

Granulomatous glossitis: a case report

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Abstract: A 50-year-old man was admitted to our clinic with a complaint of lingual enlargement. Detection of non-caseous epithelioid granuloma on histopathological examination led to a diagnosis of a granulomatous glossitis. Extensive investigation for the presence of associated disorders yielded negative results. Metranidazole and clofazimine were totally ineffective and tetracycline led to a minimal improvement. No associated disorder was detected at a 4-year follow-up examination. The position of granulomatous glossitis within the spectrum of orofacial granulomatous conditions is discussed. (*J. Oral Sci.* 46, 199-202, 2004)

Key words: granulomatous glossitis; orofacial granulomatosis; Melkersson-Rosenthal syndrome.

Introduction

The term orofacial granulomatosis was introduced to encompass the broad spectrum of non-necrotizing granulomatous inflammation in the oral and facial region, including patients with the complete triad of Melkersson-Rosenthal syndrome (MRS), chelitis granulomatosa, sarcoidosis, Crohn's disease and infectious disorders such as tuberculosis (1,2). There may be several underlying etiologic mechanisms, with similar clinical and pathologic presentations, often manifesting at different points in time (3).

Granulomatous glossitis was first described as a peculiar manifestation of MRS by Schuermann in 1952 (4). The typical triad of MRS is rarely seen simultaneously, and involvement of the tongue as a sole manifestation of MRS is much rarer. In monosymptomatic cases, making a clear diagnosis is difficult, and therefore a complete differential diagnosis for the other recurrent or persistent disorders characterized by macroglossia has to be done (5).

Herein we report a case of granulomatous glossitis with no associated systemic disorder that was unresponsive to clofazimine and metronidazole, yet showed minor improvement with tetracycline.

Case Report

A 50-year-old man presented with a complaint of enlargement of the tongue associated with small glossal tags. The papules had developed at the edge of the tongue and gradually increased in number during the previous five years. The patient complained of speech impairment, hypersalivation and a burning sensation on eating. He denied swelling of the lips, buccal and labial mucosa, and the face. His medical history was unremarkable except for hypertension that had been controlled with anti-hypertensive drug therapy for the previous 10 years.

Dermatologic examination revealed slight enlargement of the tongue with a deep central furrow, multiple shallow radial fissures and multiple white mucosal tags at the edge of the tongue (Figs. 1 and 2).

Laboratory investigations including a complete blood count, erythrocyte sedimentation rate, serum electrolytes, hepatic and renal function tests, serum iron level, anti-HIV antibodies, angiotensin converting enzyme level, thyroid function tests, IgG, IgA, IgM, IgE levels, ANA, anti-DNA, 24 hours urine calcium level, and stool examination for the presence of blood were all either negative or within normal limits. Contrast imaging of the esophagus, large

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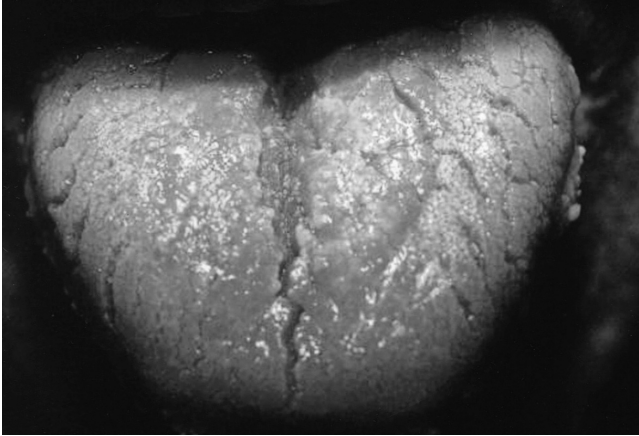


Fig. 1 A deep central and multiple shallow radial fissures on the tongue.



Fig. 2 Multiple white mucosal tags at the edge of the tongue.

and small intestine, computed tomographic examination of the thorax and temporal bone, pulmonary function tests, abdominal ultrasound and gallium scintigraphy of the bones all gave normal results. A patch test for European standards (commercially available) was negative. The European standard series includes the 22 most commonly encountered allergens and is used to document and validate a diagnosis of allergic contact sensitization and identify the causative agent. Substances to be tested are applied to the skin in shallow cups (Finn chambers), affixed with tape and left in place for 48 hours. Contact hypersensitivity, if present, results in a papular-vesicular reaction that develops within 48 to 72 hours when the test is read. Results of neuropsychological testing of taste sensation, perception of temperature and pressure were within normal limits. Complete systemic examinations as well as neurologic, pulmonary and ophthalmic examinations showed unremarkable findings. A dental examination revealed dental caries for which root canal treatment had been done. A tuberculin skin test (PPD) revealed a positive 20-

mm induration at 48 hours. However, this was considered insignificant because of normal chest X-ray findings and the fact that routine immunization for tuberculosis is done routinely in Turkey. Histopathologic examination of the biopsy specimen obtained from the lateral zone of the tongue revealed non-caseating epithelioid granuloma with Langhans-type giant cells and lymphocytes in the muscle fibers with surrounding plasmocytic infiltration (Figs. 3 and 4).

