,26,27]. The institutional cohort showed trauma in 7 of 11 cases (63.6 percent), including irritation after endodontic treatment. Four cases lacked any recorded traumatic history. This supports trauma as the principal trigger, while a minority may relate to immune or systemic influences.

Clinical features: Comparison of institutional cases with literature

Induration and pain were the most frequent findings. Firm or tender lesions were reported in 41.2 percent of literature cases and fibrinopurulent exudate in 35.3 percent [2–14]. Ulcers frequently showed raised or rolled borders that caused clinical confusion with squamous cell carcinoma during initial examination. In published cases, tongue involvement represented the dominant site distribution, especially along the lateral border, followed by buccal mucosa [1–35]. Institutional cases showed comparable ulcer morphology, including nodular forms not always emphasized in earlier reports. All institutional cases were symptomatic, with pain levels influenced by trauma severity and duration. Difficulty in swallowing was noted in cases where the lesion approached the palatoglossal region.

Histopathological variations: Comparison of institutional cases with literature

A mixed eosinophil rich inflammatory infiltrate was present in 79 percent of literature cases and in all institutional cases [3–6,9,13,15,16,19,20,23–25]. The infiltrate commonly extended into underlying muscle fibers, which corresponded clinically to the firm palpation. Granulomatous or deeper muscle involvement was noted in 7 percent of literature cases and 18 percent institutionally [5]. Occasional cases demonstrated pseudoepitheliomatous hyperplasia, which may resemble early invasive carcinoma during routine light microscopy. Angiocentric infiltration with atypical mononuclear cells appeared in 7 percent of literature cases and 9 percent of institutional cases [26]. These histologic variations explain why biopsy is essential even when trauma is evident in clinical history (Figure 3-5).

Investigations

Special investigations were conducted in 7 cases (24.1%) of the 29 reviewed cases. These investigations were primarily carried out to confirm the diagnosis and identify any underlying conditions, particularly

in cases with uncertain etiology or atypical clinical presentations. Immunohistochemistry (IHC) have been used to further evaluate the lesions, Markers used are CD3, CD30, CD68 to confirm the inflammatory and immunological nature of the lesions[11,18,19,26,28,29]. Additionally, molecular techniques such as T-cell receptor γ gene rearrangement and PCR were used in five cases to identify T-cell lymphoma[1,2].

DISCUSSION

The present analysis demonstrates that the clinical and histopathological features of the institutional TUGSE cases closely parallel those described in published literature, particularly with respect to traumatic etiology, tongue predilection, induration and eosinophil-rich inflammatory infiltrates. At the same time, certain variations in clinical morphology, depth of inflammatory extension and use of ancillary investigations highlight the heterogeneity of this entity.

The immunopathological mechanisms described above are consistent with the histopathological findings observed in the present institutional cases, where eosinophil-rich infiltrates extended into deeper connective tissue and muscle layers, accounting for the characteristic induration. Pathogenesis of TUGSE involves a complex interplay of trauma, immune dysregulation Th2 response, eosinophil recruitment, macrophage activation and delayed wound healing mechanisms. A traumatic ulceration often triggered by mechanical injury from sharp teeth, ill-fitting dental prostheses, or accidental mucosal trauma compromises the epithelial barrier, allowing the entry of microorganisms, toxins and foreign proteins. The loss of epithelial integrity exposes the underlying connective tissue, triggering an inflammatory response. While trauma typically elicits a Th1-dominated immune response, characterized by macrophage activation and neutrophil infiltration, certain conditions may skew the immune milieu toward a Th2 phenotype, favoring eosinophil recruitment[30]. This shift may be attributed to chronicity of tissue damage, repeated mechanical insult, or dysregulated wound healing, leading to an immune environment conducive to eosinophil infiltration.

Eosinophils remain abundant within the stromal infiltrate because of a Th2 dominant immune response [9]. IL 5 supports eosinophil survival at the lesion site. IL 4 and IL 13 promote eosinophil migration and persistence. Eotaxins including CCL11, CCL24 and CCL26 attract eosinophils in response to chronic mechanical irritation[31,32].

The release of granule proteins including major basic protein, eosinophil peroxidase, eosinophil derived neurotoxin and eosinophil cationic protein contributes to tissue destruction and delayed healing. These cytotoxic effects explain why induration and muscle infiltration are frequent histologic features. Excessive fibroblast activation and collagen deposition result from transforming growth factor beta signaling in the inflamed stroma.

