Orofacial granulomatosis of the lower lip and cheek: report of a case

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Orofacial granulomatosis (OFG) is a granulomatous disease of the orofacial region. This clinicopathological entity describes patients with oral lesions characterized by persistent and/or recurrent labial enlargement, ulcers, and a variety of other orofacial features, which on biopsy have lymphedema and noncaseating granulomas. The cause is idiopathic but appears to represent an abnormal immune reaction. This may be a manifestation of Crohn's disease (CD) since some patients with oral lesions develop typical bowel symptoms of CD in ensuing months to years; tooth-associated infections, sarcoidosis, food or contact allergies, and viruses have also been implicated in causing OFG. Clinical features of OFG are highly variable and sometimes so insidious that signs and symptoms are frequently not severe enough to cause alarm. The lips are most commonly involved and demonstrate a nontender, persistent swelling. Because of the relatively nonspecific clinical findings associated with granulomatous diseases, a microscopic diagnosis of granulomatous inflammation often presents a diagnostic dilemma for clinicians. We report a case of OFG of the lower lip and cheek and describe its management to add to the current body of literature on the subject. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104:e42-e44)**

The term orofacial granulomatosis (OFG) was introduced by Wiesenfeld in 1985.[1-3] It is a disease that affects individuals of both sexes of almost all ages, races, and geographic locations. OFG comprises a group of diseases characterized by noncaseating granulomatous conditions affecting the lips and intraoral sites.[1-8] The most common clinical presentation is persistent swelling of one or both lips. It is important to establish the diagnosis accurately because granulomatosis is sometimes a manifestation of Crohn's disease (CD) or other granulomatous inflammations. A cell-mediated hypersensitivity reaction is favored as the etiology because of the presence of activated helper T lymphocytes expressing interleukin-2 receptors in these lesions. The disease may result from an exaggerated cellular immune response and females appear to be slightly more susceptible than males.[1-5] Oral involvement is often unilateral and may sometimes resemble a benign or malignant tumor. Clinically, small nodules, plaques, or ulcers resembling herpetic lesions or fever blisters, may be seen on the palate and buccal mucosa. The lesion has been described as bleb-like, containing a clear yellowish fluid, or as solid nodules mimicking a tumor. The most common differential diagnoses include foreign body reactions, infection, CD, sarcoidosis, and OFG; all are characterized by noncaseating granulomatous inflammation, thus, it is important to establish the diagnosis.[3-7]

CASE REPORT

A 55-year-old man was referred in January 2005 for a mass in the right side of the lower lip and cheek. The swelling had been present for 2 years (Fig. 1). The patient had no systemic disease and his past medical history was noncontributory. There was no evidence of foreign material or any history of trauma. Clinically, the swelling of the lower lip and right cheek was firm, indurated, and tumorlike and the overlying mucosa was erythematous and had a cobblestone appearance. There were no palpable nodes in the face and neck regions. Routine laboratory tests (CBC diff., ESR, Ca, P, platelet count, alkaline phosphatase, urinary Ca., ACE) were done and were reported to be within normal limits. Radiographic studies of the face and the chest did not reveal any abnormalities. There was no hilar lymphadenopathy on the chest radiograph (CXR). The patient had undergone prolonged antibiotic therapy for mistaken cellulitis and numerous incisions for drainage had been performed erroneously by dentists before referral. No clinical signs or symptoms of gastrointestinal (GI) disease were present. The patient was admitted for a biopsy. Upon admission, the patient underwent an intraoral incisional biopsy. Histopathologic examination revealed the presence of non-necrotizing granulomas composed of epithelioid histiocytes and giant cells with a peripheral rim

