CASE REPORT

# A rare case of primary orofacial granulomatosis of gingiva during pregnancy

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## ABSTRACT

Orofacial granulomatosis (OFG) comprises a group of diseases characterized by noncaseating granulomatous inflammation affecting the soft tissues of the oral and maxillofacial region. It is important to establish the diagnosis accurately because this condition is sometimes a manifestation of many systemic conditions like Crohn's disease or sarcoidosis. The clinical outcome of OFG patients continues to be unpredictable. Current therapies remain unsatisfactory. This article reports a rare case of isolated OFG with langhans type giant cells and inflammatory infiltrate without any systemic involvement, in which the condition was a manifestation of pregnancy. The diagnostic approach to and the treatment of OFG are reviewed.

***Key words:*** Crohn disease/diagnosis, granulomatosis, mouth diseases/diagnosis, orofacial, pregnancy

## INTRODUCTION

Orofacial granulomatosis (OFG) comprises a group of diseases characterized by noncaseating granulomatous inflammation affecting the soft tissues of the oral and maxillofacial region.[1] OFG is a chronic inflammatory disorder characterized by persistent or recurrent soft tissue enlargement, oral ulceration and a variety of other orofacial features. The recurrent chronic orofacial swelling caused by OFG can cause significant cosmetic and functional problems but can be prevented if the disease is diagnosed early and promptly treated.[1] This term was first introduced by Wiesenfeld in 1985, and it encompasses Melkersson–Rosenthal syndrome (MRS) and cheilitis granulomatosa of Miescher.[2]

The definite cause of OFG is unknown.[3] Various mechanisms have been suggested to explain the exact etiology. OFG may be a manifestation of Crohn's disease (some patients with oral lesions will develop typical bowel symptoms of Crohn's disease in ensuing months to years), tooth-associated infections, sarcoidosis and food or contact allergies, infection and genetic predisposition.[4-6] The classic presentation of OFG is a nontender, recurrent labial swelling that eventually becomes persistent.[7] This swelling may affect one or both lips, causing lip hypertrophy.[8] The swelling is initially soft but becomes firmer with time as fibrosis ensues. Intraoral involvement may take the form of hypertrophy, erythema or nonspecific erosions involving the gingiva, oral mucosa or tongue.[8,9] However, the clinical presentation can be highly unpredictable, making the diagnosis difficult to establish.

The diagnostic dilemma may be further complicated by the fact that OFG may be the oral manifestation of a systemic condition, such as Crohn's disease, sarcoidosis or more rarely, Wegener's granulomatosis.[10] In addition, several conditions, including tuberculosis (TB), leprosy, systemic fungal infections and foreign body reactions, may show granulomatous inflammation on histologic examination.[3]

Early diagnosis is important as it provides a better prognosis. This may need further clinical, radiographic,

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hematological and histopathological investigations to arrive at a correct diagnosis. The diagnosis of OFG is made by histopathologic identification of non-caseating granulomas. Local and systemic conditions characterized by granulomatous inflammation must be excluded by appropriate clinical and laboratory investigations.[3,10] The first goal of management should be the identification of the initiating cause. However, this can be difficult as often the reason is elusive at times and there can be spontaneous remission in a few cases.

The case report outlines the diagnostic approach used to investigate a patient presenting with a rare case of OFG of gingiva during pregnancy and discusses various therapeutic modalities used in treating OFG.

## CASE REPORT

A female patient aged around 32 years reported 9 months postpartum, complaining of nonresolving pregnancy tumor (as told to her by her dentist during pregnancy) in lower anterior gingiva, extending from 33 to 43. The history related to her pregnancy revealed that this was patient's second pregnancy. The first pregnancy was uneventful. History also revealed that the growth was generalized before and started at the 4$^{th}$ month of pregnancy and covered all clinical crowns by the 7$^{th}$ month.

