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Traumatic Ulcerative Granuloma with Stromal Eosinophilia

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A 41-year-old man presented with an 8-year history of recurrent mouth ulcers, previously treated with unrecalled antibiotics and vitamins but with no relief. Examination showed a 2.0 x 1.0 cm hard, immovable ulcer at the right lateral tongue. On further interview, a history of repeated biting trauma on the site of the lesion was elicited. The clinical impression was a non-healing tongue ulcer. Incision biopsy of the lesion was performed and the specimen sent for histopathologic evaluation.

The specimen consisted of three, cream-tan, irregularly-shaped soft tissues measuring up to 0.9 cm in widest diameter. The cut sections of the tissues showed a tan-pink to cream-white soft cut surface. Microscopic examination showed a squamous epithelium-lined tissue with a dense polymorphic infiltrate of inflammatory cells rich in neutrophils, eosinophils, plasma cells and large atypical mononuclear cells, and accompanying granulation tissue formation. *(Figures 1 and 2)* Immunohistochemical studies showed CD20 expression of B-cells in the lymphoid follicles, with CD3 and CD5 highlighting the surrounding T-cells. The plasma cells are staining for both kappa and lambda, with kappa-lambda ratio of 3:1. The Ki-67 showed a high proliferation index within the reactive germinal centers and scattered low proliferative activity within the interfollicular areas. *(Figure 3)* Given the morphologic and immunohistochemical profile of the lesion, we diagnosed it as traumatic ulcerative granuloma with stromal eosinophilia.

Traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) is considered a rare lesion of the oral mucosa. First described in 1881 by Riga then defined histologically in 1890 by Fede,[1,2] it has since been called by a variety of terms including traumatic ulcerative granuloma, ulcerative eosinophilic granuloma, and Riga-Fede disease in infants and neonates. The term TUGSE was first coined by Elzay in 1983 to delineate it from more aggressive conditions such as eosinophilic granuloma, eosinophilic fasciitis and carcinoma with stromal eosinophilia.[3] It is a benign, chronic, self-limiting lesion of the oral mucosa.[1,2]

TUGSE typically manifests as an isolated ulcer with elevated margins or an indurated submucosal mass, most commonly affecting the dorsal or lateral surfaces of the tongue but can be found in other locations in the oral mucosa such as the lip, palate, and gingiva.[2,4] The lesions can also be multifocal and recurrent, and can persist from several weeks to months, but will heal without treatment; a wide age range of patients can be affected, with a peak incidence in the sixth and seventh decades of life, with only a slight female predominance.[1,4] Due to its clinical manifestation, it can often be mistaken for malignancy or an infection; however, its microscopic and immunohistochemical features, self-limiting nature and spontaneous resolution indicate a benign reactive process.[1,2]

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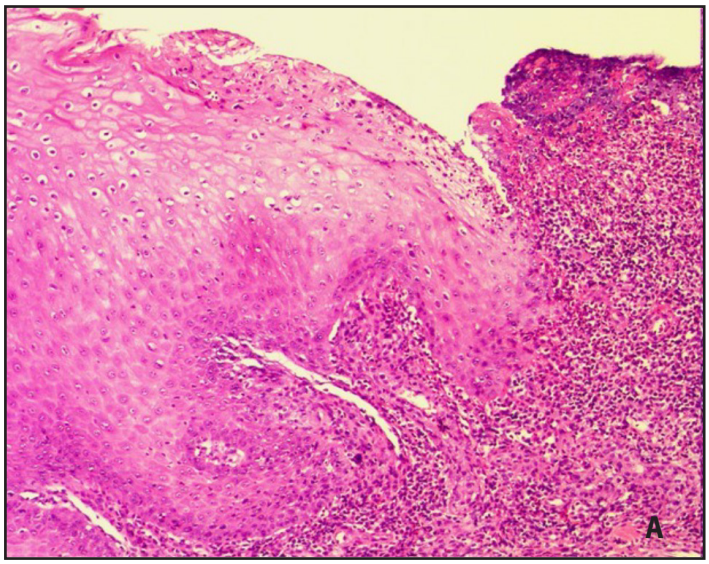
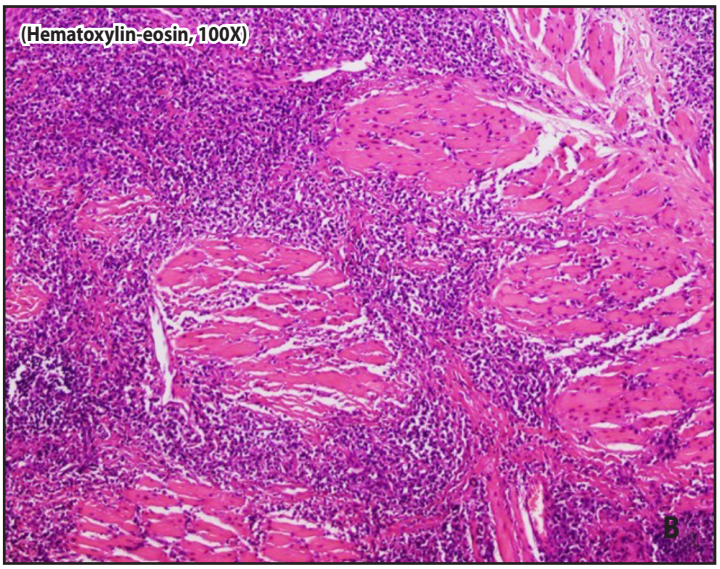


Figure 1. A. Ulcerated stratified squamous epithelium overlying dense inflammatory infiltrate.



