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TRAUMATIC ULCERATIVE GRANULOMA WITH STROMAL EOSINOPHILIA – CASE SERIES

Oral Pathology

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ABSTRACT

Traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) is relatively uncommon lesion presenting clinically as ulceration of the oral mucosa with a chronic course associated with delayed healing. Chronic irritation causing trauma to the oral mucosa is considered as major causative factor. The most commonly affected site of the lesion appears to be Tongue and Buccal mucosa. This lesion represents clinically as ulcer with indurated margins mimicking malignancy, causing diagnostic challenge for the dentists. Histologically characterized by breach in the epithelium exposing underlying connective tissue infiltrated with dense amount of inflammatory cells predominantly of eosinophils penetrating the underlying mucle. It is important to diagnose the lesion histologically to rule out malignancy and to treat appropriately. However the lesion resolves on its own or with minimal and conservative treatment. In this review we present four case series of clinically manifesting ulceroproliferative lesions on buccal mucosa and diagnosed as TUGSE,based on clinical and histopathological features.

KEYWORDS

Ulcerative lesion, Buccal mucosa, Trauma, Eosinophils, Muscle degeneration, Granulation tissue.

INTRODUCTION

TUGSE is an ulcerative lesion of oral mucosa usually affecting the tongue. This lesion has chronic benign course and is of self healing in nature.[1] Inspite of obscure etiopathogenesis, trauma is considered as one of the major contributing factor in initiating the lesion.[2,3] Although clinically the ulcer simulates malignancy with elevated and rolled out borders, most of these lesions tends to resolve after incisional biopsy or after the removal of traumatic cause.[4,5] They do not require any aggressive surgical treatment and recurrence is very rare. Popoff was the first person to described TUGSE in an adult patient in 1956 and reported it in 1960. Shapiro and Juhlin in 1970 reported this lesion as a seperate entity[6,7]. The same lesion in infants and neonates is termed as Riga–Fede disease; Riga described this lesion clinically in 1881 and histologically by Fede in 1890[5] This lesion has been described in literature using various terminologies such as ulcerative granuloma eosinophilium dictinum, traumatic eosinophilic granuloma, traumatic granuloma of tongue, eosinophilic granuloma of tongue, eosinophilic ulcer of tongue, ulcerative eosinophilic granuloma of tongue and Riga-Fede disease.[8,9] Here we present 4 case reports of TUGSE reported in our institution.

MATERIAL AND METHODS

Four cases diagnosed as TUGSE during the period 2015 to 2018 were retrieved from Department of Oral Pathology Government Dental College, Bangalore. The information was collected with detailed case history and was tabulated, which included clinical features like age, gender, site, symptoms, histopathological diagnosis, treatment along with follows-up of each case.

CASE 1: 24 year old male patient reported with a chief complaint of pain and swelling in the upper left back tooth region since 10 days. Intra oral examination revealed a solitary, firm, ulcer approximately 1.5x2 cm in size with indurated margins on the buccal mucosa in relation to 28 which was carious and fractured partly touching the ulcer (Figure 1). Sub mandibular lymph node was palpable. Provisional diagnosis of malignant ulcer was given. Histopathologically H & E stained sections showed hypeplastic epithelium with superficial spongiotic cells and Connective tissue infiltrated with dense amount of inflammatory cells predominantly of binucleated eosinophils, mast cells and lymphocytes. Endothelial lined capillaries engorged with RBC's were evident (Figure 2,3). Trauma causing tooth was extracted and the ulcer healed in a week with no recurrence.

CASE 2: 30 year old female patient reported with Pain and swelling in upper back tooth region since 15 days. Intra oral examination revealed solitary ulcer on left buccal mucosa measuring 1x1 cm in dimension in relation to sharp distobuccal cusp of 17 (Figure 4). Lymph node was not palpable and a provisional diagnosis of traumatic ulcer was given and excisional biopsy was performed. Histopathologically H & E stained sections showed Parakeratinised stratified squamous epithelium exhibiting hyperplasia and spongiotic superficial layer. Discontinuity in epithelium with fibrinous exudates was evident. Underlying Connective tissue exhibited dense amount of inflammatory cells like lymphocytes, neutrophils and predominantly of eosinophils infilterating deep connective tissue resulting in muscle degeneration. Proliferating endothelial cells with capillary formation were seen (Figure 5, 6). No recurrence was noticed after treating with antiobiotics and analgesics.