She was informed by a dentist at that time, that it was a pregnancy related lesion and would regress postpartum. The lesion started regressing postpartum except in the lower anterior region, where a granulomatous growth still remained after 9 months postpartum. There was no contributory medical history, drug use and family background, but patient reported getting treated for hormonal imbalance before marriage.

Clinical examination revealed good oral hygiene, generalized edematous gingival overgrowth with localized tumor-like growth extending from 33 to 43 on the labial side than lingual side [Figure 1]. Generalized bleeding on probing with minimal enlargement of marginal and free gingiva in the upper arch, which was erythematous compare to other area of oral mucosa was noticed [Figure 2]. Grade I mobility in 31 and 41 and presence of generalized false pockets was evident. Orthopantomogram (OPG) was advised along with complete blood picture as routine investigations before excision of the growth. There was no periodontal bone loss noted in OPG [Figure 3].

Provisional diagnosis depending on the history and clinical picture pointed towards as pregnancy tumor extending from 33 to 43. Differential diagnosis included OFG, TB, sarcoidosis, allergic reaction to food or dental materials and Crohns disease.

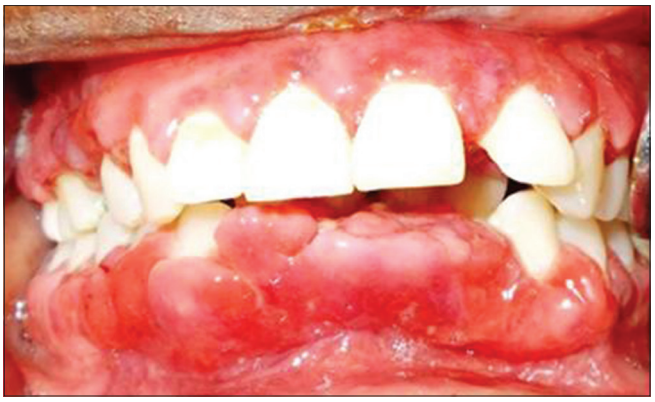

**Figure 1:** Intraoral picture during clinical examinationshowing gingival enlargement in the lower anterior region

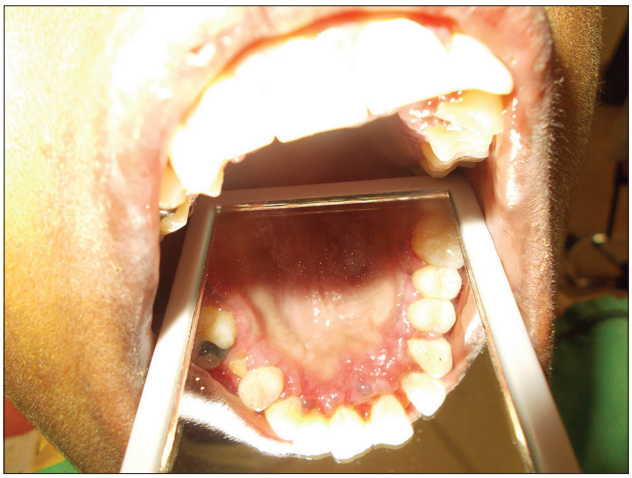

**Figure 2:** Palatal gingiva showing erythematous area and enlargement of papillary and marginal gingiva

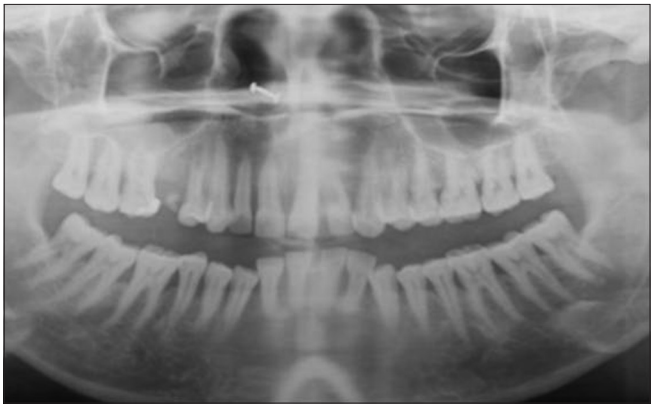

**Figure 3:** Orthopantomogram of the patient showed normal periodontal structures

Treatment included full-mouth scaling and root planning to treat possible periodontal involvement due to lack of maintenance of oral hygiene because of the growth. Following this, subgingival scaling and curettage were planned along with the excision. Excision of the tumor, under local anesthesia was carried out along with curettage in the lower anterior segment [Figure 4]. The tissue specimen was sent

