

Persistent diffuse swelling of the upper lip - A case report

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ABSTRACT

Cheilitis granulomatosa, is a rare inflammatory disorder of unknown etiology. It is a disorder characterized by recurrent or persistent swelling of one or both the lips. Histologically it shows the formation of non necrotizing granulomas with epitheloid cells and Langhan's type giant cells. Dispersed oral mucosal granulomas occur in number of conditions collectively described as the Orofacial granulomatosis. The term idiopathic Orofacial Granulomatosis is used in cases with unknown etiology. In this paper we report a case of persistent diffuse upper lip swelling which was diagnosed as Cheilitis granulomatosa. Persistent diffuse lip swellings should not be neglected. A thorough workup to eliminate other etiologies is essential.

Key Words: Cheilitis Granulomatosa, Epitheloid, Langhans, Oro facial.

INTRODUCTION

Cheilitis granulomatosa, first described by Miescher in 1945, is a rare inflammatory disorder of unknown etiology. It is clinically characterized by painless, non pruritic, firm, asymmetrical and occasionally unilateral enlargement of one or both lips, which primarily affects young adults¹. Although the swelling may initially be episodic, in the long term the enlargement of the lips often persists. Histologically, non-necrotizing granulomas are seen, as well as oedema, lymphangiectasia and perivascular lymphocytic infiltration². It is estimated that incidence of cheilitis granulomatosis is 0.08% in the population³.

CASE REPORT:

A 21 year old female patient reported to the Department of Oral and Maxillofacial Pathology, with a chief complaint of swelling of upper lip for the past 1 year. On examination there was a diffuse swelling of upper lip (Fig 1&2) without any surface ulceration. It was soft and non tender on palpation. Intra oral examination was noncontributory.

On general examination no systemic involvement was present. Haemogram was within the normal limits. Etiological agents such as food, drugs, latex, and physical and chemical factors were ruled out and there was no history of insect bite. With the detailed history and clinical findings, it was provisionally diagnosed as Cheilitis granulomatosa.

Incisional biopsy was performed. Histopathology showed presence of stratified squamous epithelium and underlying connective tissue consisting of non-caseating granuloma (Fig 3) with multiple tubercles showing langhan's type of giant cells surrounded by epitheloid cells and lymphocytes (Fig 4&5). Based on the clinical presentation of the lesion and the histopathological features confirmatory diagnosis of Cheilitis granulomatosa was given.

Patient was treated by giving 100 mg of Clofazimine twice daily for 10 days, followed by four times a week for 2–12 months.

Discussion:

Cheilitis granulomatosa or **Miescher's cheilitis** was first described in 1945 as a distinct pathologic entity by the German dermatologist Miescher, who reported the first six cases (Miescher, 1945). Consequently, **Cheilitis granulomatosa** has been associated with Sarcoidosis, Crohn's disease, Atypical tuberculosis, Anderson-Fabry disease, allergic reactions and hairy cell leukaemia. (White *et al*, 1981; Brook *et al*, 1983; Hernandez *et al*, 1986; Shaike *et al*, 1986; Ghandour).

Furthermore, some consider it as an oligosymptomatic or monosymptomatic form of Melkersson-Rosenthal syndrome (Warsaae- and Pindborg, 1980, Azaz and Nitzan, 1984; Hernandez *et- al*, 1986; Zimmer *et al*, 1992). Melkersson Rosenthal Syndrome has been described as a triad of recurrent episodes of orofacial swelling (the lips are most commonly affected), facial nerve palsy and fissured tongue or lingua plicata².

The complete triad of symptoms is uncommon, varying from 8 to 25%. The presentation of only one symptom is more common. The most frequent complaint is facial edema and enlargement of the lips⁴. In our case only cheilitis granulomatosa was present of the triad of the symptoms of Melkersson Rosenthal syndrome. Some consider Cheilitis granulomatosum as an early manifestation of Melkersson Rosenthal syndrome.

