

Orofacial granulomatosis: A case report and a proposal of a diagnostic algorithm for oral granulomatous lesions

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Abstract

Orofacial granulomatosis (OFG) is an uncommon chronic inflammatory disorder with multifactorial etiology and pathogenesis affecting the orofacial region which appears usually as a persistent and/or recurrent swelling that may involve one or both the lips and/or recurrent ulcers along with other orofacial features. The diagnosis of OFG is challenging and it should be ruled out from other conditions characterized by granulomatous inflammation. This article describes a case of a 30-year-old female patient with upper lip swelling as the main manifestation without any systemic involvement and we have also laid down a proposal of a diagnostic algorithm for differential diagnoses and treatment modalities for OFG which could be helpful for the clinician and dentists alike to rule out other granulomatous disorders thus in effective management of OFG.

Keywords: Algorithm, differential diagnosis, granulomatous, lip swelling, orofacial granulomatosis, pathogenesis

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INTRODUCTION

In 1985, Wiesenfeld *et al.* introduced the term “Orofacial granulomatosis (OFG)” to describe a uncommon chronic granulomatous condition involving the lips, face and oral cavity and that are histologically associated with noncaseating granulomas and multinucleated Langhans-type giant cells.^[1] Tilakaratne *et al.* proposed the term “Idiopathic OFG” when lesions are restricted to the oral region without the identifiable granulomatous disease. The diagnosis should not be changed until the patient develops systemic manifestation of a specific granulomatous condition.^[2]

Its etiology being unclear, multifactorial processes have been implicated with very little evidence supporting each of the causes making it as a disease of exclusion.

Since OFG may be the oral manifestation in systemic conditions such as Crohn’s disease, sarcoidosis or Wegener’s granulomatosis in addition to several other conditions such as tuberculosis, leprosy, systemic fungal infections and foreign-body reactions which may show granulomatous inflammation on histologic examination, it can lead to many diagnostic challenges.^[3,4]

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CASE REPORT

A 30-year-old female patient who was a daily wages laborer was referred to the Department of Oral and Maxillofacial Surgery with a chief complaint of upper lip swelling, along with periods of exacerbation and remission, for the past 7 to 8 months. The patient gave a history of swelling which was sudden in onset with no history of trauma, pain or burning sensation. The swelling was noticed 8 months back, with discomfort in mouth opening for a year. She visited a local general practitioner for the same who prescribed medications for the swelling (topical steroids and antibiotics) which provided temporary relief. The swelling recurred again to which she was referred to our hospital for its management. The patient had no previous medical history and was not aware of any food or drug allergies.

Extraoral examination revealed a diffuse swelling of the upper lip [Figure 1] with no palpable lymph nodes. The swelling was nontender, noncompressible soft to firm in consistency, with no evidence of ulceration, fissuration, sinus or discharge, bruit or pulsations. There was no paralysis of facial muscles. Intraoral examination revealed slightly erythematous gingiva with granular appearance with respect to maxillary and mandibular arches. Bleeding on probing or tooth mobility was absent. The left buccal mucosa showed cobblestone appearance in the pterygomandibular raphae region extending anteriorly till the first molar, along the occlusal line [Figure 2]. There were no evident changes in the tongue and other parts of the mucosa. Based on clinical features, a provisional diagnosis of OFG was given. The other conditions that were considered under differential diagnosis included angioneurotic edema, Crohn's disease, tuberculosis, sarcoidosis, cheilitis granulomatosa, foreign-body reaction, fungal infections and contact allergy. We ruled out Melkersson–Rosenthal Syndrome because there was no facial paralysis and the tongue was clinically normal. Since there were no signs of anemia or symptoms suggestive of Crohn's disease, comprehensive gastrointestinal investigations were not justified in this case. The absolute eosinophil count was $400/\text{mm}^3$ suggestive of an allergic etiology and erythrocyte sedimentation rate was 35 mm in 1 h. Incisional biopsy of the upper lip was obtained for histopathologic examination which revealed an overlying parakeratinized stratified squamous epithelium with underlying stroma showing areas of vascularity along with circumscribed aggregates of noncaseating granulomas that composed of epithelioid histiocytes and Langhans-type giant cells with peripheral lymphocytes and plasma cells suggestive of a granulomatous lesion [Figures 3a and b]. Staining for acid-fast bacilli (AFB) and periodic acid–Schiff (PAS) yielded negative results.

