Clinicopathological diagnosis of orofacial granulomatosis

ABSTRACT

Orofacial granulomatosis is a rare chronic inflammatory disorder characterized by persistent or recurrent soft tissue swellings, oral ulceration, and other orofacial features in the absence of an identifiable granulomatous disease. We report a case of a 61-year-old woman with recurrent ulcerations and swellings in her oral mucosa. She was diagnosed as orofacial granulomatosis based upon clinicopathological correlation after exclusion of other granulomatous diseases and showed a favorable response to systemic corticosteroid treatment.

Key Words: *Oral mucosa, orofacial granulomatosis, pathology*

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Introduction

Orofacial granulomatosis (OFG) is a rare and heterogenous clinical condition which is characterized by orofacial granulomas presenting in the absence of recognized systemic condition.[1] The classic presentation of OFG is a nontender recurrent labial swelling that eventually becomes persistent.[2] However, the clinical presentation can be highly variable, making the diagnosis difficult to establish.[3] We report the case of a 61-year-old woman with persistent swollen masses on the tongue and the retromolar trigone, swelling of the lower lip mucosa and cobblestoning, representing OFG which showed a favorable response to systemic corticosteroid treatment.

Case Report

A 61-year-old female patient presented with a 20-year history of swollen masses in her oral mucosa, which sometimes ulcerated. Clinical examination revealed firm nontender infiltrating masses involving the right lateral side of the tongue (3 × 2 cm) [Figure 1a] and right retromolar trigone (2 × 2 cm) [Figure 1b] with granular surfaces, swelling of the lower lip mucosa with cobblestoning [Figure 1c], and multiple palpable, nontender, firm, and mobile lymph nodes on both sides of the neck. She had no symptoms of fever, fatigue, weight loss, or gastrointestinal disturbance, and she had not undergone any investigation or treatment for her complaints before, except using occasional topical corticosteroids and antiseptic mouthwashes. She denied the role of diet on the lesions. Her medical history revealed diabetes mellitus and family history was positive for hypertension in her mother.

Laboratory data including complete blood cell count, serum biochemistry analysis, urinalysis, and serum C reactive protein, calcium, vitamin B12, folate, and angiotensin converting enzyme values were normal except elevated serum fasting glucose (143 mg/dl). The erythrocyte sedimentation rate was 41 mm/h, and chest radiography was normal with no signs of sarcoidosis or tuberculosis. The Mantoux test and pathergy test were also negative.

An incisional biopsy of the lesion involving the retromolar trigone was performed, and the biopsy materal was split into two pieces for histopathologic examination and mycobacteriologic culture. Soft tissue ultrasonography of the neck revealed lymphadenitis, and the biopsy of the lymph nodes showed noncaseating granulomatous lymphadenitis. The histopathologic examination of the oral lesion together with Erlich-Ziehl-Neelsen stain for acidoresistant bacilli (ARB) and periodic acid schiff (PAS) stain showed well-demarcated granuloma formation consisting of epitheloid cells surrounded by lymphocytes

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in an edematous stroma [Figure 2]. Although the patient had no gastrointestinal symptoms, a colonoscopy was performed. Minor ulcerations were seen in the descending colon. Mucosal biopsies from the observed lesions revealed aphtous ulcerations; inflammatory bowel disease, neoplasia, and tuberculosis were ruled out. Mycobacterial culture of the oral biopsy sample showed no growth.

Based on history, clinical findings, histopathologic examinations, and laboratory data, sarcoidosis, tuberculosis, systemic fungal infections, and Crohn's disease were excluded, and the patient was finally diagnosed as idiopathic orofacial granulomatosis.

Oral prednisolone 50 mg/day was started for ten days and then tapered 10 mg every week. The treatment was well tolerated by the patient except for slight increases in serum glucose levels, which were regulated by adjusting the insulin dosages. Lesions showed marked improvement, and no recurrence was observed in a 2-year follow-up.

Discussion

OFG is a diagnosis of exclusion.[4] It is an uncommon disorder characterized by persistent and/or recurrent labial enlargement, oral ulcers, and a variety of orofacial features in the absence of identifiable Crohn's disease or sarcoidosis.[5]

The diagnosis of OFG is made by histopathologic identification of noncaseating granulomas. Local and systemic conditions characterized by granulamatous inflammation must be excluded by appropriate clinical and laboratory investigations.[6] OFG characteristically presents with lip swelling along with affecting the gingivae, buccal mucosa, floor of the mouth, and a number of sites in the oral cavity.[7] However, the clinical presentation can be highly variable, making the diagnosis difficult to establish. For example, intraoral involvement may take the form of hypertrophy, erythema, or nonspecific erosions involving the gingiva, oral mucosa, or tongue.[6,8]

Upon microscopic identification of granulomatous inflammation, special stains are used to rule out deep fungal infectons [periodic acid schiff stain (PAS)] or specific bacterial infections (Ziehl-Neelsen, Gram).[6] Blood tests, radiology, and endoscopy are other tools used to differentiate OFG from Crohn's disease, sarcoidosis, tuberculosis, and foreign body reactions.[5] A diagnosis of idiopathic OFG is made on the basis of negative results of a thorough investigation.[3]

