Case Report

A Case Report on Oral Granulomatous Lesion

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Abstract

Granulomatous infections are chronic inflammatory disorders caused by a variety of infectious and noninfectious factors. They can be localized or a symptom of a systemic, disseminated disease. Oral signs of granulomatous inflammation, like skin indications, are frequently vague in appearance. As a result, identifying the underlying source of inflammation can be difficult in the absence of overt foreign material or a known infectious pathogen. This review aims to discuss a case report which imposed a diagnostic challenge. The etiology and histopathogenesis of commonly encountered oral granulomatous lesions are also reviewed.

Keywords: *Foreign body reaction, oral granulomatous lesion, orofacial granulomatosis, sarcoidosis, tuberculosis, Wegener's granulomatosis*

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Introduction

The orofacial tissues can be affected by a wide range of granulomatous disorders. Infections, immunological, reactive, and foreign body granulomas are all examples of granulomatous lesions. Most of the granulomatous lesions are sessile, lobulated, moderately firm, and relatively nontender nodules and papules with normal coloration and little or no surrounding inflammatory mucosal erythema. Histologically, the granulomatous lesions are characterized by small, nonnecrotizing, or noncaseating granulomas with peripheral lymphocytes, central epithelioid histiocytes, and multinucleated giant cells. Some of the granulomas may ulcerate centrally and present as a squamous cell carcinoma as time passes on. Granulomas are most commonly caused by the presence of a nondegradable product or hypersensitivity reactions. Microorganisms can act as foreign bodies as well as antigens for immunological responses, so these two mechanisms are often combined in most infectious diseases. As a result, granulomas are normally the result of defensive mechanisms that form when invading agents are not destroyed by acute inflammatory processes. The main objective of this article is to present a case of granulomatous lesion of the oral cavity, as well as a comprehensive literature review of the facts and variations surrounding its nomenclature, clinical presentation, and etiology. It also represents the difficulties that a professional face when diagnosing and treating such cases.

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Case report

A female patient of 52 years old reported a chief complaint of pus discharge and pain in her upper left cheek region for 1 month. The patient revealed the history of a previous lesion in the same region 5 years back, growing over a period of 4 months, associated with pain. On extraoral examination, evidence of irregular scar in the left cheek region with hyperpigmentation was present with an obvious asymmetry in the middle third of the face. There was a difference in the width of the palpebral fissure, elevation on the left of the dorsum of the nose, fullness in the left infraorbital region, and obliteration of the left nasolabial fold. Moreover, on palpation, pus discharge was evident in the left infraorbital area and overlying skin pigment was firm and tethered [Figures 1-7]. On intraoral examination, evidence of scar of previous surgery in the left upper vestibule was seen and the overlying mucosa appeared normal. On palpation, tenderness in the buccal vestibule in 26 region was evident.

Based on the history, clinical features, and other examinations, a provisional diagnosis of fatty fibrous

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growth/basal cell carcinoma was given. Following this, an incisional biopsy was done in the left infraorbital area through an intraoral approach and the specimen was sent for histopathological examination. The diagnosis was given as chronic granulomatous inflammation. Further, an excisional biopsy was done in the left infraorbital and the specimen along with the maxillary sinus lining was sent for histopathological analysis. The final diagnosis was given as chronic granulomatous inflammation, and the patient was advised for ACE-inhibitor test to rule out sarcoidosis and BAC-TEC test for tuberculosis (TB).

Histopathological findings

The histopathological picture of incisional biopsy showed fibrovascular connective tissue with numerous blood vessels, and few of them are filled with red blood cells. Foci of dense chronic inflammatory cell infiltrate including lymphocytes, plasma cells, macrophages, and multinucleated giant cells are seen suggestive of granuloma formation. Following this, the excisional biopsy specimen revealed connective tissue with multiple granuloma formation and the granulomas were made up of chronic inflammatory cells, namely lymphocytes, plasma cells, and macrophages. In addition, areas of caseating necrosis were also present. Numerous multinucleated giant cells with their nuclei arranged in horseshoe-shaped pattern toward the nuclear periphery known as Langhans-type giant cells are seen characteristically. Further, periodic acid–Schiff staining was done and there was no evidence of fungal hyphae. A final diagnosis of chronic granulomatous inflammation was given. The patient was advised to take Mantoux test to rule out TB, but the patient did not turn back after that.