The characteristic ulcer with rolled margins arises from mucosal degeneration, potentially involving cytotoxic T cells and the release of toxic products from degranulating eosinophils. Chronic inflammation in TUGSE induces the activation of fibroblasts, which proliferate and deposit excessive extracellular matrix components, particularly collagen. This fibroblastic activity results in fibrosis and the palpable firmness of the lesion margins. Transforming growth factor-beta (TGF-β), released by eosinophils and other immune cells, plays a pivotal role in this fibrotic response, giving rise to the induration observed clinically[10,11]. The inflammatory infiltrate involves underlying muscle fibers and stimulates the activation of myofibroblasts, which contribute to wound contraction and further collagen deposition. The resulting scarring and tissue remodeling accentuate the indurated margins of the lesion. Eosinophils release granule proteins, including major basic protein (MBP) and eosinophilic cationic protein (ECP), which cause direct cytotoxicity to surrounding tissues. This tissue damage leads to further inflammation and perpetuates the recruitment of immune cells, amplifying the thickened, elevated borders of the ulcer.

Experimental studies by Lambrecht BN et al. and Pelaia C et al. highlight the role of IL-4, IL-5 and IL-13 in sustaining chronic inflammation in asthma and oral mucosal injuries [11,12]. Fonseca FP et al. demonstrated that TLRs on immune cells recognize microbial PAMPs, triggering pro-inflammatory cytokines, chemokines and type I interferons, which regulate innate and adaptive immunity in TUGSE. Histopathology of traumatic oral lesions reveals dense eosinophilic infiltrates and mast cell activity, suggesting a shared immunopathological mechanism [13]. CD68+ macrophages interact with eosinophils via TGF-β, promoting fibrosis and delayed healing, sustaining chronic inflammation [33]. Unlike mast cells in acute responses, macrophage-eosinophil interactions establish persistent inflammation in TUGSE [14]. IHC shows T-cell markers and CD30 positivity, with some cases exhibiting monoclonal T cells, suggesting an oral counterpart of cutaneous lymphomatoid papulosis (LP) per WHO classification [15]. T lymphocytes outnumber B cells, while antigen-presenting cells, including Langerhans and non-Langerhans cells, predominate over KP I-positive macrophages, reinforcing T-cell-driven immunity in EUOM [34]. Trauma may trigger TUGSE, but T-cell activation sustains lesion development, with some cases showing polyclonal or monoclonal T-cell populations [16,21].

The marked clinical and histological overlap between TUGSE and malignant or lymphoproliferative disorders explains the frequent diagnostic dilemma encountered in both the present cases and prior reports. TUGSE mimics SCC, lymphoma, eosinophilic granuloma and Riga-Fede disease (Table 3), with SCC showing dysplastic invasion, lymphoma requiring IHC/molecular analysis and Riga-Fede linked to natal/neonatal teeth. While primarily reactive, its overlap with lymphomatoid papulosis (LyP) suggests a possible oral counterpart of CD30+ cutaneous lymphoproliferative disorders (LPDs), including ALCL [35]. IHC, TCR gene rearrangement and clinical correlation are crucial for differentiation. Findings include CD3+ T-cell infiltration, CD68+ histiocytes and α-SMA+

myofibroblast activity [19], with some cases showing CD30+ atypical cells, lymphoproliferation, eosinophils and monoclonal TCRγ rearrangement, linking TUGSE to cutaneous CD30+ LPDs [30]. Resemblance to cutaneous LyP type C raises concerns about lymphoma transformation, though TUGSE is typically self-limiting, making differentiation from ALCL challenging [2][31].

Management strategies employed in the institutional cases mirrored those recommended in the literature, with biopsy serving both diagnostic and, in some instances, therapeutic roles. Management of TUGSE generally involves removing the source of trauma if any and monitoring the lesion. Due to its tendency for spontaneous resolution and removal of the inciting factor, conservative treatment is often sufficient [41]. Reported treatment options include corticosteroids (administered topically, systemically, or via intralesional injection), antibiotics, 0.1% triamcinolone acetonide mouthwash, as well as methods like irradiation, electrocoagulation and liquid nitrogen therapy[42]. Biopsy is both diagnostic and curative in some cases, as removal of the lesion often initiates healing. Despite its alarming clinical presentation, TUGSE has a favorable prognosis with appropriate management.