The case was diagnosed as granulomatous glossitis and treated with metronidazole for six months, clofazimine for three months and tetracycline for six months. Because of hypertension, systemic corticosteroid therapy was not offered and the patient refused treatment with intralesional corticosteroids. Tetracycline therapy produced a mild clinical improvement of the mucosal tags. However, the tongue enlargement and furrows were not altered by this therapy. Since the patient denied any complaints, no further therapy was administered and he was followed up for four years with no progression or complication. During follow-up no associated systemic disease has arisen.

Discussion

The clinical features of granulomatous glossitis include gross enlargement of the tongue with a cobblestone appearance on its surface and firm induration on palpation. Granulomatous infiltration of the tongue may be observed in various disorders, including MRS, sarcoidosis, Crohn's disease, leprosy, tuberculosis, tertiary syphilis and deep mycotic infections. However tissue cultures, bacteriologic examination, serologic tests, systemic examination of the lung and intestinal tract can be helpful for differential diagnosis.

The typical triad of MRS signs - peripheral facial paralysis, recurrent perioral swelling and stable lingua plicata - is rarely seen simultaneously. Frequently, oligo- and monosymptomatic forms are present (5). Although the upper lip is the most commonly affected site, involvement of the tongue is seen in less than 10% of patients with MRS. Granulomatous glossitis as the unique symptom of MRS is even more uncommon. The differentiation of major and minor clinical signs may facilitate the recognition of MRS even in incomplete cases. Minor signs such as paroxysmal epiphora, nasal hypo- or hypersecretion, episodic facial sweating, tinnitus, blurred vision, blepharospasm, and migraine-like headaches are nonspecific symptoms themselves; however, in association with one or more major criteria they may allow a diagnosis of MRS to be made.

Granulomatous glossitis must be differentiated from lingua plicata, which is frequently associated with MRS.

This congenital condition of the tongue is harmless, painless and the tongue is of normal size and consistency. Histopathologic examination of the tongue may aid the diagnosis.

The suggestion that orofacial granulomatosis is a variant of sarcoidosis has not been confirmed, although occasional patients have a positive Kveim reaction or a raised serum concentration of angiotensin-converting enzyme (6,7). Nevertheless, only very few patients with MRS have manifestations of sarcoidosis or Crohn's disease. Atopy has been found in 12-60% of the patients, and specific intolerance to foods or additives has been proposed (1,8). Potential allergic factors should be evaluated early in the diagnostic process by querying any history of contact allergies, patch testing and elimination diets, particularly for oral hygiene products such as toothpaste and mouth-rinses, foods, food additives, flavorings, metals and cosmetics (9).

On the other hand, granulomatous lesions of the oral cavity may be seen in patients with proven Crohn's disease, or these lesions may antedate bowel symptoms by several

years and may be the only obvious site of the disease. Some patients with oral lesions may have symptomless intestinal disease (1,10,11). Kano et al. (12) reported that some patients with cheilitis granulomatosa are predisposed to Crohn's disease, and cheilitis granulomatosa has been reported to precede intestinal Crohn's disease by up to several years (13,14). In only 2 of 13 patients reported by van der Waal et al. (3), cheilitis granulomatosa preceded Crohn's disease, and therefore routine investigation of the gastrointestinal tract in patients with cheilitis granulomatosa or MRS with a negative history of gastrointestinal complaints is not recommended.

The distinction between orofacial granulomatosis and other conditions with non-caseating granulomas may not be easy. The histologic findings of tuberculoid or sarcoid-like granulomas or lymphocellular infiltrates surrounded by plasma cells intermingled in the edematous connective tissue are considered diagnostic for granulomatous glossitis. Management should include biopsy of the lesion and exclusion of systemic diseases by hematological and biochemical investigations. If there are gastrointestinal