Discussion

Granulomatous inflammation is a type of chronic inflammation that is unlike any other. Granulomas are clusters of macrophages with epithelioid shapes, multinucleated giant cells, lymphocytes, and fibroblasts. Clinical manifestations of granulomatous inflammation, on the other hand, are frequently variable and indistinct. Granulomatous inflammation can be caused by a variety of factors, including environmental or genetic factors, infectious organisms, or it can be idiopathic. A typical differential diagnosis of the present case includes:

1. Foreign body reactions and infection
2. TB
3. Sarcoidosis
4. Orofacial granulomatosis (OFG)
5. Wegener's granulomatosis (WG)
6. Microbial infections.

There are two types of granulomas, foreign body granulomas and immune granulomas.

Foreign body reactions

Foreign body granulomas are the most common source of granulomatous inflammation in the oral cavity.[1] Foreign bodies may be endogenous or exogenous. Microscopically, the granulomas are usually seen enveloping the foreign particles. In some cases, foreign material also may be identified within the cytoplasm of the giant cells, representing an effort by the giant cells to phagocytose and eliminate the material. Whereas some foreign substances, such as glass, suture material, hair fibers, and silica, may be easily visible under the microscope, other substances may require the use of polarized light to be visualized. If there is no identifiable foreign material, other causes of the granulomatous inflammation must be considered. There is an extensive list of substances, including common dental materials, that may induce foreign body reactions in the oral cavity. Retained impression material, amalgam, pumice, gutta-percha,