CONCLUSION

TUGSE is a reactive oral ulceration commonly associated with trauma. Induration and deep inflammatory infiltration can resemble malignancy, which makes biopsy necessary. Removal of traumatic irritants or excision leads to healing in most cases. Occasional T cell rich infiltrates require follow up to exclude lymphoproliferative disorders.

CONFLICTS OF INTEREST

There are no conflicts of interest among the authors

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Table 1: Summary of reviewed cases of TUGSE

S.NO	AUTHOR NAME	AGE	GENDER	ETIOLOGY	SITE	CLINICAL FEATURE	HISTOPATHOLOGICAL FEATURES	INVESTIGATION	REFERENCE
1.	Wright et al	66 years	Female	History of multiple cutaneous and nodal relapses of marginal zone lymphoma	Lateral border of the tongue	Painful oral ulceration	Ulcerated squamous mucosa with a polymorphous inflammatory infiltrate consisting of small lymphocytes, histiocytes, eosinophils and large atypical lymphoid cells	CD30-, CD3-, CD2 –, EBV -, PCR-based T-cell receptor γ gene rearrangement	[34].
2.	Venkatesh et al	64 years	Female	Trauma from supra-erupted teeth	Lateral border of the tongue	Non-healing ulcer; indurated base and tenderness on palpation	Hyperparakeratinized epithelium with pseudoepitheliomatous hyperplasia and a mixed inflammatory infiltrate of eosinophils, extending into connective tissue and muscle.	Not reported	[35]
3.	Sidana et al	27 ye	Male	Toothbrush trauma; history of chewing tobacco	Buccal Mucosa	Ulcer which later on progressed to a painless submucosal lump, sessile, smooth surface and firm	Connective tissue with complete epithelial ulceration. An intense mixed inflammatory infiltrate, predominantly composed of eosinophils.	Not reported	[36]
4.	Pushpa et al	45 years	Female	Chronic trauma; history of tobacco chewing	Lateral border of the tongue	Painful erythematous ulcer with irregular borders and everted margins	Ulcerated parakeratinized stratified squamous epithelium with fibrovascular connective tissue showing ulceration and chronic inflammatory infiltrates, predominantly eosinophils	Not reported	[37]
5.	Mohamad et al	13 years	Male	Trauma from lip biting	Labial mucosa	Solitary ulcer; mild pain and swelling affecting facial appearance.	Ulcerated with fibrinopurulent exudate rich in eosinophils. The stroma showed dense heterogeneous inflammatory infiltrates, including eosinophils, small lymphocytes, large mononuclear cells and histiocytes.	CD3+ CD20+, CD68+, CD1a+, CD30+ positive large mononuclear cells.	[38]
6.	Banerjee et al	35 years	Female	Trauma due to carious maxillary molars (17, 16)	Buccal mucosa	Solitary, irregular ulcer; erythematous floor, irregular hyperkeratotic white borders	Infiltrative lesion with dense granulomatous stroma and chronic inflammation extending into connective tissue and musculature, showing macrophages, budding vascular channels, lymphocytes and eosinophils.	Not reported	[39]

