Oral Medicine Case Book 57: Orofacial granulomatosis

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CASE REPORT

A 17-year old female presented at the Oral Medicine Clinic with the complaint of persistent swelling of the upper lip and anterior attached gingiva, causing her discomfort when eating and talking. The swelling started approximately ten months earlier. At the time she was seen by her physician who prescribed an antibiotic that gave mild symptomatic relief, but no clinical resolution. She was also seen by an oral hygienist on three occasions with no improvement of the gingival swelling. The patient also reported that she had been diagnosed with depression and type 2 diabetes approximately two years ago and was currently using Citalopram (a selective serotonin re-uptake inhibitor) and Glucophage® (metformin hydrochloride, an anti-hyperglycemic drug). Extra-oral examination revealed a firm, swollen and superficially cracked upper lip with a red granular appearance. No enlarged cervical lymph nodes could be palpated. Intra-orally, the anterior maxillary and mandibular gingivae were hyperplastic and erythematous, with a granular surface (Figures 1, 2 and 3). The differential diagnosis included contact allergy and granulomatous disease, including mycobacterial infection.

An incisional biopsy of the labial surface of the upper lip was performed and the patient was provided with an antibacterial mouthwash, (0.2% aqueous solution of chlorhexidine gluconate) and instructed to return for further management two weeks later. Histological evaluation of the incisional biopsy from the upper lip disclosed non-necrotising granulomatous inflammation. The non-necrotising granulomas were composed of epitheloid histiocytes and Langhans-type multinucleated giant cells, surrounded by a rim of lymphocytes (Figures 4 and 5). The Ziehl-Neelsen stain was negative for acid-fast bacilli and the Periodic Acid Schiff stain failed to reveal any fungal elements. Based on the histological features, the clinical findings and the special stain results, the clinical diagnosis of orofacial granulomatosis (OFG) was established.

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ACRONYMS

ANCA: Anti-Neutrophil Cytoplasmic Antibody
CT: Computerised Tomography
NSAID: Nonsteroidal Anti-Inflammatory Drug
OFG: Orofacial Granulomatosis
PCR: Polymerase Chain Reaction

Since OFG could be associated with other systemic conditions or linked to a hypersensitivity reaction ,(some elements in the diet or present medication), the patient was referred to the Department of Internal Medicine at the local academic hospital to establish the underlying aetiology. At the time of publication of this report a definitive cause was still awaited.

DISCUSSION

Orofacial granulomatosis (OFG) is an uncommon inflammatory disorder, typically presenting as a granulomatous cheilitis, resulting in non-tender swelling and enlargement of one or both lips and usually also of the oral tissues.[1] The condition may cause significant cosmetic and functional discomfort and although unequivocal evidence lacks, the swellings appears to be the result of lymphoedema, caused by granulomas disrupting normal lymph drainage. The age of onset is usually during adolescence or young adulthood with an equal gender and racial distribution.[2] The clinical signs may be persistent or present as recurrent episodes.[3] The initial swelling usually subsides within a couple of days, however with subsequent attacks, the swelling becomes permanent and increases in severity. The swelling is asymptomatic and non-pruritic and has a soft, firm or nodular texture on palpation. The normal lip architecture is eventually altered by persistent lymphoedema and non-caseating granulomas. Once the swelling has become chronic, the enlarged lips tend to become painful due to the formation of cracks and fissures and may eventually develop a reddish brown discolouration with a scaly, rubbery texture.[2,4]

Oral lesions are seen in most cases of OFG. The oral lesions appear as enlargements of the lingual, palatal, gingival or buccal mucosa, with a granular surface texture and may eventually give rise to a "cobblestone" appearance, frequently with the presence of mucosal tags. In some cases linear ulcers can develop in the buccal sulcus. The dorsum of the tongue may present with fissuring and rarely, palsy of the facial nerve may arise, due to granulomatous involvement of the nerve trunk.[1,4] The simultaneous presence of tongue fissuring, labial enlargement and palsy of the facial nerve are the classical features of the Melkersson-Rosenthal syndrome.[5] OFG may be accompanied by systemic symptoms of fever and other mild constitutional symptoms, including headache and visual disturbances. The patient may also complain of loss of taste sensation and a decreased saliva flow. Cervical lymph node enlargement may also be present.

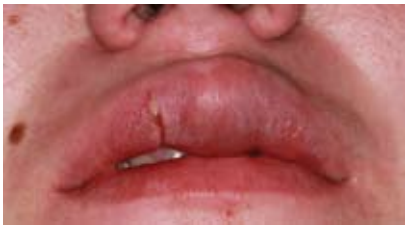

Figure 1: The patient presented with chronic swelling of the upper lip. Note the superficial cracks and fissures.

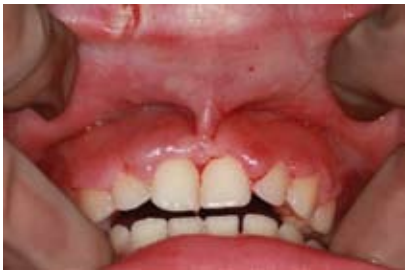

Figure 2: Marked hyperplasia of the upper anterior attached gingiva.