for histopathological analysis, but there was a recurrence of granulomatous growth within 15 days [Figure 5].

Microscopically the lesional connective tissue consisted of keratinized stratified squamous epithelium with some areas of ulceration and necrosis [Figure 6] and the connective tissue showed collagen fibers with spindle-shaped fibroblasts with a diffuse chronic inflammatory cell infiltrate [Figure 7] composed predominantly of lymphocytes. Focal areas showed the presence of a tubercle-like structure consisting of chronic inflammatory cells, Langhan's giant cells and histiocytes [Figure 8]. This picture was suggestive of a chronic granulomatous disease. Following this, we thoroughly investigated the patient to rule out the granulomatous diseases [Table 1].

Granulomatous lesion pointed towards sarcoidosis and Crohns disease, whereas the presence of langhans cells was suggestive of TB.

Based on history, clinical examination, initial treatment, histopathological report and further investigations, the diagnosis was confirmed as primary OFG of gingiva.

The evidence pointed to the treatment of OFG with systemic corticosteroids depending on the severity of systemic manifestations or intralesional administration of triamcinolone 10 mg/ml.

**Table 1: Investigations carried out for the diagnosis**

| Investigations | Results |
|---|---|
| ESR | 40 |
| To role out diabetes: FBS, RBS | Normal range |
| AFB | Negative |
| Monteux test | Negative |
| Tissue TB PCR | Negative |
| Progesterone levels | normal |
| Serum angiotensin converting enzyme levels for sarcoidosis | Negative |
| Urine calcium levels | Negative |
| HIV | Negative |
| OPG | Normal |
| Detailed history about gastrointestinal disturbances (to role out Crohns disease) | Negative |
| Chest radiograph | Negative |

RBS: Random blood sugar, FBS: Fasting blood sugar, OPG: Orthopantomogram, TB: Tuberculosis, PCR: Polymerase chain reaction, ESR: Erythrocyte sedimentation rate, AFB: Acid-fast *Bacillus*