7.	Hannan et al	21 years	Male	previous root canal with composite semi-crown	Palatoglossal fold region	Sore throat and mild odynophagia radiating to left submandibular region;	Reported but details not provided in the published article	Not reported	[8]
8.	Sethi et al	17 ye	Male	Unknown; no history of trauma provided	Retromolar area, with additional lesions on right buccal mucosa, hard palate	Soft, tender, yellowish-white lesion with irregular surface texture and white keratotic margin	Reported but details not provided in the published article	Not reported	[40]
		70 ye	Female	Trauma due to teeth impingement	lateral border of the tongue	Non-healing asymptomatic ulcer	Reported but details not provided in the published article	Not reported	
9.	Benitez et al	48-years	Male	Unknown; no history of trauma provided	Retromolar buccal plane	Not reported	The ulceration displayed an infiltrative granulomatous morphology involving the superficial mucosa, fatty tissue and deep muscle fibers, with abundant lymphocytes, histiocytes, eosinophils.	PCR: Biclonal T-cell receptor rearrangement was detected.	[24]
10.	Axelrod et al	70	Male	Not reported	Anterior maxillary gingiva	Large yellowish ulcer with elevated margins and central induration	Reported but details not provided in the published article	CD3+, CD4+, CD5+, CD30+ CD1a-, CD8-, CD20-, CD56-, CD117-, ALK1-, Langerin-, EBER-	[41]
11.	Bordignon et al	59 years	Male	Ill-fitting denture causing mucosal trauma	Base of the tongue extending to the floor of the mouth	Indurated ulcer with white-yellow fibrinous pseudomembrane and slightly raised red borders	Ulcerated mucosa with polymorphonuclear infiltrate, granulation tissue displayed dense capillary networks with lymphocytes, macrophages, neutrophils and eosinophils and cell proliferation included fusiform, ovoid and histiocytoid cells.	CD3+ CD68+ α-SMA- CD30-	[32]
12.	Lakkam et al	65	Male	Local trauma by adjacent teeth	Lateral border of the tongue	Erythematous ulcer with a whitish surrounding halo, Smooth, tender, firm consistency, well-defined margins with everted rolled induration, Tender and palpable submandibular lymph nodes	Irregular, intensely inflamed connective tissue stroma. Loose to dense collagen bundles with plump to spindle-shaped fibroblasts Predominantly lymphocytes, eosinophils and macrophages/histiocytes	Not reported	[42]
13.	Butler et al	81	Male	Not reported	Dorsal surface of the tongue	Rapidly enlarging vascular-appearing nodule with a collarette of mucosal epithelium	reported	Not reported	[43]
14.	Rose et al	63 years	female	Sharp teeth near the ulcer	Lateral border of the tongue	Single ulcer with elevated, paler borders and a pale area near the border. Firm, indurated and keratotic	Reported but details not provided in the published article	Not reported	[44]

						borders with a base fixed to underlying structures			
		38 years	Male	Sharp root stumps	Lateral border of the tongue	Painful single ulcer on the left side of the tongue with a red base, indurated, white elevated border	Reported but details not provided in the published article	Not reported	
15.	Gagari et al	28 years	Male	Picking at the ulcer once it started forming	Dorsal surface of the tongue	Raised and rolled margins, reddish-yellow borders, moderate discomfort on palpation, firm base and borders	Chronic inflammation with eosinophils, lymphocytes and histiocytes dispersed among muscle fibers.	Not reported	[45]
16.	Kuriyama	32 years	Female	Not reported	Commissure of the mouth	Deep ulcer	Dense mixed inflammatory cell infiltrates composed of eosinophils, lymphocytes and histiocytes, extending from submucosal tissue to underlying striated muscle fibers.	Not reported	[46]
17.	Boffano et al	60	Male	Ill-fitting Prothesis	Retromolar region	Asymptomatic, whitish fibrinous ulceration with indurated borders	The lesion exhibited an inflammatory submucosal infiltrate composed of mixed inflammatory cells, including lymphocytes, histiocytes, neutrophils, eosinophils, plasma cells and large cells.	IHC: CD68+ histiocytes, polyclonal plasma cells, CD20+ B lymphocyte.	[47]
18.	Sharma et al	75	Female	Sharp teeth	Postero-lateral aspect of the tongue	Erythematous ulcer with whitish surrounding halo. Smooth, tender, firm with well-defined margins and induration.	Superficial hyperplastic epithelium with hyperkeratosis and a central area of ulceration. - Dense mixed inflammatory infiltrate with eosinophils and macrophages.	Not reported	[48]
19.	Marszałek et al	53	Female	Not reported	Dorsal surface of the tongue	Ulcer with elevated, indurated margins and yellowish, necrotic bottom	Ulceration with a necrotic base Dense inflammatory infiltrate of lymphocytes, eosinophils and atypical mononuclear cells	Not reported	[49]
20.	Brasileiro et al	65	Male	Not reported	Hard palate	Ulcerative lesion with yellowish fibrinopurulent membrane and erythematous halo	Extensive superficial necrosis Polymorphic lymphoid infiltrate Eosinophils and atypical large lymphoid cells Angiocentric infiltration	IHC: CD3, CD30 and granzyme B. CD31 and CD34. positive for epithelioid-like endothelial cells	[50]
21.	Shokravi et al	51	female	denied any trauma	Anterior pillar of the soft palate	Painful, nonhealing ulcer with fibrinopurulent membrane, erythematous halo, difficulty in swallowing	Ulcerated squamous mucosa with granulation tissue Mixed inflammatory infiltrate, abundant neutrophils and lymphocytes No eosinophils present	IHC: CD3, CD20, CD21, CD30, CD56 negative, IgG4, EBV, HSV - negative	[51]
22.	Damevska et al	52	Male	Unknown	Dorsal and lateral surface of the tongue	4 indurate lesions with central ulceration and white pseudomembrane, Firm and painful on palpation.	Ulcerated surface Dense, diffuse infiltrate of eosinophils, plasma cells and large mononuclear cells. Infiltrate extending deep into tongue musculature	IHC: CD30+ cells	[52]

