

The Diagnostic Dilemma and Prognostic Implications of Orofacial Granulomatous Diseases (OGD)

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ABSTRACT

Background: Orofacial granulomatous diseases (OGD) are heterogeneous group of disorders characterized by granulomatous type of chronic reaction. Its multifactorial causes and indistinct presentations may pose diagnostic challenge with great implications on the treatment outcome.

Objective: This study aimed to evaluate the prevalence, diagnostic challenges and its implications of the orofacial granulomatous diseases seen in a tertiary hospital.

Methods: A retrospective study of all histopathologically diagnosed granulomatous diseases of the orofacial region over 30 years period (January 1990 – September 2022). The data were retrieved from the archive of the Department of Oral Pathology and Medicine and were analyzed.

Results: A total of 12 cases were diagnosed histopathologically as orofacial granulomatous diseases within the study period. The mean age was 27.3 ± 9.9 years with peak age group at 2nd decade of life ($n=5, 41.7\%$). There were 7(58.3%) males and 5(41.7%) females with male to female ratio 1.4:1. The mid-facial region ($n=9, 75\%$) was the commonest site of occurrence. Prior to biopsy, these 12 cases had clinical diagnosis of chronic granulomatous lesions ($n=2, 16.7\%$), carcinoma of the maxillary antrum ($n=1, 8.3\%$), ameloblastoma ($n=1, 8.3\%$), lymphoma ($n=1, 8.3\%$), necrotizing fasciitis ($n=1, 8.3\%$) and 6 cases (50.0%) had no clinical diagnosis. Only 3 (25%) cases did ancillary investigations and had definitive diagnosis; one case each of actinomycosis ($n=1, 8.3\%$), aspergillosis ($n=1, 8.3\%$) and ($n=1, 8.3\%$) deep mycoses. There was a case of Wegener's granulomatosis ($n=1, 8.3\%$) as the definitive diagnosis based on histopathology only.

Conclusion: The diagnostic challenge associated with OGD is due to arrays of possible aetiological factors and non-specific presentations. Hence, detailed history, prompt histopathological diagnosis with ancillary investigations is necessary for positively impact prognosis.

Keywords: Orofacial granulomatous diseases, diagnostic dilemma, prognosis

INTRODUCTION

Arriving at a definitive diagnosis when dealing with lesions that are associated with granuloma formation in orofacial region can be challenging as wide range of disorders are associated with orofacial granulomatous lesions. Orofacial granulomatous diseases (OGD) are heterogeneous group of disorders characterized by chronic granulomatous reaction due to variety of stimulus (Susan, 2019). These stimuli can be grouped into infectious such as bacteria (e.g Tuberculosis), fungi (e.g Histoplasmosis), Parasites (e.g Leishmaniasis) and non-infectious such as immunological (e.g sarcoidosis), metabolic disorders (Cronh's disease), foreign bodies

(e.g retained dental material) and idiopathic (Orofacial granulomatosis) (Susan 2019; Alawi 2013).

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Clinically, OGD usually present with variable and indistinct findings which include; facial swelling, ulceration, fissures, mucosa tags, gingival enlargement, and others (Alawi 2013). Histologically, granulomas are composed of aggregates of epithelioid histiocytes, with a peripheral cuff of lymphocytes and plasma cells. Two broad forms of well-defined

granuloma exist, based on their etiology: foreign-body giant cell granulomas and immune granulomas (Kabeer et al., 2017). The immune granulomas are further histologically characterized as necrotizing, non-necrotizing and suppurative (Kabeer et al., 2017). A careful evaluation with hematoxylin and eosin stain may reveal identifiable aetiology (Kabeer et al., 2017) but when this is not possible or there is histological overlap, there may be diagnostic challenge which may necessitate ancillary tests such as special stain, microbiological test and molecular testing. This study aimed to evaluate the prevalence, diagnostic challenges and its implications of orofacial granulomatous diseases seen in a tertiary hospital.

MATERIALS AND METHODS

A retrospective study of all histopathologically diagnosed granulomatous diseases of the orofacial

region over 30 years period (January 1990 – September 2022). The data were retrieved from the archive of the Department of Oral Pathology and Medicine and were analyzed. There were 12 cases of histopathologically diagnosed orofacial granulomatous diseases within the study period. The variables obtained included: age, sex, site, clinical diagnosis, histopathological diagnosis and definitive diagnosis after ancillary test. The Data collected were analyzed with SPSS, version 21 (Chicago: SPSS Inc.).