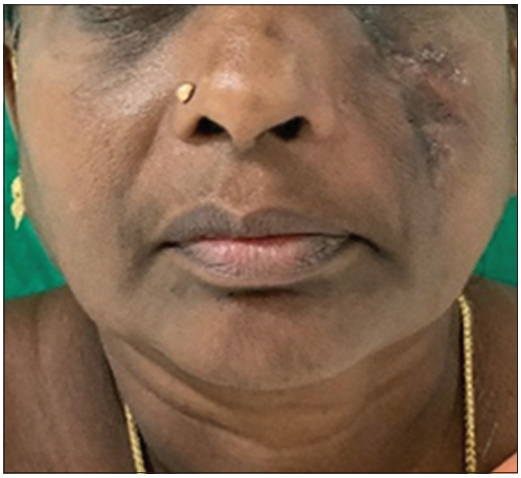

Figure 1: Patient profile

Figure 2: Intraoral view

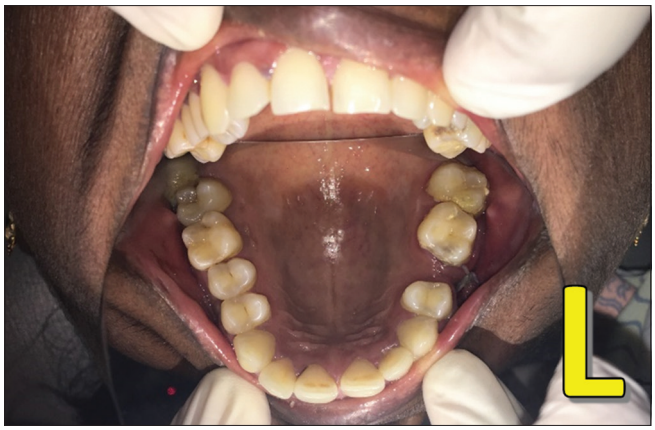

Figure 3: Left vestibule region

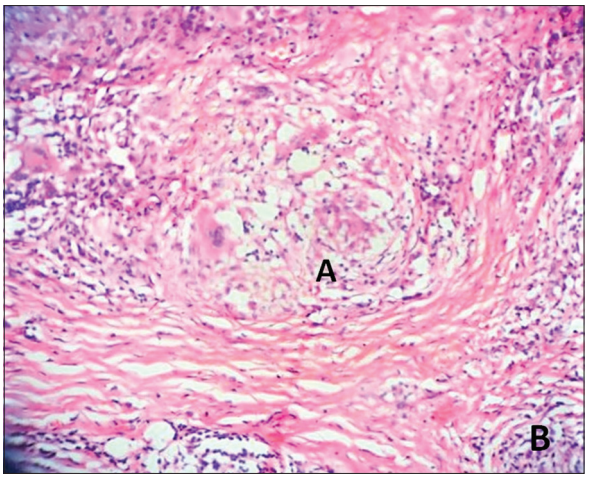

Figure 4: (A) Area of necrosis; (B) Chronic inflammatory cell infiltrate

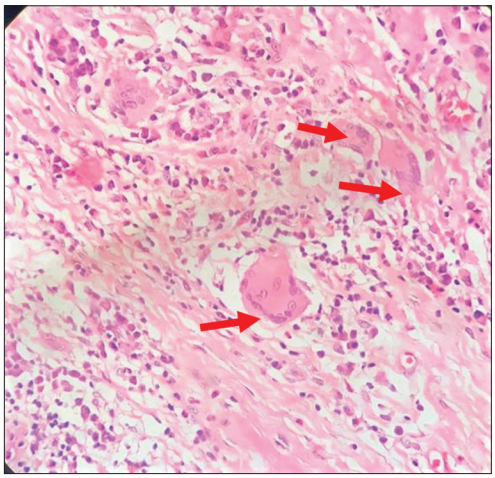

Figure 5: Arrow mark indicates Langhans-type giant cells

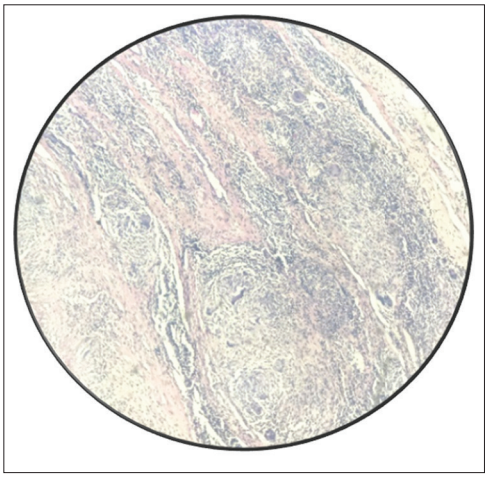

Figure 6: Periodic acid–Schiff stained section under ×10, no evidence of fungal hyphae

zinc phosphate cement, various endodontic sealers, and suture material have all been associated with granulomatous inflammation.[2]

Immune-mediated granulomatous disorders

Immune-mediated granulomatous inflammation represents a distinct form of delayed-type (cell-mediated) hypersensitivity. Immune granulomas typically develop in response to infection by various mycobacterial and fungal organisms. Upon initial exposure to a nondegradable antigen derived from an organism (usually a protein), there is an accumulation of predominantly CD4-positive T-lymphocytes around blood vessels in the area where the antigens lie. Over time, the T-cells differentiate, become activated T-helper (Th) cells, and begin secreting various cytokines that recruit macrophages to the site of the foreign antigen. If the antigens persist and remain nondegradable, the recruited macrophages eventually transform into epithelioid cells, organize, and form granulomas.[3]

Tuberculosis

TB is the prototypical example of immune-mediated granulomatous disease. TB is caused by infection with *Mycobacterium tuberculosis*, but other mycobacterial infections, including those caused by *Mycobacterium leprae* (leprosy), *Mycobacterium bovis*, and *Mycobacterium avium intracellulare*, also can induce granulomatous inflammation.[4,5]

The manifestations of TB are variable and most commonly restricted to pulmonary complications. While oral manifestations may be identified in extrapulmonary or disseminated TB, primary oral TB is uncommon. A nonhealing ulceration is the most common manifestation; localized masses or swellings may also be evident. In rare instances, infection may involve the alveolar bone and mimic periodontal disease. The pathogenesis of the disease is described in Figures 8 and 9. Epithelioid cells are formed by differentiation of activated macrophages which coalesces to form multinucleated

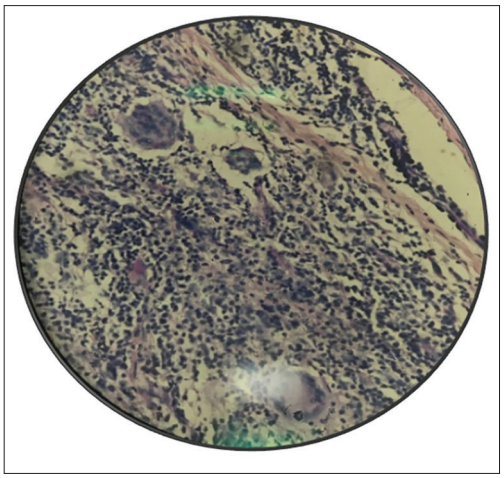

Figure 7: Periodic acid–Schiff stained section under ×40, no evidence of fungal hyphae

