Case Report

Management of orofacial granulomatosis: A case report

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ABSTRACT

The term orofacial granulomatosis (OFG) was introduced by Wiesenfeld in the year 1985. OFG describes a disease with frequent or persistent edema in the orofacial region. It may be idiopathic or may present as a localized form or generalized form as in Crohn's disease, tuberculosis, and sarcoidosis. The clinical features include facial or lip swellings, angular cheilitis, oral ulcerations, vertical fissures of lips, gingival enlargement, mucosal tags, and sometimes lymph node enlargement. The diagnosis of OFG is quite challenging and it should be excluded from other granulomatous conditions. The usual treatment for this condition includes corticosteroids, monoclonal antibodies, and tumor necrosis factor-α inhibitors. It has been suggested that intralesional triamcinolone injections are a safe and effective therapeutic strategy in controlling the permanent disfiguring swelling of OFG. Hereby, we present a case of a 34-year-old female patient who reported with swollen upper lips and gingival enlargement.

Key words: Gingival enlargement, Orofacial granulomatosis, Swelling

Orofacial granulomatosis (OFG) is a granulomatous inflammation first introduced by Wiesenfeld *et al*. in the year 1985 [1]. Although the actual prevalence of this disease is unknown, 0.8% is the advised estimate. It causes recurrent edema of orofacial tissues characterized by recurrent enlargement of the lips, gingiva, tongue, and a variety of other orofacial features but is unrelated to systemic granulomatous diseases. The sex ratio is 1:1 and symptoms usually appear in the third decade [2]. The etiopathology is exactly not known. There are different hypotheses which include genetic causes, infectious agents such as mycobacterial infections, allergic reactions to food and environment, and immune dysfunctions [3]. The clinical features of OFG are facial or labial swellings, oral ulcers, gingival enlargement, mucosal tags, fissured tongue, vertical fissures of lips, and sometimes lymph node enlargement [4]. OFG histopathologically presents as non-caseating granulomas. The diagnosis of OFG is quite challenging due to the variability of the presentations and relatively large differential diagnosis. Diagnosis of OFG is based on clinical presentation, the system involved, clinical, radiographic, histopathological assessment, and laboratory tests [5]. Treatment of OFG includes corticosteroids (intralesional steroid injections and systemic steroids), clofazimine, monoclonal antibodies such as infliximab, antibiotics, antihistamines, tumor necrosis factor-α inhibitors, biotherapies, and surgical excision.

This case is reported in view of its rarity and to document the efficacy of azithromycin pulse therapy along with intralesional corticosteroids.

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CASE REPORT

A 34-year-old female patient came to the Department of Oral Medicine and Radiology with the chief complaint of a swollen upper lip for the past 5 months (Fig. 1). History revealed recurrent episodes of edema which led to difficulty in speech and mastication. There was no history of bleeding, ulcerations, or changes in sensory functions of the lip. There was no pertinent history of drug intake or other systemic allergies. There was no history of abdominal pain or diarrhea. Personal history revealed no deleterious habits such as tobacco chewing or alcohol consumption. The family history was non-contributory.

On general examination, the patient was moderately nourished. There were no signs of anemia, cyanosis, jaundice, clubbing of fingernails, or pedal edema. Vital signs revealed a pulse rate of 74 bpm, respiratory rate of 15 cycles/min, blood pressure of 124/84 mm of Hg, and temperature of 97°F. Lymph node examination revealed bilateral, single, submandibular lymph nodes measuring 1.5×1.5 cm approximately. They were non-tender, soft in consistency, and freely mobile on palpation. Extraoral examination