23.	Didona et al	65	Female	Ulceration adjacent to sharp teeth	Lateral surface of Tongue	Painful ulcer. Initially started as a slightly red lesion with mild induration, rapidly progressing to ulceration	No histopathological information is provided	Not reported	[53]
24.	Vasconcelos et al	63	Male	Trauma related to amalgam restoration,	Lateral surface of Tongue	Painful ulcerated nodule, that was firm, raised and erythematous, with a central ulcer. The ulcer had a yellow fibrinous base.	Ulcerated lesion with dense mixed infiltrate of eosinophils, lymphocytes and epithelioid cells Infiltrate extended into the submucosa. The cells exhibited pleomorphism, voluminous cytoplasm and nuclei with prominent nucleolus	IHC: CD68+ cells	[54]
25.	Bastos et al	61	Male	Root remnants and dental calculus	Lateral surface of Tongue	Painful ulcer	Eosinophilic Ulcer (EU)	Not reported	[55]
		57	Female	Unknown	Upper lip	Crusted, itchy, painful lesion	Eosinophilic Ulcer (EU)	Not reported	
		38	Female	Lip biting habit	Lower labial mucosa	Ulcer with erythematous halo, necrotic surface,	Eosinophilic Ulcer (EU)	Not reported	
		68	Male	Trauma (tongue injury)	Dorsum of tongue	Painful ulcer with precise limits, irregular contours, elevated edges	Eosinophilic Ulcer (EU)	Not reported	
26.	Alobeid et al	45	Female	Not given	Buccal mucosa	Firm and painful buccal mucosa ulcer, no systemic symptoms	TEG (T-cell lymphoma)	D4–, CD8–, bcl-6+; CD30+ cells, negative for CD20, CD56, CD68, CD79a PCR: Monoclonal TCRγ rearrangement	
		46	Female	Systemic or recurrent form of T-cell lymphoma; history of chemotherapy treatment	Dorsum of tongue	Solitary ulcer of the tongue, developed skin nodule a year later	TEG (T-cell lymphoma)	CD4+, CD8–, bcl-6+/– or bcl-6–; CD30+ cells, negative for CD20, CD56, CD68 PCR: Monoclonal TCRγ rearrangement	
		86	Female	Peripheral T-cell lymphoma	Dorsum of tongue	Oral ulcer on the tongue, reappeared as a new lesion at the base of tongue		CD4+, CD8–, bcl-6+; CD30+ cells, negative for CD20, CD56, CD68, CD79a PCR: Monoclonal TCRγ rearrangement	
27.	Elovic et al	In a study of 12 cases TUGSE, it was found that 92% of eosinophils did not express detectable levels of mRNA for TGF-α or TGF-β. Only a small percentage of eosinophils infiltrating the lesions produced these factors. The lack of significant synthesis of TGF-α and TGF-β by eosinophils in TUGSE lesions, in contrast to eosinophils in the animal wound-healing model, may contribute to the delayed healing characteristic of TUGSE.							[14]
28.	Hirshberg et al	TUGSE cases showed inflammatory infiltrates of lymphocytes, macrophages, eosinophils and atypical cells. CD30+ cells were present in 5 cases, with T-cell receptor gene rearrangement indicating polyclonality in 6, oligoclonality in 5 and monoclonality in 1. All cases healed without recurrence, except the monoclonal case, which required long-term monitoring. The study concluded that TUGSE is mainly a reactive lesion, but monoclonal cases warrant long-term follow-up to rule out lymphoma.							[17]
29.	Salisbury et al	Immunoreactivity for CD30 and TCR gene rearrangement was detected in 7 out of 29 TUGSE cases (24%) with amplifiable DNA. These were found in large atypical mononuclear cells in some cases. However, T-cell clonality and/or CD30 positivity do not indicate malignancy in TUGSE cases without morphological or clinical signs of lymphoma.							[28]
30.	Shen et al	In a study of 49 cases, 34 were examined, with 64.7% attributed to trauma and 35.3% to other factors. Lesions were most commonly located on the tongue (67.6%), followed by buccal mucosa (17.6%). The ulcers were painful, non-healing, with hard, indurated margins and severity ranged from mild (38.2%) to severe (29.4%). These findings suggest TUGSE is often trauma-related, but severe or persistent cases require careful evaluation to rule out malignancy or other conditions.							[33]

Data labelled as Not reported indicates absence of information in the original publication.