RESULTS

A total of twelve cases of histopathologically diagnosed orofacial granulomatous diseases were retrieved. OGD occurred within second to fifth decades of life with mean age of 27.3 ± 9.9 years and peak age group at 2nd decade of life (n=5, 41.7%). There were 7(58.3%) males and 5(41.7%) females with male to female ratio 1.4:1.

Table 1. The age group and sex distribution

| Age (years) | Frequency | Gender | |
|-------------|-----------|--------|--------|
| | | Male | Female |
| 10-19 | 5 | 4 | 1 |
| 20-29 | 2 | - | 2 |
| 30-39 | 4 | 2 | 2 |
| 40-49 | 1 | 1 | - |
| Total | 12 | 7 | 5 |

The mid-facial region (n=9, 75%) was the commonest site of occurrence. The clinical diagnosis were chronic granulomatous lesions (n=2, 16.7%), carcinoma of the maxillary antrum (n=1, 8.3%), ameloblastoma (n=1, 8.3%), lymphoma (n=1, 8.3%), necrotizing fasciitis (n=1, 8.3%) and 6 cases (50.0%) had no clinical diagnosis. A

case of definitive diagnosis of Wegener's granulomatosis (n=1, 8.3%) was made based on histopathology. Only 3 (25%) cases did ancillary investigations/tests and had definitive diagnosis; one case each of actinomycosis (n=1, 8.3%), aspergillosis (n=1, 8.3%) and (n=1, 8.3) deep mycoses.

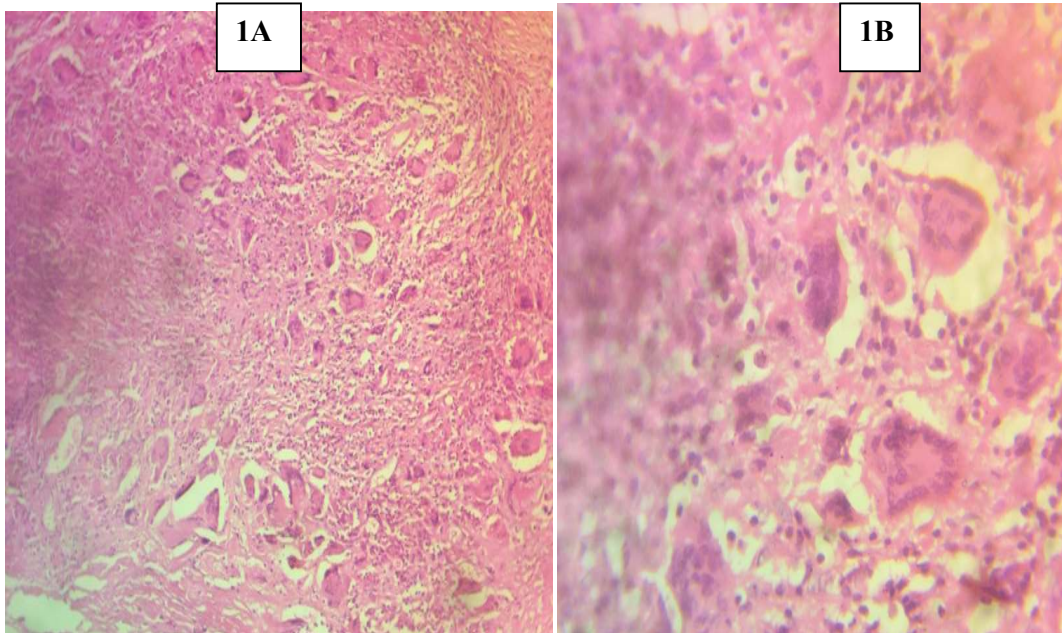
Table 2. The site distribution, clinical, histopathological and definitive diagnoses