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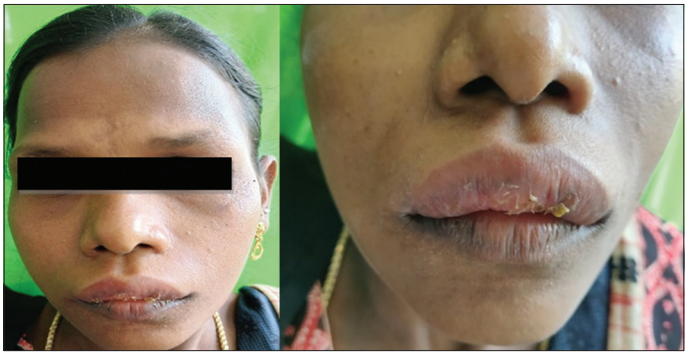

Figure 1: Initial pictures showing the swelling of the upper lip

showed a convex profile with competent lips. The upper lip showed a diffuse swelling and mild cracks and crustations were present on the surface. It was non-tender on palpation. Intraoral examination showed the absence of oral lesions and amalgam restorations. Generalized gingival enlargement involving the marginal, attached, and interdental gingiva on both facial and lingual/palatal aspects of all the teeth was present which appeared to cover almost one-third of the crowns (Fig. 2). The enlargement was profound in the mandibular arch when compared to the maxillary arch. The gingiva was reddish pink, shiny, and smooth in appearance. There was a loss of gingival scalloping and stippling. On palpation, the gingival enlargement was firm in consistency and was non-tender. There was generalized bleeding on probing. Oral hygiene status was fair; generalized supragingival plaque and calculus were present.

Panoramic radiograph revealed mild generalized interdental bone loss and horizontal bone loss in relation to 46 and 47 (Fig. 3). A provisional diagnosis of OFG was made. The absence of fissured tongue and facial palsy eliminates the possibility of Melkersson–Rosenthal syndrome [5]. Routine blood investigations and Mantoux test revealed no abnormality. Chronic inflammatory diseases such as Crohn's disease were eliminated after gastroenterological examinations.

An incisional biopsy was performed in the mandibular gingiva (site A) and upper labial mucosa (site B). Histopathological examination showed parakeratinized stratified squamous epithelium. The underlying connective tissue showed focal collections of lymphocytes and plasma cells admixed with histiocytes. Perivascular inflammatory infiltrate, blood vessels, muscle bundles, nerve fibers, and adipocytes were seen. Histopathologic findings did not reveal non-caseating granulomas, a finding that is consistent in approximately 45% of the OFG patients [6,7]. The final histopathological diagnosis was OFG which correlated with our provisional diagnosis.

After establishing the diagnosis, we treated the patient with intralesional triamcinolone injections (kenacort) 40 mg/mL solution, once a week for 3 weeks (Fig. 4). We also prescribed azithromycin, 500 mg pulse therapy weekly (3 consecutive days every week) for 1 month, as it has antimicrobial and anti-inflammatory properties [8]. The patient was also placed on an elimination diet. After 2 weeks of follow-up, the lip swelling appeared to decrease in size (Fig. 5), and after 1 month of this treatment, there was a reduction in the swelling. At the end of

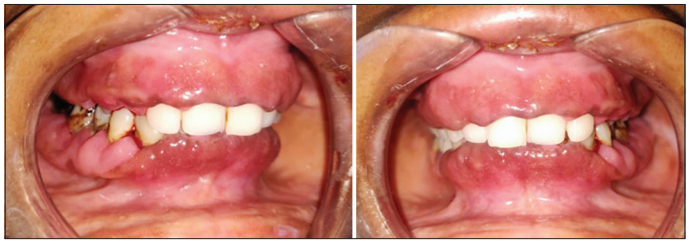

Figure 2: Generalized gingival enlargement involving the marginal, attached, and interdental gingiva