Intraoral tuberculosis is rare and always accompanied by primary lesion in the lung or elsewhere. The sites most commonly involved are dorsum of the tongue, gingiva with deep punched out ulcer⁵. A sub acute illness is characterized by cough, haemoptysis, dyspnoea, anorexia and weight loss associated with fevers & night sweats. In our case clinical presentation was not similar to the above findings and there were no associated prodromal symptoms. Mantoux test was negative. Chest X ray did not reveal any evidence of tuberculous lesion.

Sarcoidosis affects young to middle aged adults with typical swelling in the cervical lymph nodes. In the oral cavity the most commonly affected sites are salivary glands and gingiva. Lips are less commonly affected⁵. In our case there was no lymph node enlargement and chest radiograph was normal.

Crohn's disease is a chronic inflammatory bowel disease. Oral manifestations consist of ulcers, lip fissuring, cobble stone plaques, cheilitis, polypoid mucosal tags and perioral erythema⁵. In our case there were no gastro intestinal complaints.

Dispersed oral mucosal granulomas occur in number of conditions collectively described as the Orofacial granulomatosis and the differential diagnosis of the group is often difficult. Diagnosis first involves exclusion of Tuberculosis, Sarcoidosis both of which are unusual orally but may affect any site the granulomatous reaction to fungal or dental infection should also be excluded. An attempt must be made to exclude distinct entities such as oral crohn's disease, Melkersson Rosenthal syndrome and hypersensitivity reactions, which are differentiated primarily by clinical investigations⁵.

Cheilitis granulomatosis presents as a persistent, painless, non-pruritic, firm oedema of the lips. The first episode of oedema usually subsides completely in hours to days, making angioedema one of the differential diagnoses. Recurrent, painless attacks are the rule with episodes usually increasing in duration as the disease progresses, as well as leading to persistent swelling that gradually becomes firmer. The first symptom of cheilitis granulomatosa occurs in second decade of life. It has female predilection³. Most commonly upper lip is affected followed by lower lip⁶. In our case also the clinical features are consistent with the above mentioned findings.

Although the etiology of granulomatous cheilitis is unknown, a relationship with Crohn disease has been suggested due to the granulomatous nature of the lesion. Most authors, however, do not recommend routine investigations of the gastrointestinal tract in patients with a negative history of gastrointestinal complaints⁷. It is still controversial. There is no conclusive evidence that cheilitis granulomatosa is due to atopy or an infective agent. Some patients with cheilitis granulomatosa may represent a localized form of sarcoidosis, although oral manifestations of sarcoidosis usually coincide with systemic signs and symptoms and consist of focal nodular elements, as opposed to the more diffuse lip swelling in cheilitis granulomatosa.

Various factors including levels of vitamins and trace elements, other nutritional components, could be involved in pathogenesis. *Mycobacterium paratuberculosis* has not been found to be implicated in the pathogenesis of orofacial granulomatosis or oral Crohn's disease as was suggested previously⁸. When no specific condition could be diagnosed the term idiopathic orofacial granulomatosis can be used⁵. In our case, as there is no specific etiology we reported it as idiopathic orofacial granulomatosis.

Biopsy of the swollen lip or facial tissues during the early stages of the disease often only shows oedema and perivascular aggregations of lymphocytes. In some cases of long duration no other changes are seen, but in others the infiltrate of the submucosal connective tissue becomes denser and focal nonnecrotizing granulomas are formed with epithelioid cells and Langhans' type giant cells. These granulomas are often indistinguishable from those in sarcoidosis or Crohn's disease⁹. In our case also, we reported similar histopathological picture. In general, stains for mycobacteria and fungal organisms are recommended to exclude specific infectious disease⁹.

When the diagnosis is established, treatment is directed towards alleviation of symptoms. Several treatment modalities have been proposed. Removal of odontogenic foci may elicit a good response in some patients. Initial treatment with antihistamine therapy brought relief in most patients. Reactions to dietary components should be sought in the history and possible antigens avoided. Most therapeutic regimens include corticosteroid therapy, either topical, intralesional or systemic, as an empirical approach to this inflammatory disease. Patients with mild episodes of cheilitis granulomatosa benefit from treatment with triamcinolone in orabase or clobetasol in orabase. Injections of up to 1 mL triamcinolone acetonide (10 mg/ mL) into each side of the affected lip should be repeatedly given to patients with more pronounced manifestations. Cheiloplasty should only be performed in severely disfiguring cases⁹.