Based on clinical history, laboratory investigations and histopathological findings, a confirmatory diagnosis of OFG was given. A change of toothpaste was recommended suspecting an allergy to some component in it as she was unaware of any other food/drug or material allergies. The tablets levocetirizine and topical corticosteroid were prescribed. The swelling of lips and the cobblestone appearance were noticeably reduced after the first



Figure 1: Clinical photograph showing diffuse upper lip swelling of 8-month duration

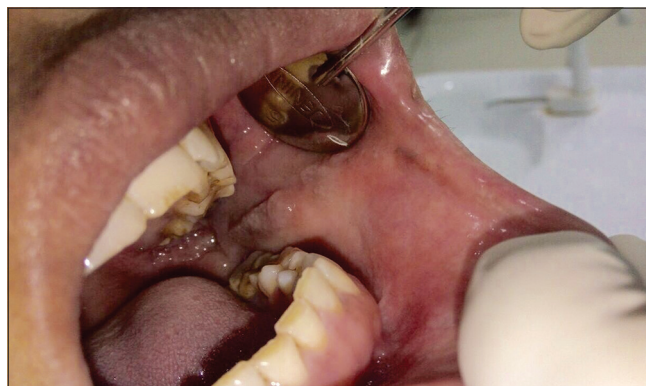


Figure 2: Clinical intraoral photograph showing thickened, hyperplastic and cobblestone appearance of the left buccal mucosa

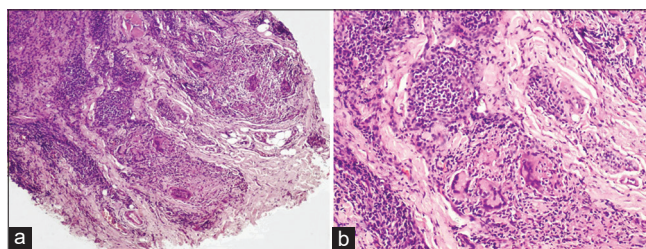


Figure 3: (a) Photomicrograph showing multiple well-demarcated noncaseating granulomas with Langhans-type giant cells (H&E stain, $\times 40$). (b) Photomicrograph showing deeper stroma showing noncaseating granulomas consisting of epithelioid cells, Langhans-type giant cells, lymphocytes and plasma cells with surrounding fibrosis (H&E stain, $\times 100$)

follow-up. Subsequent visits by the patient revealed complete remission of the lesions with no recurrence.

DISCUSSION

OFG is an increasingly yet uncommon recognized entity affecting the oral and peri-oral structures. The age range of presentation for males is 23 years (range: 5–80 years) and for females, it is 30 years (range: 6–84 years), with more of a female predilection.^[4]

The etiology of OFG has been varied in the reported literature, chief among them being genetic, allergy due to various food substances/dental materials, immunological or infective causes.^[5]

The main clinical features of OFG are recurrent nontender swelling involving face/one or both lips, angular cheilitis, which may eventually become persistent, along with intraoral features which may be present like mucosal ulcerations, fissures on lips and tongue, mucosal tags, gingival enlargements,

cobblestone appearance of the buccal mucosa, lingua plicata, cervical lymphadenopathy and neurologic manifestations.^[5-8]

The differential diagnoses of this disease include many granulomatous lesions which have to be ruled out by the clinician based on the diagnostic criteria for OFG along with other necessary clinical, laboratory and histopathological investigations that have to be carried out to rule out other granulomatous diseases. We propose a simple yet pragmatic diagnostic algorithm to help the diagnostician to arrive at a diagnosis [Figure 4]. This algorithm takes into the consideration the most common types of orofacial granulomatous lesions.

Little evidence is available in literature regarding the biochemical, hematological and immunological findings in OFG. Immunoglobulin E level assessment and patch test can be done if a hypersensitivity reaction is suspected. Chest radiographs could be done to rule out sarcoidosis. We can rule out tuberculosis by checking for AFB in the