CASE 3: 33 year old male patient was referred to the department with a chief complaint of Pain and swelling in the upper right back tooth region since 10days. Intra-oral examination revealed ulcero proliferative growth on buccal mucosa in relation to 17and 18 region. Sub mandibular lymph node was palpable and tender but not fixed to the underlying structures. Provisional diagnosis of malignant ulcer was given. Incisional biopsy was performed and Histopathologically H & E stained sections showed hyperplastic epithelium exhibiting thin & long rete ridges. Underlying Connective tissue was infilterated with moderate amount of diffusely spread inflammatory cells predominantly of neutrophils, eosinophils and lymphocytes. Numerous plump endothelial lined capillaries engorged with RBC's were also noted. Trauma causing tooth was extracted. Patient was called back for check up 2 weeks later and wound was completely healed.

CASE 4: 36 year old female patient reported with a chief complaint of pain in the lower left back tooth region and difficulty in opening mouth from past 15 days. Intra oral examination revealed a solitary ulcer approximately measuring 1x1.5 cm on left side of buccal mucosa in relation to 37. Sub mandibular lymph node was palpable, firm, tender and not fixed to underlying structures. Provisional diagnosis of malignant ulcer was given and Incisional biopsy was performed. Histopathologically H & E stained sections revealed ulcerated epithelium exposing the underlying connective tissue consisting of dense amount of inflammatory cells predominantly neutrophils, eosinophils, lymphocytes and plasma cells. Atypical large cells resembling macrophages were evident. Inflammatory cells infilterating deep in to muscle and degenerating muscles were evident. Offending tooth was removed and treated with antibiotics and analgesics. Healing of ulcer was found after 15 days of follow up.

Case Number	Age	Sex	Chief Complaint	Clinical Features	Lymph Node Assesment	Provisional Diagnosis	Histopathology	Tratment	Recurrence
1	24	M	Pain and swelling in the upper left back tooth region since 10 days	Ulcer on buccal mucosa in r/t to 28	Sub mandibular lymph node palpable	Malignant ulcer	Microscopic examination showed Hypeplastic epithelium with superficial spongiotic cells and underlying connective tissue shows dense amount of inflammatory cell infilterate predominantly binucleated eosinophils, mast cells and lymphocytes with endothelial lined capillaries.	Trauma causing tooth was extracted	No
2	30	F	Pain and swelling in upper left back tooth region since 15 days	Ulcer on buccal mucosa in r/t to 17	Sub mandibular lymph node not palpable	Traumatic ulcer	Histopathological evaluation of H & E stained sctions revealed Parakeratinised stratified squamous epithelium,with hyperplasia and spongiotic superficial epithelium. Discontinuity in epithelium with fibrinous exudates was noted. Underlying connective tissue shows abundant eosinophils along with other inflammatory cells like lymphocytes and neutrophils. Proliferating endothelial cells with capillary formation are also noted.	Antibiotics and analgesics were given	No
3	33	M	Pain and swelling upper right back tooth region since 10days	Ulcero proliferative growth on buccal mucosa r/t to 17 &18	Sub mandibular lymph node palpable and tender not fixed	Malignant ulcer	Microscopic examination showed Hyperplastic Epithelium is with thin & long rete ridges. Connective tissue showed diffuse polymorphous inflammatory cell infiltrate predominantly of neutrophils, eosinophils, lymphocytes with numerous plump endothelial lined capillaries.	Trauma causing tooth was extracted	No
4	36	F	Pain in left lower back tooth region and difficulty in opening mouth from past 15 days.	Ulcer on buccal mucosa in r/t to 37	Sub mandibular lymph node palpable firm and tender , not fixed	Malignant ulcer	Microscopic examination showed ulcerated epithelium exposing the connective tissue consisting of diffuse inflammatory cells predominantly neutrophils, eosinophils, lymphocytes plasma cells and atypical large cells resembling macrophages. Inflammatory cells are seen infilterating deep in to muscle and degeneration of muscles were evident	Trauma causing tooth was extracted and antibiotics, analgesics were given	No