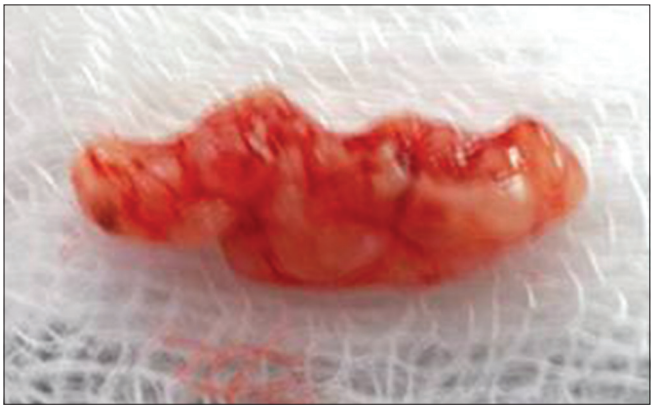

**Figure 4:** Excised specimen was reddish and firm in consistency

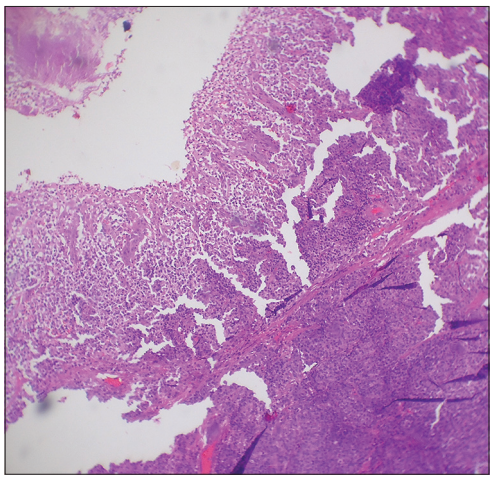

**Figure 6:** Stratified squamous epithelium with ulceration,necrotic surface and inflammatory infiltrate-low power view (H&E stain, ×40)

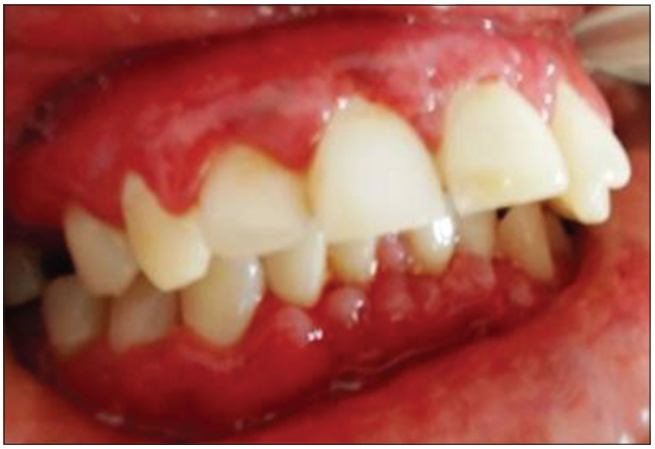

**Figure 5:** Intraoral picture after 15 days of excision

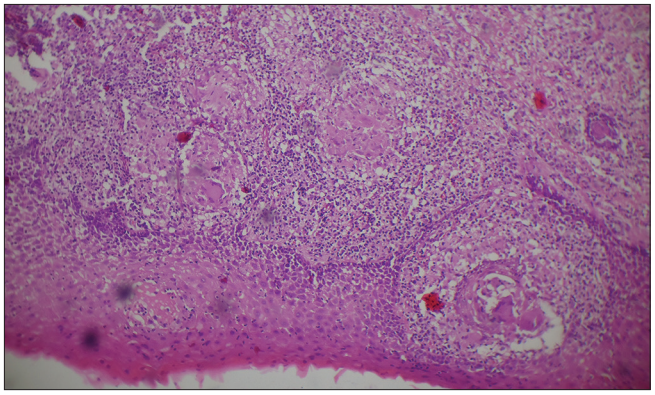

**Figure 7:** High power view shows granulomatous area in an inflammatory background below the parakeratinized epithelium (H&E stain, x200)

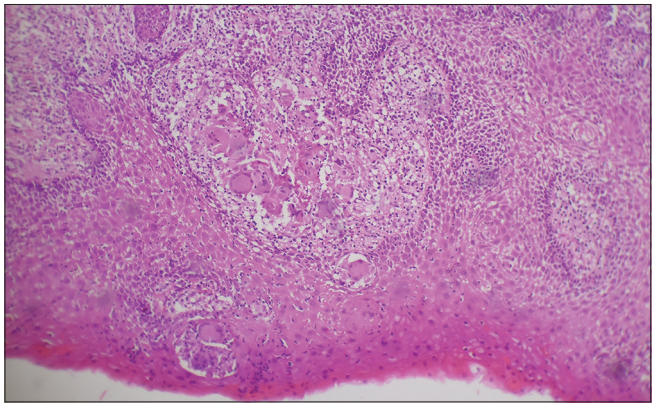

**Figure 8:** Langhans giant cells and lympho-plasmacytic cells-high power view (H&E stain, ×200)

The patient was explained about the treatment, but as she was still nursing the child, the treatment was deferred until the nursing stopped. The patient was put on regular maintenance care during this period.

