DOI: NJLM/2015/12314.2034

Case Report

Dentistry Section

Orofacial Granulomatosis- A Circuitous Route to Diagnosis

KARTHIKEYA PATIL, MAHIMA V GULEDGUD, USHA HEGDE, ANKITA SAHNI, BHUVAN NAGPAL

ABSTRACT

Orofacial granulomatosis(OFG) is a rare multifactorial clinicopathologic disorder which can exhibit wide spectrum of orofacial manifestations. Its clinical presentation is indistinguishable from numerous systemic conditions making its diagnosis and treatment a challenging task for oral health care practitioners. An extensive diagnostic work up is essential to recognize and manage this rare disease and keep a watch for development of any specific systemic granulomatoses.

A case of OFG which was identified after an elaborate diagnostic work up in a 65-year-old female patient is reported. A review of prevailing relevant literature is also put forth.

Keywords: Diagnosis, Granulomatous conditions, Orofacial granulomatosis, Lip swelling, Multidisciplinary approach

CASE REPORT

A 65-year-old female patient reported with a chief complaint of swelling of the entire upper lip since one year. The swelling was sudden in onset, not preceded by any trauma, toothache, or use of oral or local medication. The swelling had gradually progressed to the present size and thence remained static. There was no past history of similar swellings in the region of complaint or anywhere else in the body. There was no complaint of bleeding, pus discharge, numbness or parasthesia in the region of complaint as well as in the surrounding area. Patient had got her upper front tooth extracted followed by a course of antibiotics six months ago but the swelling had failed to regress. There was no history of any respiratory or gastrointestinal symptoms

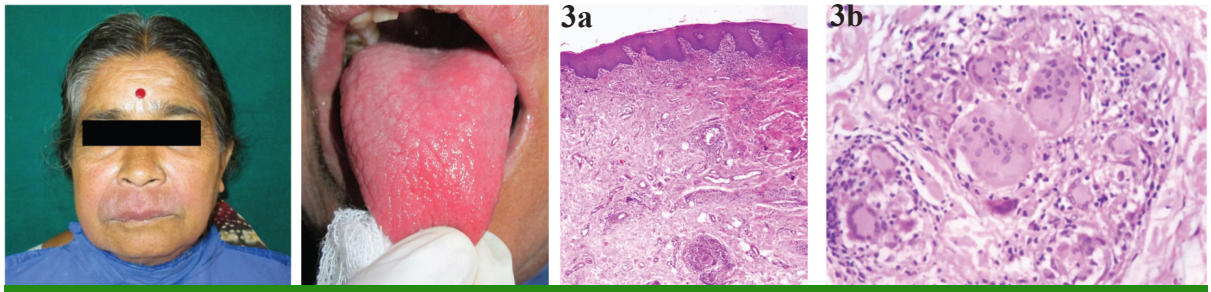
Patient was a known hypertensive and diabetic since 2 years and was on oral hypertensives and oral hypoglycaemics since 2 years.

On extra oral examination a diffuse erythematous swelling involving the upper lip and supralabial area was noted resulting in loss of contour and diminution of nasolabial angle. Bilateral erythema on the cheeks was also noted [Table/Fig-1].

The swelling was non-tender on palpation, no local rise in temperature or palpable bruit was elicited. It was firm in consistency. On intraoral examination the dentition was found to be periodontally compromised with generalized attrition and abrasion. Fissures were noted on the dorsum surface of the tongue [Table/Fig-2].

The clinical differential diagnoses considered were Angioedema, Foreign body granuloma, Chelitis Glandularis, Chelitis Granulomatosa, Melkerson Rosenthal Syndrome, Sarcoidosis, Crohns disease, Tuberculosis, Leprosy and Deep fungal infections. A screening orthopantamograph illustrated generalized horizontal alveolar bone loss. Chest radiograph did not delineate any pathology. Complete hemogram including ESR, serum ACE and serum IgE values were within normal range. Mantoux test was found to be negative and patient was seronegative to HIV. Patient was referred to a Gastroenterologist and Allergy and Immunology expert. A thorough gastrointestinal examination and lack of symptoms excluded the need for a GI endoscopy. A patch test to evaluate for allergic reactions to common food items/ additives was found to be negative.