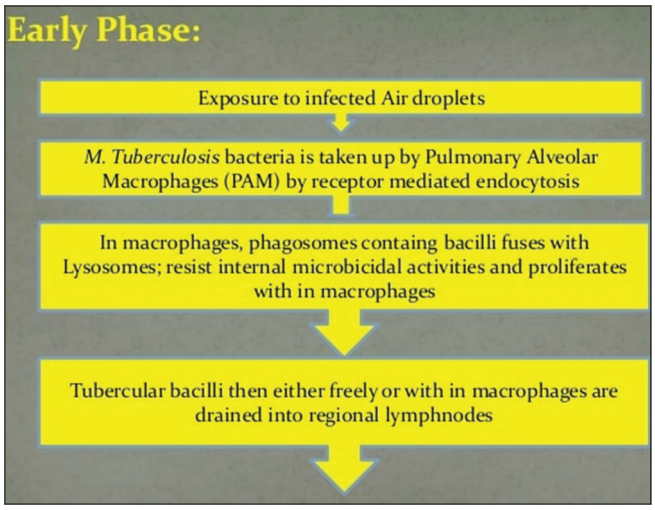

Figure 8: Early phase of tuberculosis pathogenesis

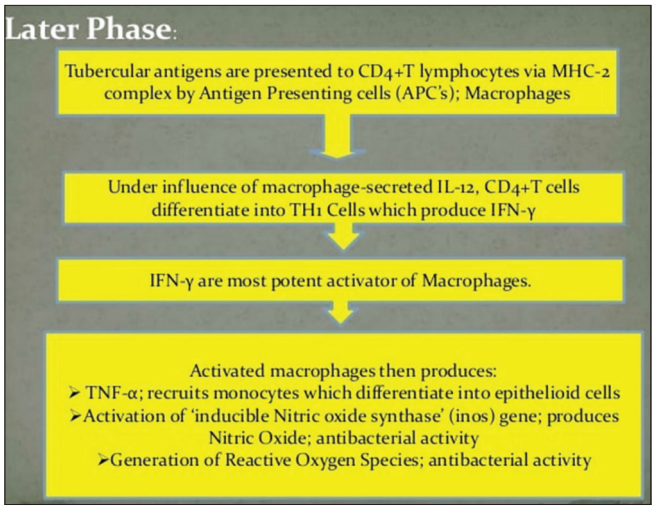

Figure 9: Later phase of tuberculosis pathogenesis

giant cells. Production of nitric oxide and reactive oxygen species which are highly oxidative causes oxidation of cells forming caseous necrosis. In addition, macrophages produced chemokines causes recruitment of lymphocytes and fibroblast. Microscopically, they resemble cell-mediated hypersensitivity reaction. Oral lesions are histopathologically similar to pulmonary lesions. Formation of typical granuloma consisting of central caseous necrosis circumscribed by epithelioid histiocytes and Langhans-type giant cells will be present. The Langhans giant cells will be surrounded by a rim of fibroblast and lymphocytes.[6]

Sarcoidosis

Sarcoidosis is a relatively common, multisystem disease of unknown etiology. A number of studies have suggested that both host and environmental factors have a role in the disease's progression. Despite the lack of specific environmental factors or infectious agents, a number of studies have found regional, seasonal, and occupational clustering of sarcoidosis patients. Furthermore, there is abundant evidence that sarcoidosis is a Th1 condition, implying that some external substance is involved in the disease's progression. Furthermore, oligoclonal growth of T-cells expressing specific T-cell receptors has been discovered through tissue sampling. This finding supports the idea that sarcoidosis is an antigen-driven illness, implying that an external agent is involved in its development.[7,8]

In up to one-third of all patients, cutaneous manifestations may be the first signs of sarcoidosis. The majority of skin findings are nonspecific and range from common (papular eruptions, erythematous scaling plaques, scar, and erythema nodosum) to uncommon (hypopigmentation and ulcerations) to rare (hypopigmentation and ulcerations) (alopecia). Lupus pernio is a cutaneous manifestation marked by indurated, brownish-red plaques that typically affect the nose and cheeks, enlarge, and become confluent over time.[9] Involvement of the oral cavity in sarcoidosis is uncommon. Although oral lesions may be the first signs and symptoms of sarcoidosis in some patients, the majority of patients will have other signs and symptoms. Any mucosal site can be affected, and multiple oral sites are occasionally involved. The majority of lesions appear as painless nodular or multinodular growths or swellings under the mucosa. The most common symptom of gingival sarcoidosis is a diffuse enlargement. Minor or major salivary gland tissue may be affected by sarcoidosis.[10]

