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Case Report Open Access

Case Report: Orofacial Granulomatosis

Michelle Pratt, Patricia Wadden, Robert Fowler and Wayne Gulliver*

Memorial University of Newfoundland, NL, Canada

***Corresponding author:** Dr. Wayne Gulliver, 187 Le Marchant Road, St. John's, NL, Canada, A1C 2H5, Tel: +1 (709) 753-2255; Fax: +1 (709) 753-5478; Email: wgulliver@newlabresearch.com

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Abstract

Orofacial granulomatosis (OFG) is an uncommon condition that presents as non-tender, non-pruritic, chronic oral labial swelling. It is a diagnosis of exclusion, and requires a full systemic workup to exclude other causes of granulomatous inflammation, such as Crohn's disease, sarcoidosis, and tuberculosis. The cause of OFG is unknown, and there is significant debate as to whether it is in fact a separate entity, or merely an initial and/or localized form of Crohn's disease (CD).

We describe a case of OFG in a 37 year-old male from Newfoundland, Canada, and discuss in detail the systemic workup, and the reasoning behind the diagnosis. A photo of the lesion is included, as well as histopathology showing non-caseating granulomatous inflammation. Short discussions of etiology and treatment options are also included.

Keywords: Orofacial Granulomatosis; Crohn's disease; Inflammation

Abbreviations

OFG: Orofacial Granulomatosis; TB: Tuberculosis; PPD: Purified Protein Derivative; TNF: Tumor Necrosis Factor

Case Report

The patient, a 37 year-old Caucasian male, presented with an approximately two-year history of a persistent and progressive swelling of the lower lip, as well as the mid portion of the upper lip (Figure 1). There was no associated pain or pruritus. Upon examination, the mouth appeared normal, with no apparent dental lesions, and no obvious amalgam adjacent to buccal mucosa. The patient had no other medical issues and was taking no medications. His family history was unremarkable.

Serology was negative for C-ANCA, P-ANCA, and ANA, but positive for rheumatoid factor antibody (80 IU/mL). CBC, ESR, CRP, blood chemistries, urinalysis, and serum immunoglobulin levels were within normal ranges. Patch-testing and PPD skin testing results were negative.

A 4 mm punch biopsy of the lower lip showed non-caseating, granulomatous inflammation (Figure 2). Sarcoidal-type organoid granulomas were noted in the dermis; many in perivascular distribution. No epidermal change or mucin deposition was present. Acid fast and fungal stains were negative and no birefringent material was seen on polarized microscopy.

Axial CT images were collected from the palate to the iliac crest using IV contrast. Findings were unremarkable. Endoscopy performed from the nasopharynx to the glottis revealed a deviated nasal septum, but otherwise no abnormalities.

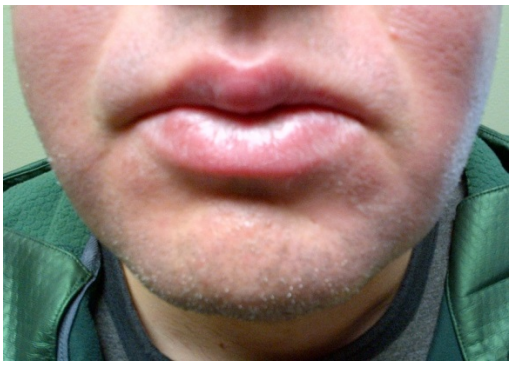

Figure 1: Persistent swelling of the bottom lip as well as the mid portion of the upper lip after several treatments with intralesional Kenalog injections (triamcinolone acetonide, 10 g/mL).

Given the clinical and histologic findings, with a negative workup for systemic disease, a diagnosis of orofacial granulomatosis (OFG) was established. The patient was treated with Hydroval cream (0.2% hydrocortisone valerate) and intralesional Kenalog (triamcinolone acetonide, 10 mg/mL) injections. Significant clinical improvement has been achieved, but not complete remission. No relapses have occurred during a three year follow-up period.

Discussion

OFG refers to disorders that present with granulomatous inflammation of the lips, face, and oral cavity, in the absence of systemic disease. The term encompasses both Melkersson-Rosenthal syndrome (MRS) and cheilitis granulomatosis (also known as Miescher cheilitis). MRS refers to the clinical trial of orofacial swelling, facial paralysis, and lingua plicata. Cheilitis granulomatosis is often

thought of as a monosymptomatic variant, with the exclusive presence of orofacial swelling. These two conditions were originally reported as separate conditions, but are now thought to represent a continuation of the same disease process [1].