B. Dense polymorphous inflammatory infiltrate extending into skeletal muscle. (Hematoxylin-eosin, 100X magnification).

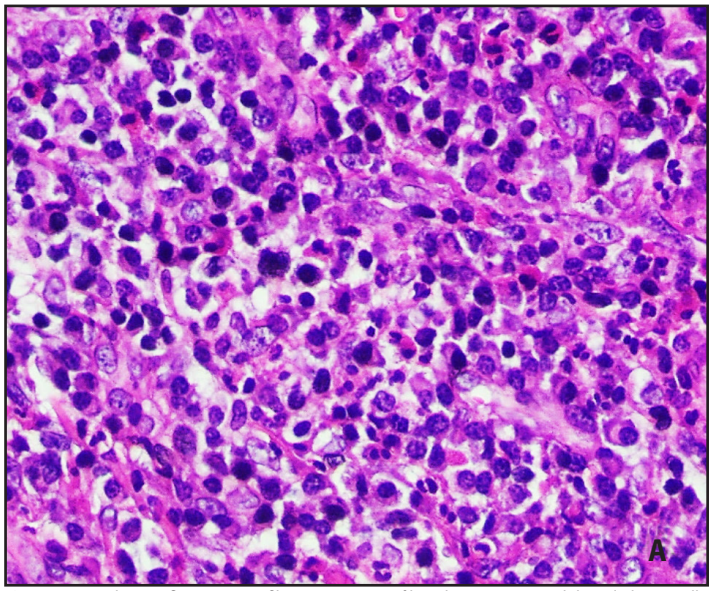
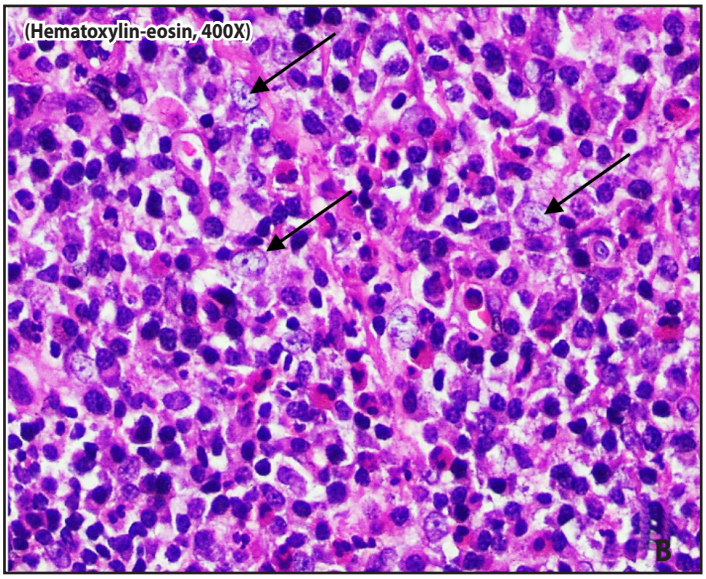


Figure 2. A. A dense inflammatory infiltrate consisting of lymphocytes, eosinophils and plasma cells, with granulation tissue formation.



B. Atypical mononuclear cells (black arrows) showing pale cytoplasm, irregular nuclear contour, with small nucleoli. (Hematoxylin-eosin, 400X magnification).

Histologically, TUGSE is characterized by a diffuse polymorphic infiltrate of inflammatory cells that can extend deep into the submucosa and skeletal muscle; it is predominantly composed of eosinophils, B and T lymphocytes, macrophages, with atypical large mononuclear cells.[1,2,4] These atypical cells have abundant pale cytoplasm, irregular nuclear contours, small nucleoli and fine chromatin.[1,2,4] The origin of these large mononuclear cells are still disputed and have been reported to originate from lineages such as histiocytes (CD68), dendritic cells (factor XIII), myofibroblasts (vimentin) and T-lymphocytes due to their variable immunohistochemical characteristics.[1,2,4] The immunostains performed in our case showed intact B-cell compartment highlighted using CD20, and intact T-cell compartment using CD3 and CD5. The plasma cells are polyclonal to kappa and lambda. The proliferation index using Ki-67 is high within the reactive germinal centers, and low in the interfollicular area. The immunohistomorphologic features are compatible with a reactive process.