Table 2: Comparison of our institutional experience with Literature

Factor	Institutional Cases	Literature Overview
Age	51–70 years common	Wide age range (13 to 81 years), but several reports show clustering in older adults (e.g., 60s, 70s)
Gender	Female > Male (54%)	Mixed findings; some reports show male predominance (e.g., Sidana, Sethi), while others show female cases (e.g., Wright, Prabhu)
Etiology	Trauma in 63.6%	Trauma common (sharp teeth, dentures, dental work), but idiopathic/systemic also reported (lymphoma, immune-related)
Clinical Presentation	Ulcerative lesions, sometimes indurated	Similar ulcerative features with variations like nodules, firm induration, erythematous base
Histopathology	Chronic inflammation (eosinophils, lymphocytes, histiocytes); some aggressive cases (granulomas, T-cell lymphoma-like)	Consistent with literature (eosinophils, lymphocytes, macrophages), but lymphoma-like changes noted in a few reports.

Table 3: Comparative clinical, histological and molecular features of TUGSE, atypical histiocytic granuloma, ALHE, LCH and LyP

	TUGSE	Atypical Histiocytic Granuloma	Angiolymphoid Hyperplasia with Eosinophilia (ALHE)	Langerhans Cell Histiocytosis (LCH)	Cutaneous Lymphomatoid Papulosis (LyP)	References
Clinical Features	Ulcerative lesion, indurated margins, painful, often on tongue or buccal mucosa, self-limiting	Ulcerated or nodular lesion, often painless, slow-growing	Erythematous to violaceous papules or nodules, usually on the head and neck, occasionally pruritic	Solitary or multiple bone or soft tissue lesions, oral ulceration rare	Recurrent papules or nodules on the skin, often self-healing	[1]
Histology	Dense infiltrate of lymphoid cells, eosinophils, large atypical cells (lymphocyte and histiocyte-like)	Granulomatous inflammation with histiocytes and eosinophils	Vascular proliferation with eosinophils, lymphocytes	Atypical Langerhans cells, epidermotropism, eosinophils	Atypical lymphoid cells, skin papules, eosinophils	[1]
IHC	CD30+ atypical cells, partial T-cell markers (CD3, CD4, CD5, CD7), CD8 negative or few	CD68+, CD1a-, CD30-, CD3+ (varies with subtype)	CD30+, CD3+, CD4+ in atypical lymphoid cells	CD1a+, CD207+ (Langerhans cells), CD30-	CD30+ in atypical lymphoid cells, T-cell markers vary	[36,37]
PCR	Monoclonal TCRγ chain rearrangement in lesions	No consistent rearrangement reported	Monoclonal TCR rearrangement or polyclonal expansion	TCRγ chain rearrangement, clonal expansion	Monoclonal TCRγ chain rearrangement in some cases	[38,39]
Molecular Sequencing	TCRγ chain monoclonal rearrangement in oral and cutaneous specimens (in some cases)	No specific genetic mutations identified	No specific genetic mutations identified	Mutations in the BRAF gene or other oncogenes in some cases	TCR gene rearrangement detected in some cases, involving T-cell expansion	[1,40]

Figure Legends

Figure 1: Schematic illustration of PRISMA flow chart search strategy employed for the study

Figure 2: Schematic representation depicting the etiopathogenesis of TUGSE

Figure 3: Low-power photomicrograph showing epithelial rete ridges overlying connective tissue with inflammatory cell infiltrate. Hematoxylin and eosin stain, original magnification ×10.