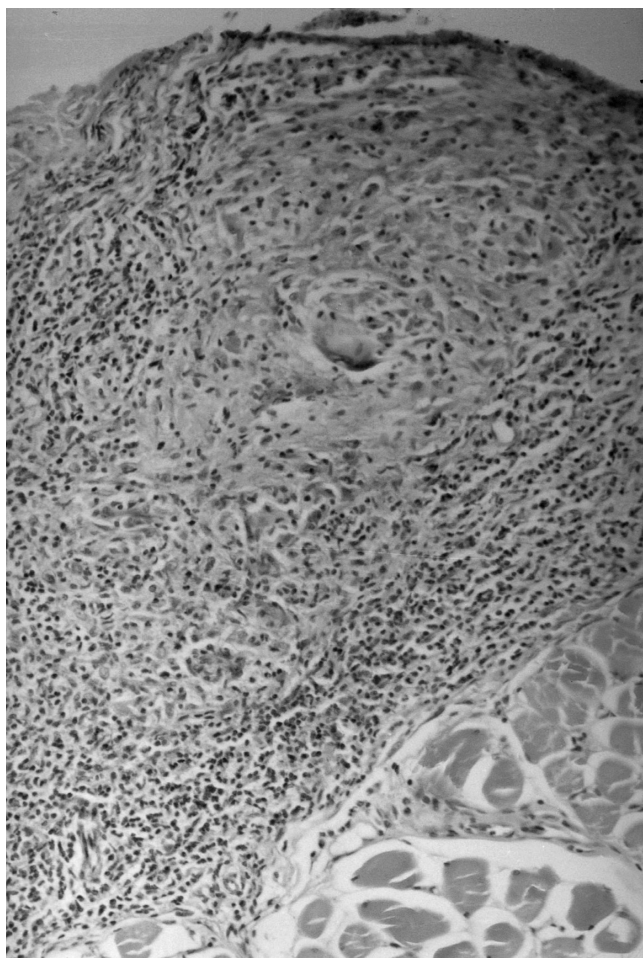


Fig. 3 Non-caseating epithelioid granuloma of the tongue.

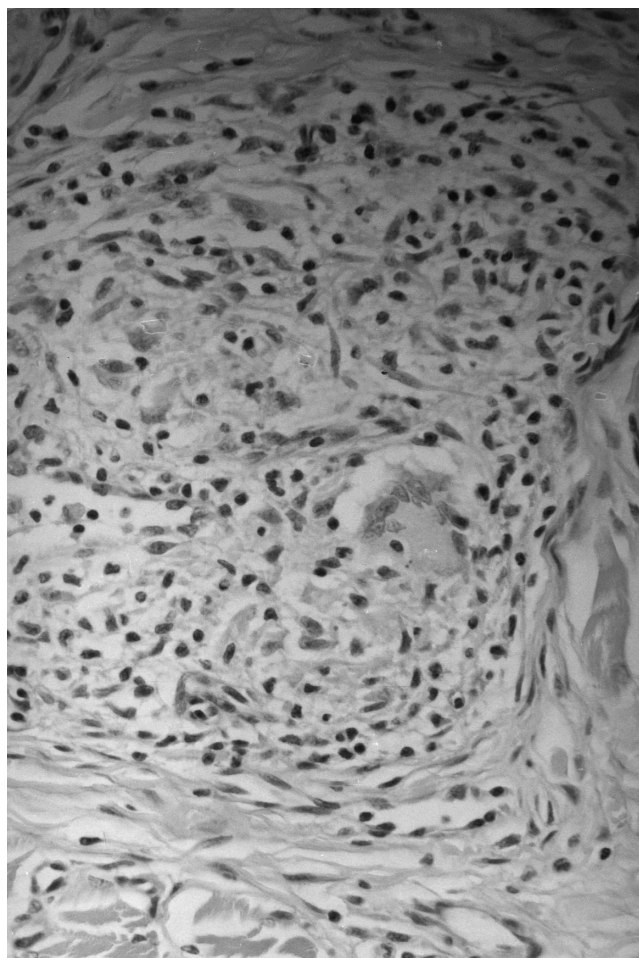


Fig. 4 Close-up view of a Langhans-type giant cell.

symptoms, bowel radiography and intestinal biopsy are indicated.

Oral sulfapridine or hydroxychloroquinsulfate and intralesional application of corticosteroids have been tried as therapeutic alternatives to clofazimine or corticosteroids with varying success. Surgical reduction is also a therapeutic option. Mahler et al. (5) have presented a case of granulomatous glossitis as an unusual form of MRS. In this case, after treatment with clofazimine, perioral and lingual swelling disappeared within two weeks.

For the present case a thorough systemic investigation revealed no remarkable features, and the diagnosis of granulomatous glossitis was established on clinical and histopathological grounds. Since the patient had no gastrointestinal complaints and showed normal contrast imaging of the gastrointestinal tract, intestinal biopsy was not recommended. In the absence of minor symptoms, it is difficult to establish a definite diagnosis. In our opinion, this condition may be either a unisymptomatic form of MRS or may form part of the spectrum of orofacial granulomatosis. Since granulomatous glossitis is a rare condition, extensive investigation for any underlying disease must be performed in order to classify this condition as a separate entity under the disease spectrum of orofacial granulomatosis.

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