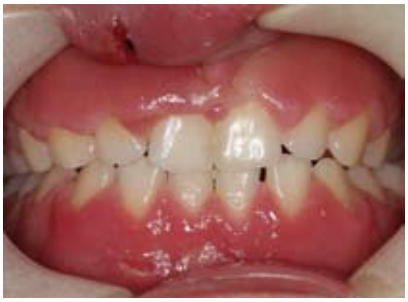

Figure 3: The gingival tissue of the anterior lower arch showed slight enlargement with a granular surface.

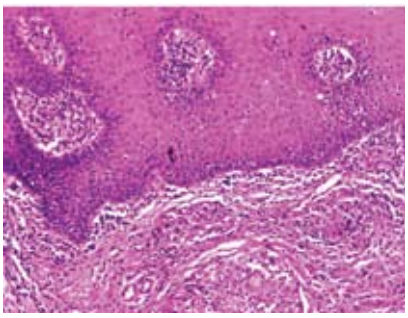

Figure 4: This photomicrograph shows several non-necrotising granulomata within the sub-epithelial connective tissue (H&E, x100)

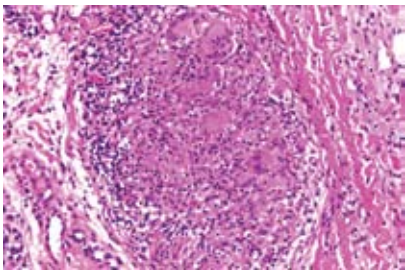

Figure 5: This photomicrograph shows a non-necrotising granuloma, consisting of epithelioid histiocytes, Langhans-type multi-nucleated giant cells and a rim of lymphocytes (H&E, x200)

Histopathological examination typically shows non-caseating granulomata.[5] The exact aetiopathogenesis of OFG is unknown and therefore the ideal treatment and long-term prognosis is uncertain. It is thought that the condition is due to a delayed type of hypersensitivity reaction, but the responsible antigen(s) inducing the immunological reaction is/are uncertain and appear to vary from case to case. In many patients there is a strong history of atopy and the condition may develop in response to metals, such as cobalt, or various food additives and preservatives, including cinnamon, benzoates, butylated hydroxyinosole, dodecyl gallate (found in margarine), menthol, chocolate and tartrazine. Patients have also reported reactions occurring in response to certain toothpastes and possibly drugs.[2,3,5]

OFG is a diagnosis of exclusion, as various conditions produce similar histopathologic and clinical features.[2] The early stages of OFG are clinically difficult to differentiate from angioedema but the persistence of the swelling between attacks should raise suspicion of OFG. Other conditions to be excluded, include Crohn's disease, sarcoidosis, foreign body reactions, mycobacterial infection (such as tuberculosis and leprosy) and contact allergy.[6] About 10 % of patients with OFG have associated Crohn's disease which should be excluded by ileocolonscopy and approximately 3% of cases have sarcoidosis, best excluded by radiological studies, (eg, chest CT for hilar adenopathy).[1,2] Other causes of non-caseating granulomatous inflammation, even though highly unlikely, such as Wegener's granulomatosis, (which hisotologically presents with subacute inflammation, abscess formation and vasculitis), should be excluded by appropriate clinical investigations, (eg. measurement of serum c-ANCA and p-ANCA antibodies). Although special stains for mycobacterial and fungal infections were negative in this case, such infections can only be definitively excluded by culture or PCR.

The treatment of OFG can pose a challenge and spontaneous remission of orofacial swelling is rare. Elimination diets should be utilised to identify possible precipitating dietary substances and likewise, other possible precipitating antigens. Topical, intra-lesional and systemic corticosteroids can be utilised for conservative management of the condition. Triamcinolone acetonide, used at a dose of 0,5-1ml of a 10mg/ml solution, is often used for the intra-lesional injections and for systemic administration, prednisone is prescribed at a dosage of approximately 1mg/kg body weight. Chronic corticosteroid administration should, however, take cognisance of the associated side effects produced, by adrenal cortex suppression and the dosage adjusted accordingly. If there is severe oral or extra-oral involvement, clofazimine (an immunosuppresive drug, originally developed as treatment for leprosy), is used at a dosage of 100-200mg daily for 3-6 months. Other therapies include NSAIDs, sulfasalazine (a sulfa drug, used for the treatment of inflammatory bowel disease and Crohn's disease), antibiotics (such as metronidazole) and anti-malarials (such as hydroxychloroquine). Patients with OFG must be regularly reviewed to identify any gastro-intestinal involvement.[5,6,7]

CONCLUSION

Although OFG is a rare condition, the dental practitioner should keep this condition in mind when a patient presents with unexplained swelling of the lip and hyperplastic oral lesions. In such cases, a careful clinical history should be taken and the patient referred to a specialist if no reason can be identified for the lip swelling and/or gingival enlargement. The diagnosis of OFG requires careful clinico-pathological correlation and elimination of all possible causative antigens.

Declaration - No conflict of interest declared.

References and *recommended reading

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