For sarcoidosis to be considered a clinical diagnosis, a microscopic finding of granulomatous inflammation is required. An initial screening for all patients with suspected or diagnosed sarcoidosis should include a detailed history, including family history, a thorough

physical examination, chest radiographs and pulmonary function tests if necessary, serum chemistries, ophthalmologic evaluation, and complete blood cell counts. It should be noted, however, that there are no specific assays or analyses that can be used to diagnose this disease. As a result, sarcoidosis is frequently used as an exclusionary diagnosis.[11]

Orofacial granulomatosis

OFG is a rare granulomatous inflammatory disorder that affects only the oral and perioral tissues. OFG can affect anyone at any age, has no sex preference, and has no known cause. Infectious agents and genetic factors have both been suggested, but neither has been consistently linked to the disease. OFG is thought to be the result of an unusual allergic reaction to foods, dental materials, or some other environmental factors.[12] OFG has been linked to a number of different clinical manifestations. A persistent, painless swelling of the orofacial tissues is the most common finding. The lips are the most commonly involved areas. The swelling can affect one or both lips, and it can be unilateral or bilateral and symmetric. Within the affected lip, a vertical fissure frequently develops. Most patients experience facial swelling, which can also affect the eyelid, as the disease progresses. Intraorally, generalized edema and erythema, superficial ulcerations, and papules are examples of nonspecific clinical findings.[2]

Although noncaseating granulomas are a hallmark of OFG, foreign body reaction, infectious disease, CD, and sarcoidosis must all be ruled out before a diagnosis of OFG can be made. As a result, OFG is an exclusionary diagnosis.

Wegener's granulomatosis

WG also known as granulomatosis with polyangiitis is an organ- and/or life-threatening autoimmune disease of as yet unknown etiology. The classic clinical triad consists of necrotizing granulomatous inflammation of the upper and/or lower respiratory tract, necrotizing glomerulonephritis, and an autoimmune necrotizing systemic vasculitis affecting predominantly small vessels.[13]

Hyperplastic gingiva, which is red to purple and has many petechiae, is the most common oral lesion. Tooth mobility, tooth loss, and wounds that do not heal are all common symptoms. Before multiorgan involvement, the disease may remain localized in the oral cavity for an unusually long time. While the cause of the disease is unknown, it appears that both cellular and humoral factors are involved. The inflammatory process includes T-cell-mediated immunity, which produces tumor necrosis factor-alpha (TNF-α) and interferon-gamma. Neutrophils are also important in the tissue injury caused by WG. TNF-α and other inflammatory cytokines stimulate the surface expression of antigens on activated neutrophils. Some of these interact with antineutrophil cytoplasmic antibodies (ANCAs), causing neutrophil degranulation and toxic product production, resulting in tissue injury. Serologic testing for ANCA is recommended as part of the diagnostic process.[14]

Vasculitis, granulomatous inflammation, multinucleated giant cells, and necrosis are histopathologic criteria for WG diagnosis. The histopathologic findings in WG gingival lesions are less specific in most cases but may show acute or chronic inflammation, multinucleated giant cells, and pseudoepitheliomatous hyperplasia. While these findings may be considered nondiagnostic, they would be helpful in confirming a WG diagnosis in the presence of strawberry gingivitis or other signs of systemic or organ system involvement.[14]

Conclusion

Granuloma formation in the oral cavity can be caused by a number of factors. Foreign body responses, infection, TB, sarcoidosis, OFG, and WG are the most prevalent differential diagnosis. A microscopic diagnosis of granulomatous inflammation sometimes provides a diagnostic problem for the clinician due to the nonspecific clinical symptoms associated with these granulomatous diseases. As a result, identifying the etiology of the granulomatous inflammation may necessitate a thorough clinical, microscopic, and laboratory examination. A patient with granulomatous infection may have a favorable to excellent prognosis if the etiology and histopathological features are adequately recognized and the condition is appropriately treated.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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