The clinical presentation of OFG may sometimes be similar to sarcoidosis, which can affect any organ or part of the body. Sarcoidosis may present as facial, labial, mucosal, and gingival granulomatous proliferation.[1] However, the presence of hilar lymphadenopathy on chest radiographs and raised serum angiotensin converting enzyme levels suggest a diagnosis of sarcoidosis rather than OFG.[1,9] The patient had normal chest radiography with normal serum angiotensin converting enzyme level. An extensive review of the literature reveals that there may be considerable overlap with OFG presenting as a distinct clinical disorder or as an initial presentation of Crohn's disease.[7,10] However, OFG appears to be more frequently related to systemic disease, with intestinal inflammation significantly more likely if OFG onset is under 30 years of age.[7,11] Considering her age at the onset of the lesions, the patient was unlikely to have systemic disease with intestinal inflammation. In addition, the colonoscopy and histopathological evaluation of the intestinal mucosal biopsies ruled out Crohn's disease. At present, it is suggested that both orofacial granulomatosis and oral Crohn's disease appear to be distinct clinical disorders. They are separated on clinical grounds where OFG tends to present with more labial pathology and less oral ulceration.[12]

A differential diagnosis of any granulomatous disorder should also include leprosy, tuberculosis, and in tropical parts of the world, certain fungal infections. Tuberculosis can be confirmed by a Mantoux test and chest radiographs and is characterized histologically by caseation necrosis and

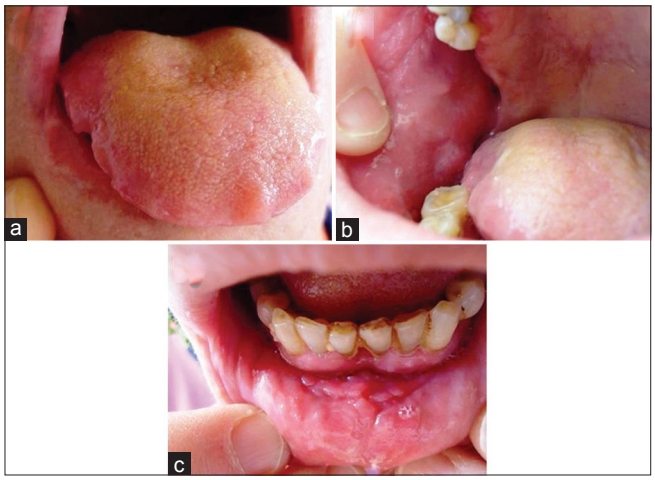

Figure 1: (a) Mass with a granular surface involving the lateral border of the tongue. (b) Mass with a granular surface in the right retromolar trigone. (c) Cobblestone like swelling in the lower lip mucosa

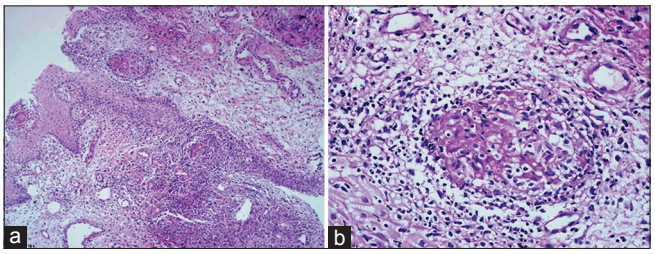

Figure 2: (a) Well-demarcated granulomas in an edematous stroma under the hyperplastic stratified squamous epithelium (hematoxylin-eosin stain, original magnification: ×100). (b) Granuloma formation consisting of epitheloid cells surrounded by lymphocytes in an edematous stroma (hematoxylin-eosin stain, original magnification: ×400)

acid and alcohol fast bacilli.[9] In the patient, tuberculosis was ruled out by normal chest radiography, negative Mantoux test, and no growth in the mycobacteriologic culture of the biopsy sample.

The etiology of OFG is uncertain, but a number of causes have been implicated such as genetic, allergic, infective, and immunological factors.[10,13] Hypersensitivity reactions to various food, preservatives, or components of oral hygiene products have been implicated in inducing tissue changes consistent with OFG.[14] The cause can be a protracted one, ranging over many years.[9]

The treatment of OFG is difficult, particularly in the absence of an etiologic factor. However, rare spontaneous remission is possible.[6,15] First line treatment involves the use of local or systemic corticosteroids or both.[6] Other alternative treatment agents have been reported in the literature including hydroxychloroquine, methotrexate, azathioprine, clofazimine, metronidazole, minocycline, thalidomide, dapsone, danazol, and TNF-α blocking agents such as infliximab and adalimumab.[3,6,9,16] The response to elimination diets has in some cases been encouraging but not all patients respond to this regime.[9] Surgery may be necessary to manage the complications of the disease and is used in cases that do not respond to medical treatment.[6] The patient showed a favorable response to systemic corticosteroid treatment without any sign of recurrence during a 2-year follow-up period.

In conclusion, the use of the term OFG in cases of noncaseating granulomatous inflammation has the advantage of describing a clinicopathologic situation without linking it to a specific disease entity,[3] and OFG defines a group of conditions in which granulomatous inflammation occurs in the oral cavity, especially the lip. In some cases, the inflammation appears to be limited to the oral cavity.[7] Patients with severe OFG may have cervical lymphadenopathy, which can be localized or generalized, tender or nontender of variable size, and usually of rubbery consistency.[5,17] The patient represented a case of idiopathic OFG with histopathologically proven noncaseating granulomas involving the lower lip mucosa, tongue, and the oral cavity with cervical lymphadenopathy. Hence, orofacial granulomatosis should be considered as the diagnosis when noncaseating granulomas involving the orofacial area are established histopathologically in the absence of recognized systemic disease.

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Conflicts of interest

There are no conflicts of interest.

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