Administration of Clofazimine, an oral phenazine that has been used to treat leprosy for many years. Now it has demonstrated its utility in granulomatous diseases such as granulomatous cheilitis due to its antibacterial, anti inflammatory, and immunomodulatory properties⁷. In our case also we treated the patient with Clofazimine.

CONCLUSION:

A case report of persistent diffuse upper lip swelling (Cheilitis granulomatosis) was discussed. Persistent diffuse lip swellings should not be neglected. A thorough investigations to eliminate other etiologies is essential. Regular follow up is necessary as, with time the patient may show specific signs related to other lesions that constitute the orofacial granulomatosis, alerting the clinician to pinpoint a precise diagnosis.

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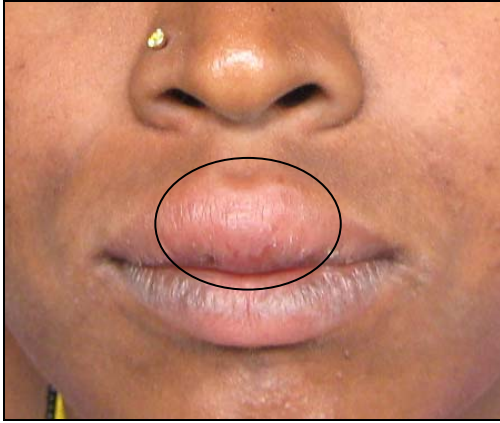
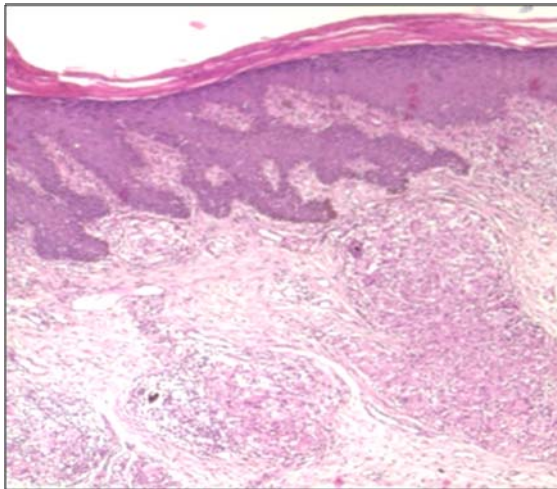


Fig 1,2: Clinical picture showing diffuse upper lip swelling



10X

Fig 3: Para keratinized surface epithelium with underlying connective tissue revealing multiple tubercle like areas.

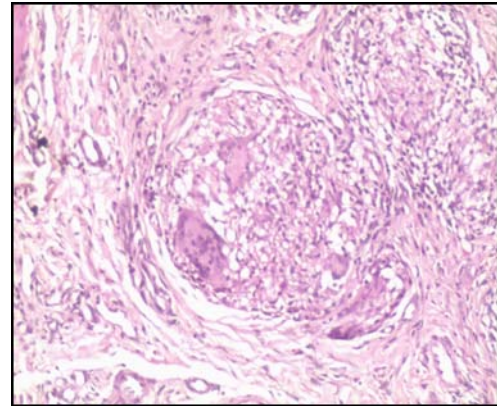


Fig 4: Tubercle – Like Area

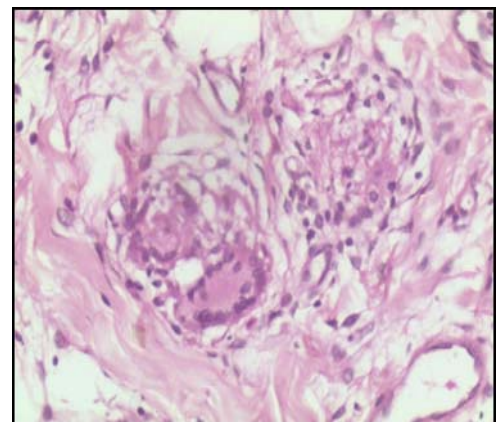


Fig 5: Each tubercle containing multiple langhan's type of giant cells surrounded by epithelioid cells and lymphocytes.