An upper lip incisional biopsy was performed. Hematoxylin and eosin stained sections revealed presence of parakeratinzed stratified squamous epithelium along with non-caseating granuloma formation consisting of collagen fibres with fibroblasts, inflammatory cells, blood vessels and multinucleated giant cells in the connective tissue [Table/Fig-3]. Periodic acid shiff staining (PAS) was done in order to rule out fungal hyphae and was found to be negative [Table/Fig-4]. Ziehl Neelsen staining was also found to be negative which ruled out the presence of mycobacterium tuberculosis and mycobacterium leprae [Table/Fig-5]. On the basis of radiographic, laboratory and histopathological findings a final diagnosis of Orofacial Granulomatosis was rendered.

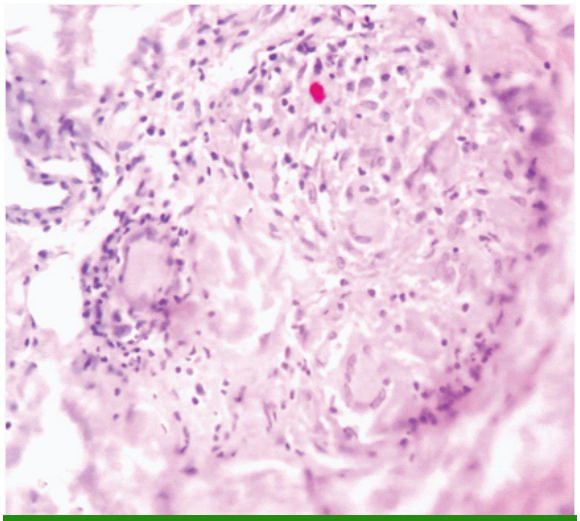


[Table/Fig-1]: A diffuse erythematous swelling involving the upper lip and supralabial area along bilateral erythema on the cheeks was evident
[Table/Fig-2]: Fissures were noted on the dorsum of the tongue
[Table/Fig-3a]: Section showing epithelium and connective tissue stroma. [H & E 40x magnification]
[Table/Fig-3b]: Section showing non-specific non-caseating granuloma in connective tissue stroma. [H & E 400x magnification]

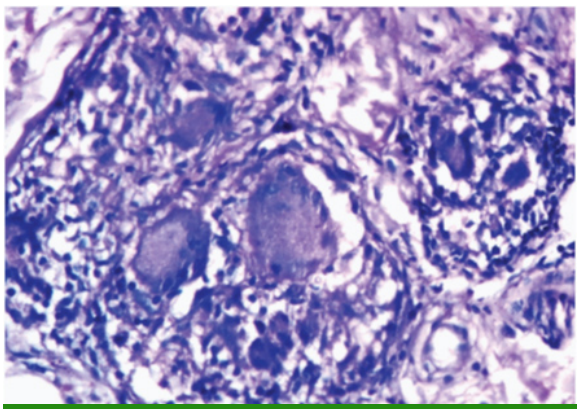
Patient underwent periodontal therapy and extraction of all teeth with poor prognosis followed by two sittings of intralesional injections of triamcinolone acetonide 10mg/ml on two visits one week apart. The treatment resulted in mild resolution of the lip swelling. However, the patient was lost to follow up.

DISCUSSION

The term orofacial granulomatosis (OFG) was introduced by Wisenfield et al., to illustrate the presence of granulomas in the head and neck region in the absence of any systemic condition. According to Wisenfield term OFG encompasses two entities Melkersson- Rosenthal syndrome (MRS) and cheilitis granulomatosa (CG) of Miescher. MRS has been illustrated as triad of persistent lip or facial swelling, recurrent facial paralysis and fissured tongue. Cheilitis granulomatosa (CG) of Miescher is characterized by swelling constrained to the lip region [3]. According to Neville and some authors they should not be considered as discrete entities and should be included in the continuum of OFG [4].