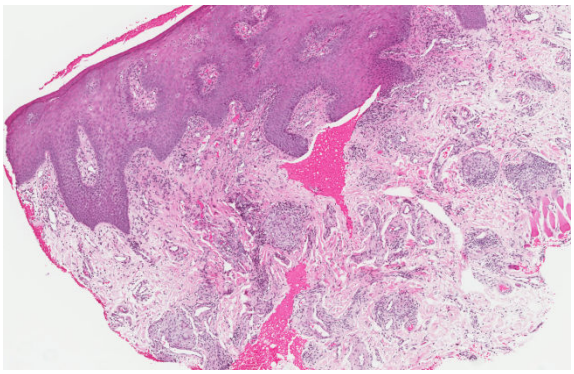

Figure 2: 4 mm punch biopsy of the lower lip showing non-caseating, granulomatous inflammation. Sarcoidal-type organoid granulomas within the dermis; many in perivascular distribution (Hematoxylin and Eosin, 120X).

OFG typically presents as painless and non-pruritic recurrent oral labial swelling. Other presenting features may include cobblestoning, ulceration, mucosal tags, gingival enlargement, lingua plicata, facial palsy, facial swelling, and facial erythema [1]. Cases of OFG have been reported in men and women of varying ages and ethnicities, with the average age of onset reported within the twenties or thirties [1-3].

The severity and pattern of onset of the oral labial swelling associated with OFG may vary significantly from patient to patient [2]. Typically, a patient presents with recurrent outbreaks of oral labial swelling, separated by intermittent periods of complete resolution. These outbreaks tend to become more frequent and longer lasting until finally a state of permanent induration is reached. In our case, the patient did not experience "outbreaks", but rather, persistent swelling that became progressively more disfiguring over a period of approximately two years. Initially, it may be difficult for a clinician to differentiate the transient swelling of OFG and the short lasting swelling associated with angioedema. However, the latter is usually associated with pruritis, and urticarial lesions elsewhere on the body.

A biopsy of our patient's lower lip revealed non-caseating granulomatous inflammation that would be consistent with a diagnosis of OFG, as well as tuberculosis (TB), sarcoidosis, and Crohn's Disease (CD). A full systemic workup was initiated in order to rule out these conditions. TB was excluded based on a lack of clinical symptoms, normal CT images, and a negative PPD test. Sarcoidosis was considered unlikely since there was no evidence of lung involvement. Furthermore, oral involvement in sarcoidosis is uncommon, and oral involvement as the initial presenting feature is rare [4]. CD was considered, however, the patient did not have any symptoms to suggest inflammatory bowel disease, and abdominal CT images were unremarkable.

Although several theories have been implicated in the etiology of OFG, the exact cause remains widely debated and largely unknown. The general consensus is that OFG is an immunological disease, however, pathways involving genetics, dietary allergies, allergies to dental materials, and infections have been proposed [5]. It is unclear whether OFG is in fact a distinct disease, or a localized or initial form of CD [6]. Certainly, the clinical and histologic features of oral CD and OFG are indistinguishable, and many patients with CD have been known to present with oral manifestations prior to the onset of diffuse disease.

In 2007, Freysdottir et al. conducted an immunohistochemistry study that analyzed the inflammatory infiltrates within labial lesions of ten OFG patients [7]. Their results suggested a cell-mediated response similar to the Th1 mediated response seen in CD. Despite the similarities between OFG and CD, in the largest retrospective case series of OFG (conducted by Campbell et al. in 2007) involving 207 patients, the 25-year risk of developing CD after being diagnosed with OFG was only 20% [8]. Several human leukocyte antigen (HLA) alleles have been associated with the CD [9], but interestingly, these alleles do not appear to be associated with OFG.[10] Overall, the relationship between OFG and CD is still up for debate, and additional research is required to gain further insight.

There is no standardized protocol for the treatment of OFG, and treatments tend to be individually tailored depending on the clinical presentation. Corticosteroids are considered the mainstay of OFG treatment, and have been quite effective in alleviating facial swelling [5]. Patients who are unresponsive to topical corticosteroid treatments are managed with short courses of systemic corticosteroids (eg. prednisone) and/or intralesional corticosteroid injections (eg. triamcinolone acetonide). If adequate responses are not achieved, long-term systemic immunosuppressants (eg. azathioprine), anti-TNF-α agents, or thalidomide may be required [1,5,11]. Spontaneous remission in OFG is rare, and most patients need long-term topical treatments and/or combination therapies. Surgery may be performed in cases where the swelling is severe and the disease has reached a quiescent phase [3].

Conclusion

In summary, a case of OFG has been presented with discussion of clinical features, differential diagnoses, potential etiologies, and treatments. Although OFG is a relatively benign condition, the labial swelling can be very psychologically distressing, and may also interfere with a patient's ability to speak and eat properly. Further research is required to gain insight into the etiology of OFG, its relationship to CD, and to develop more effective treatments.

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