| S/N | Site | Clinical diagnosis | Histopathological diagnosis | Definitive diagnosis |
|-----|---|---|--|----------------------|
| 1 | Left maxillary swelling | Chronic granulomatous lesion R/O T-cell Lymphoma | OGD | |
| 2 | Nasal swelling | Granulomatous lesion | OGD (leprosy) | |
| 3 | Cervical lymph node swelling | - | Infective OGD (tuberculosis or Systemic mycoses) | |
| 4 | Palatal swelling | Carcinoma of the maxillary antrum | Ulcerated OGD | |
| 5 | Left antral swelling | - | OGD | Actinomycosis |
| 6 | Right maxillary swelling | Ameloblastoma | OGD | Aspergillosis |
| 7 | Maxillary swelling | - | Wegener's granulomatosis | |
| 8 | Right mastoid swelling | - | OGD | |
| 9 | Oral mucosa and lacrimal (right eye) swelling | Lymphoma | OGD | |
| 10 | Cervical lymph node swelling | - | OGD | |
| 11 | Left maxillary and preauricular swelling | - | OGD | Deep mycoses |
| 12 | Ulceration of right inferior border of the mandible | Necrotising fasciitis | OGD | |

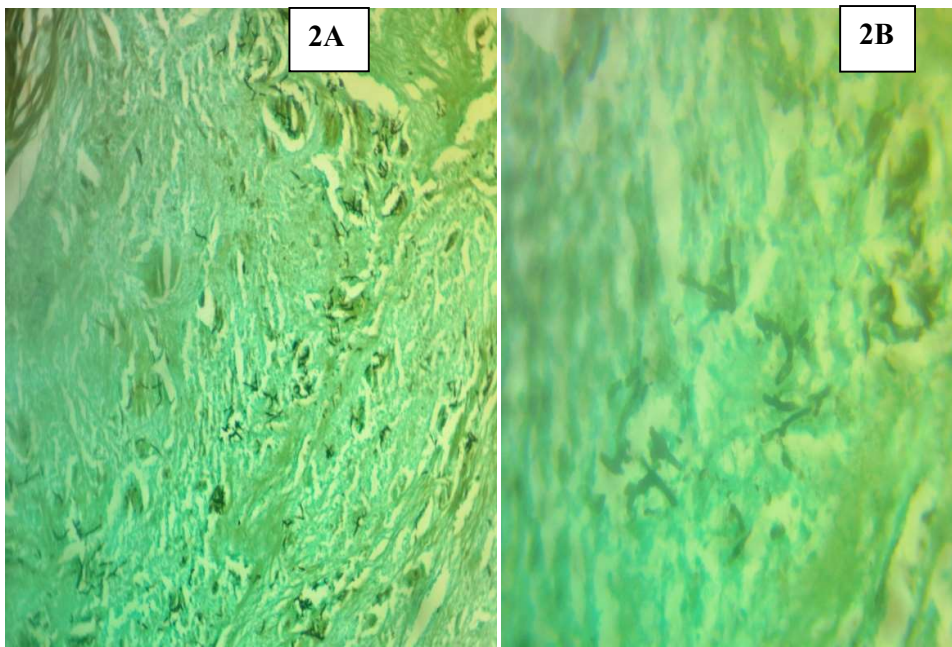
Key: OGD: Orofacial granulomatous disease, R/O: Rule out

Table 3. Frequency and percentage of clinical diagnosis and definitive diagnosis

| | Clinical diagnosis | Definitive diagnosis Histopathology | Ancillary Test |
|----------------|--------------------|--|-------------------|
| Frequency(n) | 6 | 1 | 3 |
| Percentage (%) | 50.0 | 8.3 | 25.0 |



Figures 1A and 1B: Photomicrograph showing granuloma, composed of numerous multinucleated giant cells admixed with lymphocytes within a loose fibrocellular stroma. 1A(H & E X100) and 1B (H & E X400).



Figures 2A and 2 B: Photomicrographs showing the hyphae of the deep mycoses highlighted by the special stain (Grocott methenamine silver). 2A (H & E X100) and 2B(H & E X400).

DISCUSSION

Granulomatous diseases are group of conditions characterized by a histological denominator of granuloma formation (Ahmed, 2020). Granulomatous diseases affecting orofacial region are uncommon, but when present, they may present a diagnostic dilemma (Susan 2017). The aetiologlogical factors are infectious, non-infectious and sometimes idiopathic (Susan 2017, Alawi 2013). The commonest cause in this study is infectious and is in consonant with studies done by Adhikari et al (2013) and Pawale et al (2011)..