[Table/Fig-4]: PAS stained section showed absence of fungal hyphae. [400x magnification]



[Table/Fig-5]: Z-N stained section showed absence of tubercle bacilli. [400x magnification]

The etiopathogenesis of OFG is debatable. Number of factors have been implicated such as genetics, food allergy, allergy to dental materials, infective and immunological factors. Delayed type of hypersensitivity reaction seems to have a considerable role but the exact antigen responsible for it varies from person to person [2]. Clinical manifestations of OFG are highly variable. It is commonly associated with painless swellings of the orofacial tissues. Most common manifestation is that of a recurrent non tender labial swelling which may become relentless with time. It may involve one or both lips resulting in its hypertrophy and fibrosis [5]. A number of other features may also develop such as oral ulcers, mucosal tags, fissuring of the tongue, facial nerve palsy, cervical lymphadenopathy and erythema of the face [5].

Capricious clinical manifestations of OFG mimicking numerous granulomatous conditions results in a diagnostic enigma for oral health care practitioners. Hematological evaluation, radiological assessment, endoscopy and incisional biopsy are required to differentiate OFG from crohns disease, sarcoidosis, tuberculosis, deep fungal infections, foreign body and allergic reactions as well as to confirm its diagnosis. In the present case complete systemic evaluation and appropriate investigations were performed to rule out each disease following which a clinicopathologic correlation was made and a final diagnosis of Orofacial granulomatosis was given [Table/Fig-6] [6-11].

Tilakaratne et al., proposed the term 'Idiopathic Orofacial Granulomatosis' for those cases confined to the head and neck region without any specific granulomatous disease and suggested that diagnosis should not be altered until the patient develops clinical manifestations

Disease	Differentiating factor	Pertaining to the case
1. Foreign body granuloma	Presence of foreign body	No evidence of foreign body on clinical as well histopathological examination
2. Mycobacterial infections (Tuberculosis, Leprosy & atypical mycobacterial infections)	Lip involvement is rare and usually contains caseating granulomas. AFB/ZN staining, Chest radiograph, Mantoux test should be done to rule out	AFB staining – Negative Chest radiograph No pathology Mantoux test - Negative
3. Sarcoidosis	Patient will have pulmonary, cutaneous, lacrimal, salivary, neurological and skeletal manifestations. S. ACE level, Chest radiograph, Kveim – Silltzbach test should be done to rule out	S. ACE levels –Normal Chest X-ray – No pathology Kveim test – not done (obsolete investigation)
4. Fungal infections (Histoplasmosis, Blastomycosis, Coccidiodomycosis, Cryptococcosis	PAS staining should be done to rule out	PAS staining - negative
5. Crohn's disease	Patients usually have illeal and/or rectal disease. Endoscopy & colorectal biopsy should be done to rule out	Our patient did not have any gastrointestinal symptoms
6. Angioedema	Patients may present with soft tissue swelling accompanied with urticaria	Our patient did not have urticaria and gave no historyof allergy. Patch test- Negative

[Table/Fig-6]: Diagnostic work up of orofacial granulomatosis

of systemic involvement of any specific granulomatous condition [2].

As no specific causative agent was detectable even on extensive investigation, the present case was considered as a case of idiopathic orofacial granulomatosis. Absence of an etiological factor makes the treatment of orofacial granulomatosis a challenge for oral health care practitioners. Corticosteroids remain the choice of treatment which can be administered both locally as well as systemically. Intralesional triamcinolone injections 10mg/ml have often been used in the past with promising results. Recently, administration of higher concentration of corticosteroids up to 40 mg/ml has been suggested offering advantage of reduction in volume of drug to be injected and maintenance of remission [5].

On the contrary, long term intake of systemic corticosteroids is frequently associated with numerous adverse reactions making this therapeutic modality a less preferred choice in the treatment of OFG [5].

Other treatment modalities such as hydroxychloroquinine, methotrexate, clofazamine, minocycline alone or in combination with a corticosteroid have been reported in literature with varying results [6].

Recently low level laser therapy has also been tried in the management of OFG with promising results [12]. Our patient responded well to intralesional corticosteroid injection, however, the patient was lost to follow up.

CONCLUSION

Idiopathic orofacial granulomatosis is an imitator of numerous granulomatous conditions and results in diagnostic ambiguity for oral health care practitioners. It is a disease of exclusion hence, a meticulous diagnostic work up is pivotal to conclude it as a final diagnosis. A multidisciplinary approach is indispensible towards a positive outcome in the diagnosis and management of this rare condition and to thwart esthetic and functional tribulations.