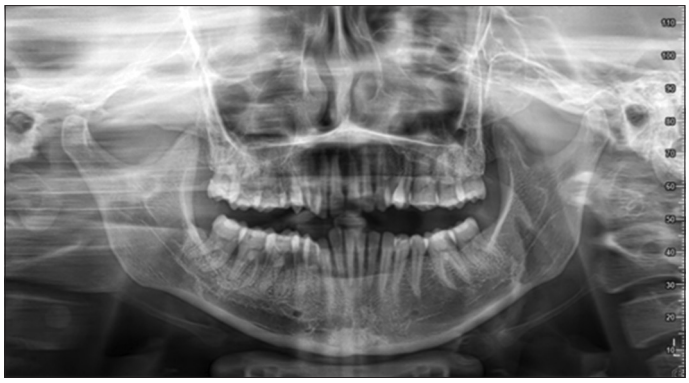

Figure 3: Panoramic radiograph revealed mild generalized interdental bone loss and horizontal bone loss in relation to 46 and 47

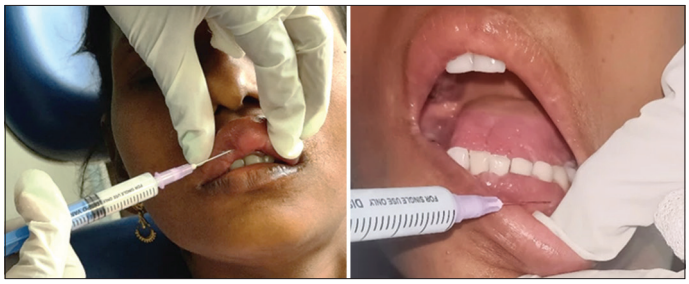

Figure 4: Intralesional triamcinolone injections (kenacort) 40 mg/mL solution, administered once a week for 3 weeks

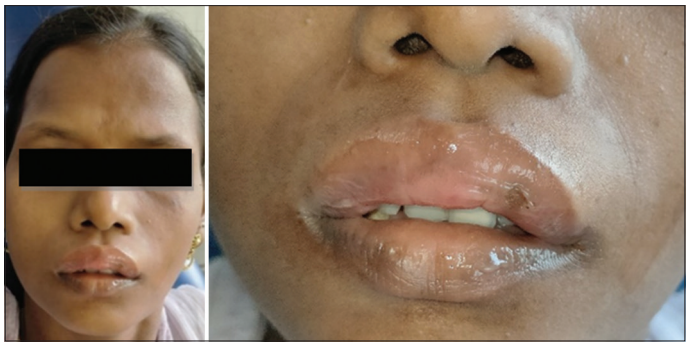

Figure 5: After 2 weeks of follow-up, the lip swelling appeared to decrease in size

3 months, the patient showed appreciable improvement (Fig. 6). There were no recurrences or treatment-related complications during the 3 months follow-up period.

DISCUSSION

OFG is a non-specific granulomatous inflammation presenting as facial or lip swelling, ulcerations, gingival enlargement, mucosal

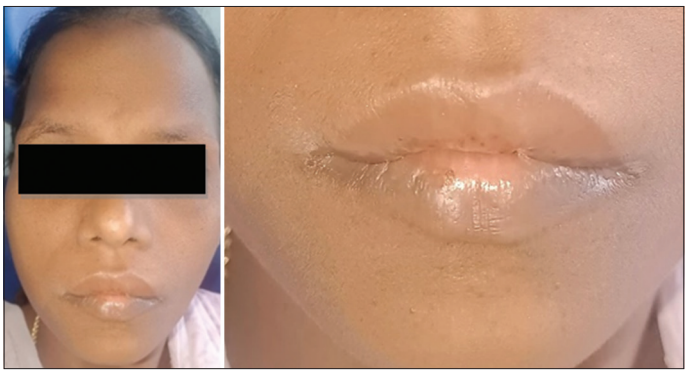

Figure 6: At the end of 3 months, the patient showed appreciable improvement

tags, and sometimes lymphadenopathy [1]. Although several factors such as infection, genetic predisposition, and allergy have been found to be causative agents for this disease, the exact etiology of OFG is unknown, and therefore precise treatment and long-term prognosis are uncertain [4].