Granulomatous diseases can occur in all age groups and all tissue site (Kabeer, 2020). OGD in this study occurred in age range of 2nd to 5th decades with 2nd decade as peak age. Though OGD can occur in any site, there was high incidence of OGD in the mid facial region, followed by the cervical lymph nodes in this study and study done on granulomatous inflammation showed lymph nodes to be the commonest site of occurrence (Adhikari et al., 2013). Though there is no sex predilection of OGD in the literature, this study observed slight male preponderance.

OGD present clinically with variable and indistinct findings which include; facial swelling, ulceration, fissures, mucosa tags, gingival enlargement, and others (Alawi, 2013; Ahmed, 2020). However, the clinical presentation in this study was mainly swelling involving hard and soft tissues and lymph nodes. Also, there was a case of ulceration. These presentations are not disease specific and as such only 16.7% of cases had clinical diagnosis of OGD while 50.0% of cases had no clinical diagnosis and other 33.3 % of cases had different clinical diagnosis other than OGD. Oral involvement of deep fungal infections is uncommon especially in immunocompetent individuals and clinicians are often unaware of the clinical spectrum of the disease, which may lead to delayed diagnosis and negatively impact prognosis (Mutalik, 2021). This was the case in an immunocompetent young female patient that presented with maxillary swelling involving the antrum that was suggestive of neoplastic mass clinically and was surgically managed but histopathology was suggestive of OGD of fungi origin. Special stain with Grocott methenamine silver stain confirmed diagnosis of deep mycoses but this was rather too late for the patient. Therefore, an extensive clinical, microscopic, laboratory, molecular evaluation may be required in order to identify the source of the granulomatous inflammation (Alawi 2013; Kabeer 2020; Mamatha 2017). Also in this study was a case of Wegener's granulomatosis that may have been missed at clinical evaluation. This disease is characterised by necrotising granuloma affecting multiple organs. Oral manifestations which are rare (only in 2% of cases)

present characteristically as strawberry gingival with other oral lesions and as early signs of the disease when present (Siar, 2011). These lesions may remain localized in the oral cavity for unusually long periods of time before multi-organ involvement (Siar 2011). Hence, timely recognition of this often overlooked oral finding can help to establish an early diagnosis of this life threatening disease (Ahmed, 2020).

Histopathologically, granulomatous inflammation encompasses array of findings, ranging from well-formed granulomas to loose collections of multinucleated giants cells admixed with inflammatory cells. A well-formed granulomas offer potential diagnostic etiologies, while the loose type is a non-specific findings (Kabeer, 2020). This type of loose presentation of granuloma may be the reason majority of the histopathologically diagnosed OGD was not specific of the etiology in this study and ancillary tests requested. The two broad forms of well- defined granuloma based on etiology are: foreign body giant cell granuloma and immune granulomas (Kabeer, 2020). The immune form is further characterised as necrotizing, non-necrotizing and suppurative which can help to narrow the differential diagnosis. The non-necrotizing pattern is usually associated with non-infectious etiologies while all the patterns can be seen in infectious cases (Kabeer 2020). Often times, no single histological feature separate an infectious necrotizing granuloma from other granulomas (Aubry, 2012). Hence the need for ancillary studies like special stains (Ziehl-Neelsen for TB, Grocott methenamine silver for deep mycoses), microbiological evaluation, molecular test such as real-time PCR, in situ hybridization is perform to find the cause of granuloma (Aubry 2012). However, only 25.0% of cases in this study had definitive diagnosis following ancillary investigations. It's worthy of note, that some granulomas may remain unexplained even with ancillary test, hence well detailed clinical history and clinicopathological correlation are essential in making a final diagnosis (Adhikari, 2013).

CONCLUSION.

OGD are uncommon with non-specific clinical presentations and sometimes histopathological overlap which may lead to missed-diagnosis or delayed diagnosis with negative or fatal outcome. Therefore, a comprehensive clinical evaluation, prompt histopathological diagnosis and appropriate ancillary investigations where necessary is of utmost importance for better and positive treatment outcome.

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