REFERENCES

[1] Leo JC, Hodjson T, Scully C, Porter S. Review article:Orofacial granulomatosis. *Aliment Pharmacol Ther.* 2004; 20:1019-27.

[2] Grave B, McCullough M, Wiesenfeld D. Orofacial granulomatosis - a 20 year review. *Oral Disease.* 2009; 15:46-45.

[3] Wiesenfeld D, Ferguson MM, Mitchell DN, MacDonald DG, Scully C, Cochran K et al. Oro-facial granulomatosis — a clinical and pathological analysis. *Q J Med.* 1985;54(213):101–13.

[4] VG Mahima, Patil Karthikeya, Malleshi N Suchetha. A Clinicohistopathologic Diagnosis of Inimitable Presentation of Orofacial Granulomatosis. *International Journal of Clinical Cases and Investigations.* 2010;1(1):13-19.

[5] Kauzman Adel, Mercier Annie, Lalonde Benoit. Orofacial granulomatosis: 2 case reports and literature review. *J Can Dent Assoc.* 2006;72(4):325-29.

[6] L Suresh, L Radfar. Oral sarcoidosis: a review of literature. *Oral Diseases.* 2005;11:138–45.

[7] Neville BW, Damm DD, Allen CM, Bouquot JE. Oral and maxillofacial pathology. 3rd ed. Philadelphia: *Saunders*; 2010.

[8] R. Eversole. Orofacial granulamatosis and other inflammatory lesion. In Sol Silverman, Lewis R. Eversole, Edmond L Truelove, editor. *Essential of Oral Medicine*. Hamiliton: BC Decker;2002 p. 245–25.

[9] G. Karthikeyan, M. Arvind, N. D. Jayakumar, M. Khakar. Idiopathic Orofacial granulamatosis in a young patient: a rare entity. *J Oral Maxillofac Pathol.* 2012;16(3):432–34.

[10] Sujatha S Reddy, N Rakesh, Thanuja Ramadoss, Deepa Jatti. Orofacial Granulomatosis -A Rare Case Report with Review of Literature, *J Clin Exp Dent*. 2010;2(3):e138-41.

[11] Tomislav Duvani, Liborija Lugovi-Mihi, Ante Brekalo, Mirna Šitum, Ana Šinkovi. Prominent features of allergic angioedema on oral mucosa. *Acta Clin Croat.* 2011;50:531-38.

[12] Elisabetta Merigo, Carlo Fornaini, Maddalena Manfredi, Marco Meleti, Federico Alberici, Luigi Corcione, et al. Orofacial Granulomatosis treated with low level laser therapy- a case report. *Oral Surg Oral Med Oral Path Oral Radiol.* 2012;113(6):e25-29.

AUTHOR(S):

1. Dr. Karthikeya Patil
2. Dr. Mahima V Guledgud
3. Dr. Usha Hegde
4. Dr. Ankita Sahni
5. Dr. Bhuvan Nagpal

PARTICULARS OF CONTRIBUTORS:

1. Professor and Head, Department of Oral Medicine & Radiology, Affiliation- JSS Dental College and Hospital, JSS University, Mysore, India.
2. Professor, Department of Oral Medicine & Radiology, Affiliation- JSS Dental College and Hospital, JSS University, Mysore, India.
3. Professor and Head, Department of Oral Pathology and Microbiology, Affiliation- JSS Dental College and Hospital, JSS University, Mysore, India.
4. Postgraduate Student, Department of Oral Medicine & Radiology, Affiliation- JSS Dental College and Hospital, JSS University, Mysore, India.
5. Postgraduate Student, Department of Oral Pathology and Microbiology, Affiliation- JSS Dental College and Hospital, JSS University, Mysore, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Karthikeya Patil
Room No 4, Department of Oral Medicine & Radiology, JSS Dental College and Hospital, JSS University,S.S Nagar Mysore – 570015, India.
Email: patilkarthik@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS:
None.

Date of Publishing: **Apr 01, 2015**