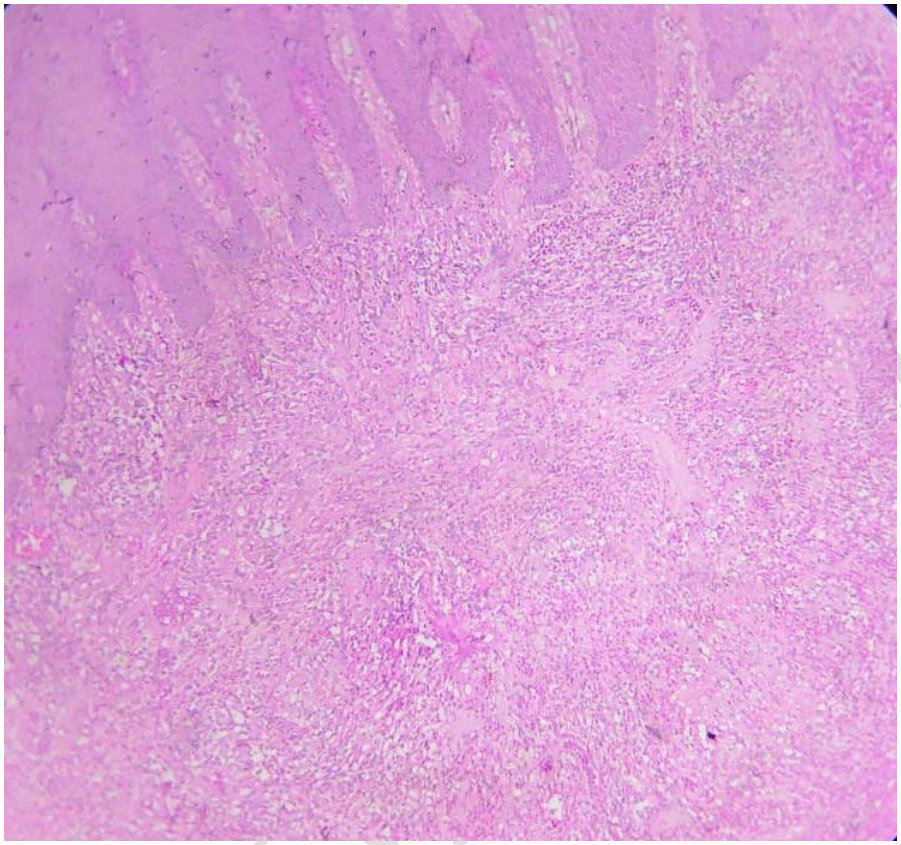

Figure 4: Low-power photomicrograph showing granulation tissue with intense inflammatory cell infiltrate. Hematoxylin and eosin stain, original magnification ×10.

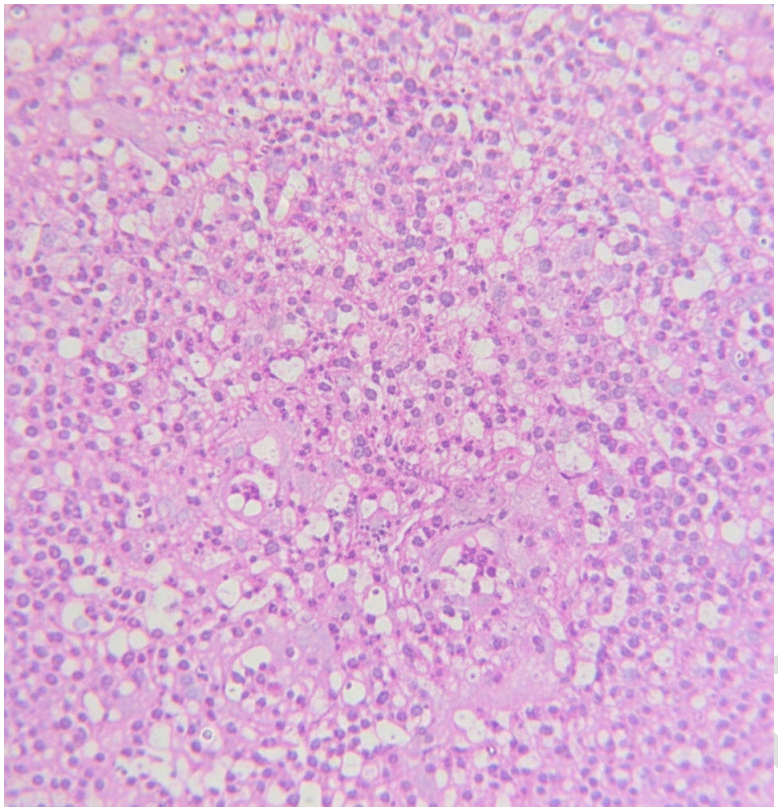

Figure 5: Photomicrograph showing dense inflammatory cell infiltrate and prominent eosinophils. Hematoxylin and eosin stain, original magnification ×40.