DISCUSSION

TUGSE is clinical and histopathological diagnosis of a reactive ulcer of oral mucosa.[2,10] Duration of the lesion ranges from weeks to months. Clinically manifesting as ulcer with indurated borders simulating malignant ulcer which makes it a diagnostic challenge.[7] Various etiological factors has been described in literature which includes external, internal, physical, chemical, thermal or electrical. The source of trauma can be in the form of sharp tooth, ill fitting dentures, defective orthodontic appliances and chronic irritations from malpositioned tooth. The nature of the lesion depends upon the etiologic factor and duration[5] The major evoking factor is trauma, but most of the studies show no correlation between trauma and the lesion.[11,12,13] Pathogenesis of TUGSE remains uncertain, in most of the cases initiation of the lesion following trauma results in discontinuity of epithelium creating a path way for invasion of foreign bodies, micro-organisms and their toxins. These influxed agents can result in exaggerated inflammatory response, thereby the mast cells and eosinophils will be assembled at the site. Eosinophils in turn releases the mediators like aryl sulfate, arid histamines, tissue necrosis factor, major basic protein etc which will enhance tissue damage and delay wound healing and also inhibit degranulation by mast cells.[2,3,5,14] Delayed healing nature of TUGSE is attributed to lack of transforming growth factor beta which is a secretary product of eosinophils. Tumor necrosis factor along with inflammatory and regulatory cytokines secreated by eosinophils further enhance tissue damage.[6] Massive collection of eosinophils suggest a tissue response to mucosal trauma, most of the studies suggest that high density of eosinophils are not mandatory in traumatic ulcers,[7,10] shen et al found uniform distribution of eosinophils and was found rarely infilterating deep muscles. In contrary, Marszalek et al stated that the eosinophils were more concentrated around the muscle fibres indicating consequent muscle damage. [3,15,16] Atypical cells were observed one among 4 case series, controversies exists regarding the origin of atypical large mononuclear cells. IHC studies by Regezi et al reported positive for CD68 for these atypical mononuclear cells suggesting macrophage origin,[17] Factor XIII –positive (dendritic cells) and vimentin positive suggesting myofibroblasts.[12] CD30-positive mononuclear cells raise the possibility of lymphoproliferative disorder as they are commonly expressed on activated B and T lymphocytes. [5] Alobeid et al stated that TUGSE lesion seems to be oral counter part of cutaneous CD30 positive lympho proliferative disorders.[18] only few cases of oral manifestations of lymphoproliferative are reported.[19,20,21] Ficarra *et al*. reported an ulcerated lesion of oral mucosa histologically resembling TUGSE that presented with multiple episodes of recurrent self-healing eosinophilic ulcers in which CD30 + cells were found[11] Fonesca et al suggested oral eosinophilic ulcers must be diagnosed based on the clinical, histopathological and immunohistochemical characteristics, as these lesions are self-limiting reactive condition.[14]

Lesion can be seen in wide age group ranging from 1 week to 92 years with mean age of 44 years, common in 4th to 6th decade.[13] On the contrary all 4 cases in our report was in 3rd decade of life with equal gender predilection which is in agreement with many studies[22] but study by Fonesca and wei –Ren et al shows slight male predilection

while Salisbury reported slight female predilection[14,23,16] Pain and swelling was the common complaint in 3 cases and trismus in one case. Duration of the lesion was limited to 10-15 days. All four cases exhibited single ulcer with central area of fibropurulent exudates and indurated, elevated borders simulating malignant ulcer. Buccal mucosa was involved in all 4 cases, previous studies reported tongue as most common site (60% of cases), followed by buccal mucosa, gingiva, lip, retromolar pad and palate[7] Ficarra *et al*. reported multiple and recurrent ulcers involving the buccal mucosa[11] Provisional diagnosis of malignant ulcer was given in 3 cases and traumatic ulcer in one case. Lymphadenopathy was noticed in 3 out of 4 cases which were tender and palpable but not fixed.

Histopathologically stained sections revealed ulceration with adjacent keratinized stratified squamous epithelium. Underlying connective tissue was made up of granulomatous tissue consisting of mixed inflammatory cell infiltrate predominantly eosinophils and lymphocytes, admixed with atypical mononuclear cells looking like histiocytes with large nucleus and single prominent nucleoli. Massive infiltration of eosinophils deep in to the muscles leading to degeneration of mucles were also noted. The stroma consisted of endothelial cell proliferation and blood vessels engorged with RBC's.[5,7,9] In our case series similar histopathological features were observed.