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Received for publication Feb 21, 2007; returned for revision May 11, 2007; accepted for publication May 11, 2007.
1079-2104/$ - see front matter

doi:10.1016/j.tripleo.2007.05.012

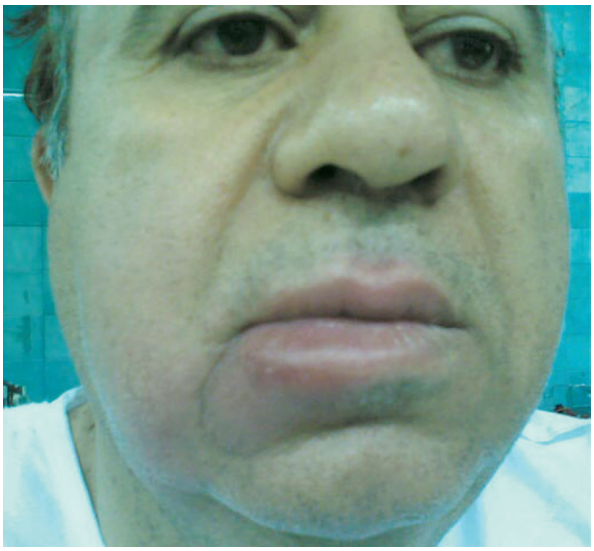

Fig. 1. Photograph of the patient on admission with swelling of the right cheek and lower lip.

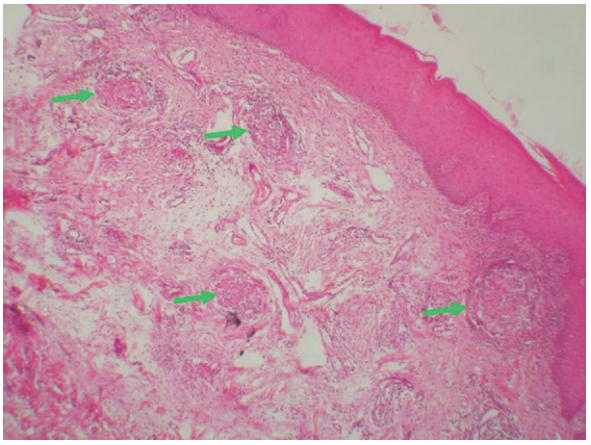

Fig. 2. Low-power photomicrograph of the oral mucosa revealing granulomatous masses without caseation or necrosis (*arrows*) (hematoxylin and eosin [H&E]; magnification ×100).

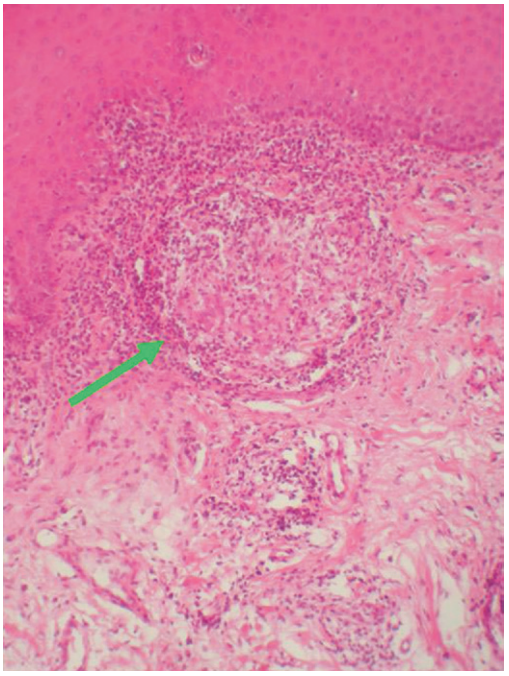

Fig. 3. High-power magnification demonstrating granulomatous inflammation beneath the mucosa (*arrow*) (H&E; magnification ×200).

of lymphocytes. A diagnosis of OFG was made based on correlation of the histopathologic findings with normal laboratory test results and normal CXR findings (Figs. 2 and 3). The patient was given prednisolone 1mg/kg for 4 weeks followed by a slow tapering over 2 to 3 months to suppress the lesion (Fig. 4). The patient has been symptom-free since; however, he is being followed periodically for possible recurrences or development of CD.