The etiology and pathogenesis of TUGSE have not been completely established but is postulated to be associated the with trauma,

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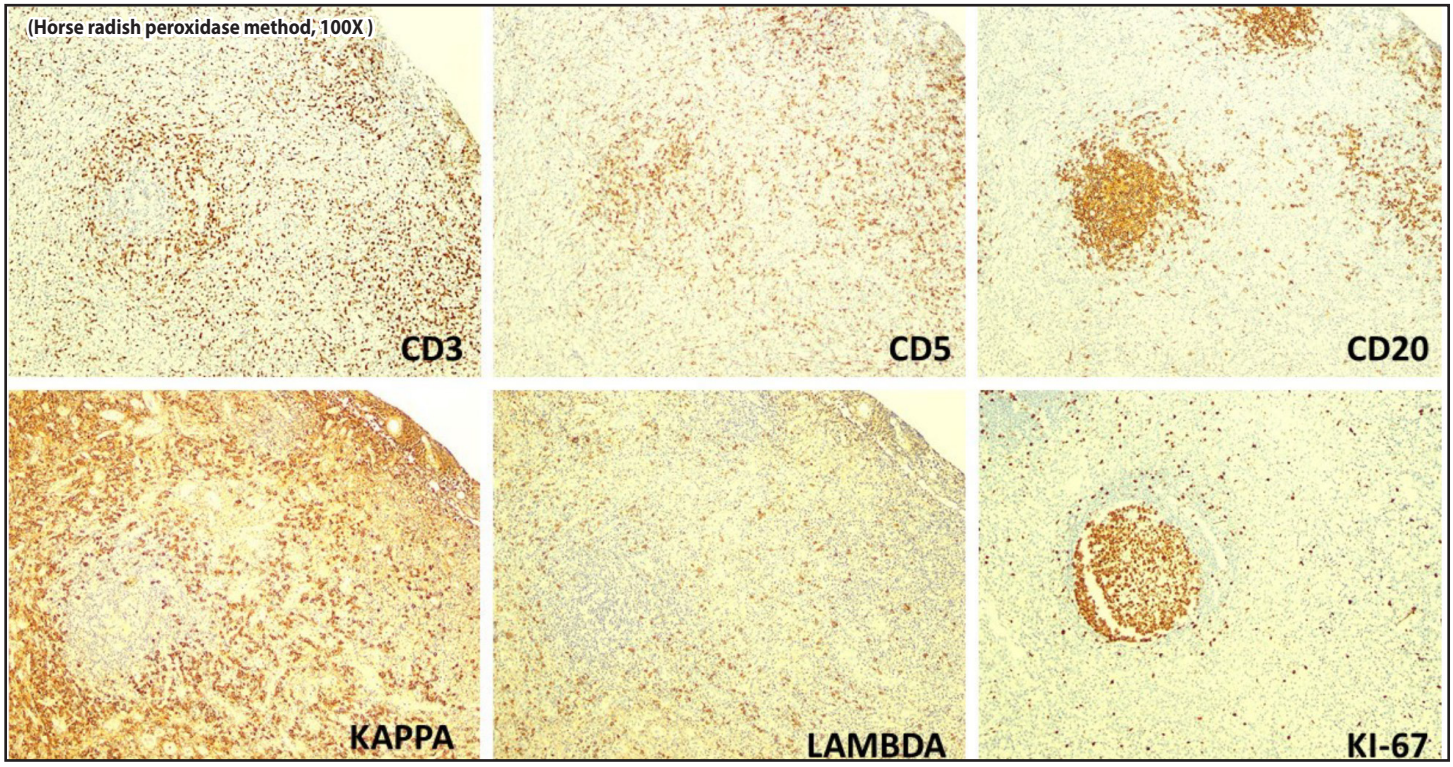

Figure 3. Immunohistochemistry showing CD20-positive B-cells in the lymphoid follicles, with the surrounding T-cells highlighted by CD3 and CD5. The plasma cells are polytypic for kappa and lambda. Ki-67 shows a high proliferation index within the reactive germinal centers and low proliferative activity between the follicles. (Horse radish peroxidase method, 100X magnification).

although obvious trauma could only be demonstrated in 50% of the cases.[1,4] Traumatic disruption of the mucosa facilitates a cell-mediated immune response due to the action of a non-identified etiologic factor such as microorganisms, toxins and/or foreign proteins; this induces an eosinophilic and mast cell reaction, including a release of cytotoxic T-cells ultimately leading to local tissue destruction.[1,5] It has also been suggested that it may be a CD30+ lymphoproliferative disorder.[1,4-6] A CD30 positivity can be seen in lymphomas, lymphoproliferative diseases, Reed-Sternberg (RS) cells, and activated T and B cells, but also occur in benign cutaneous disorders such as drug reaction, atopic dermatitis and molluscum contagiosum; however, involvement of the oral mucosa with lymphoproliferative diseases is rare.[1,4,5]

The pathogenesis and etiology of the entity remains unclear, and can mimic malignant conditions due to its clinical, histological, and immunohistochemical features thus the diagnosis of TUGSE should be made by the combination of clinical data, histopathologic, and immunohistochemical features.[1] The condition has a benign course and is characteristically self-healing.[1,2]

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