The treatment of OFG is challenging, particularly in the absence of an etiological factor at the initial visit. Various treatment modalities include dietary modification, antibiotics (metronidazole, azithromycin, and dapsone), topical corticosteroids (clobetasol 0.05% ointment with orabase), topical calcineurin inhibitors (tacrolimus 0.1% ointment), intralesional corticosteroids (triamcinolone acetonide 40 mg/mL), systemic corticosteroids such as prednisolone (25–50 mg), immunosuppressive agents (azathioprine, methotrexate, and infliximab), and surgical intervention [9].

Certain studies have shown an increased prevalence of oral allergic reactions in persons with OFG. Diets eliminating cinnamon and benzoate (preservatives E211, E212, and E213) seem to show a marked improvement in symptoms and a decrease in recurrence in these patients [10]. It has been found that in 80% of OFG patients, a history of immunoglobulin E-mediated allergy in the form of eczema and asthma can be observed when compared to 15–20% of the general population [11].

Patients with OFG have shown patch test-confirmed delayed-type hypersensitivity to several food substances and additives, including wheat, dairy products, chocolate, eggs, peanuts, cinnamaldehyde, carbone piperitone, cocoa, carvone, carmosine, sun yellow dye, monosodium glutamate, benzoate, and cow's milk. Delayed hypersensitivity to certain dental materials such as amalgam, mercury, gold, and cobalt has also been reported. Elimination diet and replacement of the relevant dental material have been reported to improve clinical manifestations by some of the authors [11]. Differential diagnosis comprises Crohn's disease, sarcoidosis, allergic angioedema, Miescher's cheilitis, Melkersson–Rosenthal syndrome, cheilitis glandularis, and tuberculosis [4].

It is necessary to screen for allergic reactions such as angioedema and eliminate the allergens. Once these primary considerations are eliminated biopsy should be considered. Granulomatous diseases such as tuberculosis, and Crohn's disease have to be ruled out after confirmation of granulomatous inflammation. The histopathologic findings did not disclose any non-caseating granulomas in our patient, a finding which is congruent in approximately 45% of OFG patients.

Systemic corticosteroids attain rapid disease control when there is severe disease or worsening symptoms. However, they are only suitable for short-term use because of their side effects, typically a short course at 0.3–0.7 mg/kg/day to rapidly reduce orofacial swelling [12]. Gupta and Singh used an intralesional combination of triamcinolone, metronidazole, and minocycline, and observed a significant decrease in lip swelling after 15 days of treatment [13]. Fedele *et al*. conducted a study of the long-term effectiveness of intralesional triamcinolone acetonide therapy and demonstrated the evidence of a reduction in the orofacial swelling of OFG [14]. Bruett *et al*. reported a case treated with azithromycin pulse therapy and showed a significant improvement in 2 months with total resolution after 5 months of therapy [15]. Yadav *et al*. 2015 conducted a study in five patients with OFG, where azithromycin 500 mg weekly pulse therapy was shown to be effective and resulted in clinical improvement in 1 month and 80–90% improvement by the end of 3 months [8]. A combination of intralesional triamcinolone acetonide and azithromycin pulse therapy succeeded in treating our case which is in accordance with the above-mentioned studies.

Cheiloplasty is done only for the most intricate cases with a major lip deformity or cases that are resistant to drug therapy. The long-term benefits of surgery are largely unknown, although recurrence of the lip swelling after surgery has been reported. Although numerous studies presented above showed successful outcomes in patients, there is still a need for prospective clinical trials with larger sample size populations to better measure predictors for treatment success in patients diagnosed with OFG.

CONCLUSION

The diagnosis and therapeutic management of OFG are quite challenging. Differential diagnosis is often required to exclude Crohn's disease, sarcoidosis, and tuberculosis. There is no precise, single treatment for OFG. This patient was successfully treated with azithromycin pulse therapy, but there exists a necessity to identify a stand-alone treatment for OFG. The triamcinolone acetonide injection procedure along with azithromycin pulse therapy appears to be the most suitable and effective treatment of OFG along with a change of diet to prevent the chance of recurrences.

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