## DISCUSSION

The OFG is a descriptive term used for granulomatous disorders affecting the face and oral cavity, which can occur for a variety of reasons resulting in significant morbidity. The clinical presentation of OFG is variable. It is characterized by nontender, persistent swelling that may involve one or both the lips and/or recurrent ulcers and a variety of other orofacial features.[11] Medical history is very important in the diagnosis of OFG as medical condition like Crohn's disease can also present as an extraintestinal manifestation of OFG.[11]

Before making the final diagnosis of orofacial granulomatosis, it is necessary to exclude other entities such as sarcoidosis, mycobacterial infections and foreign body reactions. Sometimes, the pathogenesis also suggests delayed hypersensitivity with unproven genetic predisposition. The present case posed a lot of misdiagnosis and confusion because of the time of onset of the lesion. The fact that it started at the 4$^{th}$ month of pregnancy reached its peak at 7$^{th}$ month and most of the lesion regressed after delivery, all pointed towards pregnancy tumor. Progesterone levels were checked to rule out retained pregnancy gingivitis, which were normal.

To rule out various granulomatous lesions, a detailed case history and investigations were carried out. A very high erythrocyte sedimentation rate (ESR) pointed to the infectious state. The presence of langhans cells and high ESR pointed towards TB. For TB, chest X-ray was done along with TB skin patch test, tissue TB polymerase chain reaction and acid-fast *Bacillus* test (Ziehl–Neelsen stain), along with clinical examination of signs and symptoms was carried out. All investigations for TB were normal, which coincided with the histopathological finding of granuloma.[12] For sarcoidosis, serum angiotensin converting enzyme levels and urine calcium levels were carried out. The results were negative.[13] For Crohns disease, the patient was referred to a physician for detailed history regarding initial signs and symptoms of inflammatory bowel disease, which was negative [Table 1].

Two case reports presented by Adel *et al.* suggested similar difficulties in diagnosis,[14] but one of the cases had symptoms of Crohn's disease.[15] A case report by Rana *et al*. about OFG of gingiva was treated with gingivectomy and there was recurrence only after 4 years.[16] To the best of our knowledge and literature reviews regarding OFG, none of the cases were reported with such clinical scenario. However, in the present case, recurrence was fast, limiting the option of repeated surgical interventions and treatment with topical steroids were deferred until the nursing stopped and the patient was recalled for intralesional steroid therapy.

## CONCLUSION

OFG is an uncommon clinicopathologic disease. The available literature does not provide a clear understanding of the etiology and the underlying pathological process. OFG, being increasingly recognized nowadays, has become a topic of interest to all professionals; it should be considered as one of the differentials in diagnosing facial swellings and poses a great challenge to us at all levels starting from its diagnosis to the prognosis and treatment. Although there are several treatment options emerging, such as anti-tumor necrosis factor (TNF)-alpha antibodies, the mainstay of treatment for patients with OFG appears to be individually tailored depending on a changing clinical presentation. Although there are several treatment options emerging, such as anti-TNF-alpha antibodies, the mainstay of treatment for patients with OFG appears to be individually tailored depending on a changing clinical presentation.

### Summary

#### *Why is this case new information?*

Orofacial granulomatosis is an uncommon clinical disease. The available literature does not provide a clear understanding of the etiology and the underlying pathological process OFG, being increasingly recognized nowadays, has become a topic of interest to all professionals and poses a great challenge to us at all levels starting from its diagnosis to the prognosis and treatment.

#### *What are the keys to successful management of this case? What are the primary limitations to success in this case?*

Although there are several treatment options emerging, such as anti-TNF-alpha antibodies, the mainstay of treatment for patients with OFG appears to be individually tailored depending on a changing clinical presentation.

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## Conflicts of interest

There are no conflicts of interest.

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