DISCUSSION

The diagnosis of OFG is one of exclusion after excluding foreign bodies, microorganisms, and other disorders such as chronic granulomatous disease, CD, mycobacterial infection, and sarcoidosis.[1]

Differential diagnosis

Patients with CD may present to the clinician with GI symptoms attributed to the disease or nonspecific lesions in the oral cavity, nose, or larynx. Some OFG patients have both histopathological and immunopathological features that resemble those observed in CD patients.[9] Some of these clinical manifestations have been found to be consistent with CD, but most have not.[5,6] Often an extensive clinical, microscopic, and laboratory evaluation may be required to identify the source of the granulomatous inflammation.[5] Negative endoscopy of the GI tract, normal ESR, normal serum albumin, Ca, folate and iron levels will rule out CD. With regard to sarcoidosis, a normal CXR and ACE level would make sarcoidosis unlikely. Chronic granulomatous disease is ruled out by using the neutrophil nitroblue tetrazolium reduction test.[10] Another condition that may be associated with granuloma formation is cheilitis granulomatosa (CG). CG is a subset of OFG, which presents clinically as persistent lip swelling. It also is a granulomatous inflammation of unknown origin. CG may be part of the triad of the Melkersson-Rosenthal syndrome (MRS).[5-8] Swelling of the lips

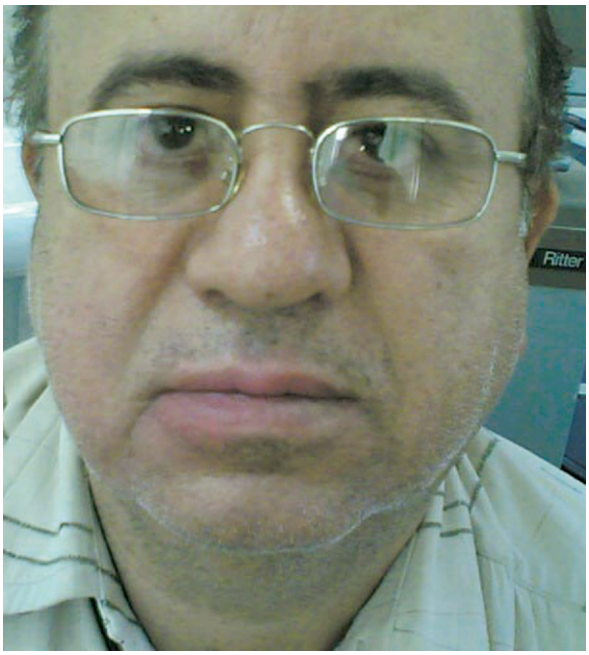

Fig. 4. Posttreatment photograph of the patient showing resolution of the lesion.

along with fissured tongue and facial paralysis constitute this syndrome.

Histopathology

Histopathologically, OFG lesions closely resemble nodules of tuberculosis (TB) and the differential diagnosis is often difficult. To make the diagnosis, other appropriate studies (special stains for acid fast bacilli, Grocott's methenamine silver (GMS) and periodic acid-Schiff (PAS) stains for fungi, cultures, and so forth) to exclude tubercle bacilli, fungi, foreign bodies, or other causes of the granulomatous condition must be done. Photomicrographs of OFG lesions show edema and scattered and clustered lymphocytes in the connective tissue, as well as several well-defined granulomas consisting of collections of epithelioid histiocytes and multinucleated giant cells.[1-8]

Therapy

A variety of drugs have been tried in the treatment of OFG, including corticosteroids. Surgery in these patients is usually unnecessary as treatment is primarily pharmacological. Systemic corticosteroids are considered the best treatment. Glucocorticoids effectively suppress the activated T-helper-induced cell process occurring at the site of disease in 50% of patients. The usual therapy is prednisolone, 1 mg/kg, for 4 to 6 weeks followed by a slow tapering over 2 to 3 months.[1,3-7] This is repeated if the disease again becomes active. Intralesional steroid injections are also an alternative treatment method that one might also consider.[3] The prognosis is generally favorable. Many of those affected remain asymptomatic and remission sometimes occurs spontaneously.

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