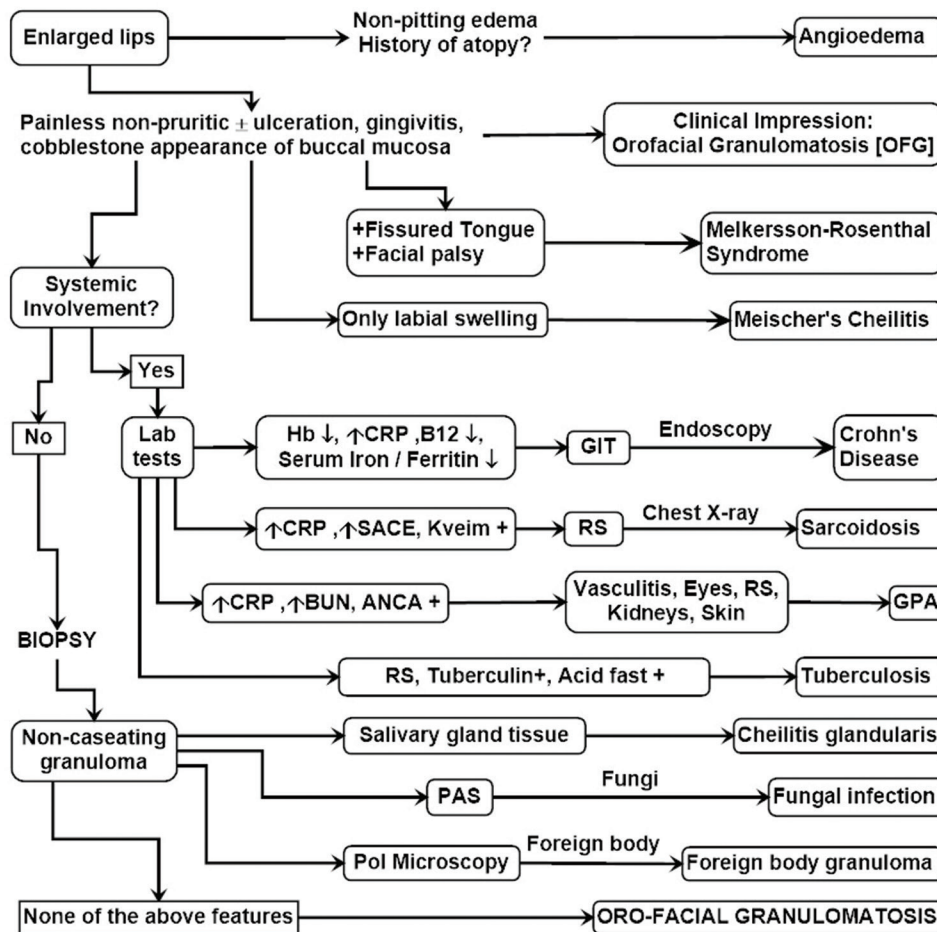


Figure 4: Diagnostic algorithm for orofacial granulomatosis. ANCA → Antineutrophil cytoplasmic antibody; BUN → Blood urea nitrogen; CRP → C-reactive protein; GIT → Gastrointestinal tract; GPA → Granulomatosis with polyangiitis, previously called Wegener’s granulomatosis; Pol → Polarizing; RS → Respiratory System; SACE → Serum angiotensin-converting enzyme ; PAS→Periodic acid–Schiff

tissue and also by chest radiography. Endoscopy along with colorectal biopsy is done when signs and symptoms of gastrointestinal disturbance are noted.^[2,6,8]

Incisional biopsy of the upper lip was done in our case and reports revealed an overlying parakeratinized stratified squamous epithelium with a fibrous connective tissue that showed circumscribed aggregates of noncaseating granulomas composed of epithelioid histiocytes and Langhans-type giant cells with peripheral lymphocytes and plasma cells suggestive of a granulomatous lesion. Staining with Ziehl-Neelsen and PAS yielded negative results. Correlating the clinical findings with histological and laboratory findings confirmed a diagnosis of OFG. The present case is unique because of the fact that it was associated with an increase in the eosinophil count. Interestingly, the patient did not give any history of allergy to drugs, food additives, cosmetics, etc. We suspected the patient might be allergic to some component in her toothpaste which she was using because she was not using any other oral hygiene product and recommended her to change it. Our educated guess proved to be correct because the change of the toothpaste resulted in a reduction in swelling of her lips and the cobblestone appearance of her buccal mucosa also disappeared. This could explain the elevated eosinophil count.

Therapeutically, a wide range of treatment modalities have been implemented for OFG [Figure 5]. Elimination diets have been advocated in many cases to identify and eliminate food allergens which have been not of much

success. Antibiotics, antihistamines, topical, intralesional, systemic corticosteroids or combination therapy have also been used for the treatment of OFG. Cheiloplasty has been advocated in certain advanced cases where lip deformities were of esthetic concern to the patient. Other alternative therapeutic agents include hydroxychloroquine, clofazimine, methotrexate, azathioprine, metronidazole, thalidomide, minocycline, dapsone, danazol and tumor necrosis factor- α blocking agents such as infliximab and adalimumab.^[5,7-11]

CONCLUSION

As OFG is a multifactorial disease and treatment of this entity could be challenging. Changes in oral and paraoral structures may be the initial signs and symptoms in OFG which may need careful evaluation of the cases by the dentists for detection and appropriate management. An algorithm has been proposed which would help in arriving at a diagnosis. This case report draws attention to allergy as an etiologic factor and timely diagnosis and appropriate management of the causative agent.

Informed Consent

Written informed consent was obtained from the patient.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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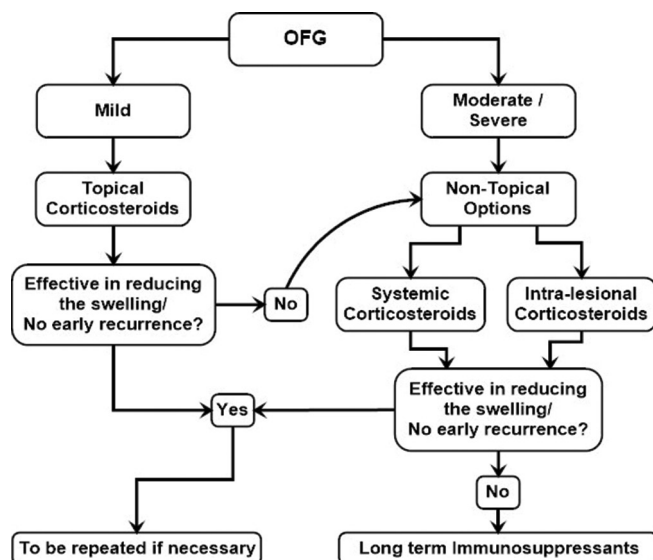


Figure 5: Treatment algorithm depicting different treatment options for orofacial granulomatosis, depending on the severity. Long-term immunosuppressants include azathioprine, thalidomide or tumor necrosis factor- α inhibitors

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