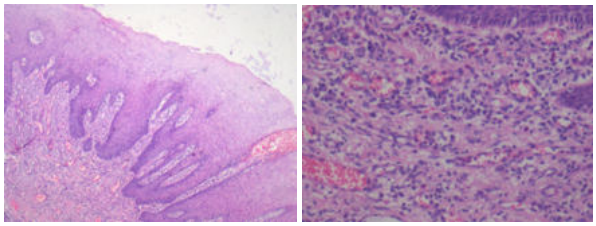
Differential diagnosis includes parasitic diseases, contact and drug allergic reactions, eosinophilic granuloma, eosinophilic fascitis, atypical histiocytic granuloma, Langerhans cell histiocytosis (LCH), angiolymphomatoid hyperplasia with eosinophilia (ALHE), pseudolymphoma, Kimura disease, certain types of lymphomas, Low-grade lymphomas.[1,5,7]

TUGSE lesions are treated with simple surgical excision. Rapid healing followed by incisional biopsy has been reported in many cases.[5,11,15] Removal of causative factor or appropriate management of the offending tooth is a baseline treatment followed by antibiotics like penicillin. Other treatment modalities includes topical application of liquid nitrogen, 0.1% triamcinolone acetonide, and electrocoagulation.[5,9] Prognosis of TUGSE is normally favorable, but minimum 2 years follow up period is compulsory.[7] No recurrences or new lesions were reported in our case series with in follow-up period of 2 years.

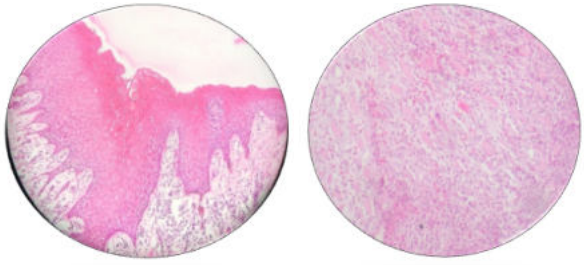
CONCLUSION:

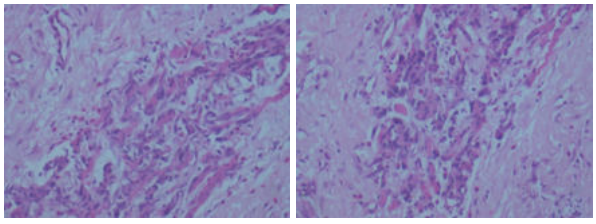
TUGSE is distinct lesion with benign, ulcerative condition of oral mucosa which can resolve without treatment, if underlying traumatic factor is removed. Clinically resembles malignant ulcer for which biopsy is mandatory to rule-out oral squamous cell carcinoma. Dentists are expected to have fundamental knowledge regarding the clinical, histopathological analysis and appropriate treatment modalities.

CASE 1



CASE 2





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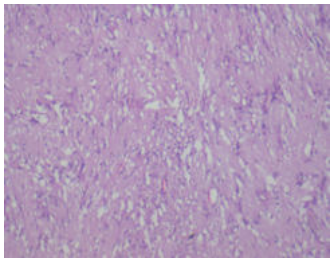
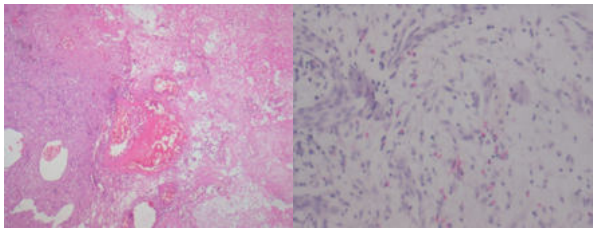
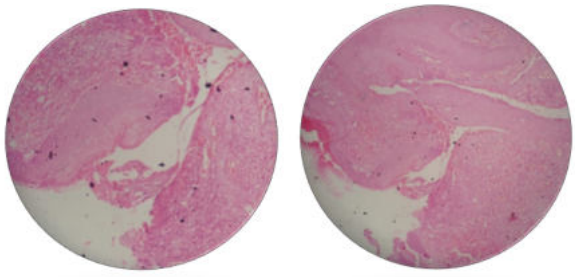
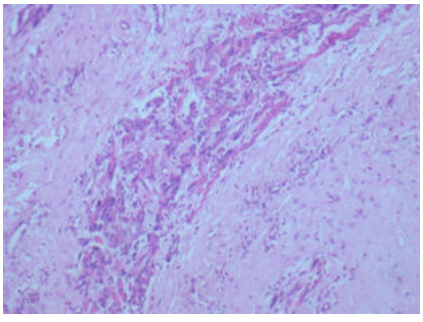




CASE 4





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