

# Infectious Granulomatous Diseases of Oral Cavity: A Concise review

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## Abstract

Infectious granulomatous conditions of the oral tissue are infrequent, but they do arise which is most of the time remain unrecognised because of the wide range of potential etiologic illnesses and the unusual presentation of the such lesions. Granulomatous inflammation are distinct form of the chronic inflammatory response which is histologically comprised of macrophages in the epithelioid form and is usually surrounded by a ring of lymphocytes. In close to the lymphocytes, fibroblasts and collagen fibres may also be detected.

This inflammatory response which manifests in several infectious, toxic, allergic, autoimmune and neoplastic disorders as well as conditions with unknown causes, is a common pathological condition. The most familiar clinical presentation include persistent swelling of the affected areas including ulceration. The most typical differential diagnosis includes tooth-associated infections, Crohn's disease, sarcoidosis and foreign body responses. Therefore, an appropriate clinical, histological and laboratory estimation is essential to recognize its source of origin.

Furthermore, it is now the dentist's role to include these conditions while making a differential diagnosis of any suspected oral lesions. Also, they should be familiar with its clinical manifestations as it is important and often serious disease. It ensures timely treatment and helping in maintaining the oral health care at primary stage.

This article emphasized the causes, pathophysiology, clinical features and histopathological features of granulomatous diseases within the oral soft and hard tissues.

**KEYWORDS:** Granulomatous inflammation, Leprosy, Syphilis, Tuberculosis.

## INTRODUCTION

A granuloma is an organized aggregation of phagocytic cells along with some other types of inflammatory cells instantaneous to infectious immune response & frequently offers a diagnostic challenge to professionals.<sup>1</sup> Moreover, it has several different potential etiology (**Table 1**) and the clinical presentations might range widely which routinely demonstrated as solitary ulceration or inflammation. Localized granulomatous inflammation in the mouth is commonly accompanied by foreign material.<sup>2</sup>

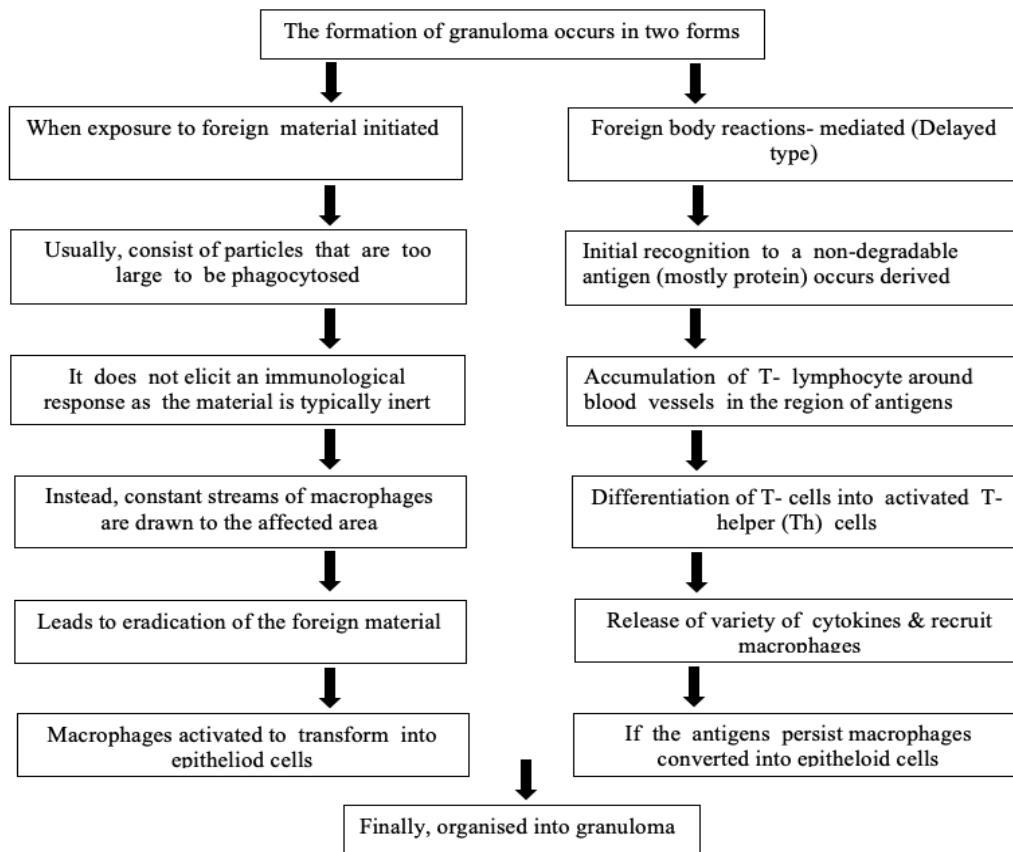
These disorders of the oral soft and hard tissues are unusual and controlling them can be still challenging for both patients and clinicians.<sup>3</sup> The macrophages in the lesion are active cells that assemble to form multinucleated giant cells. These giant cells have nuclei that are distributed either at border or frequently in the form of a horseshoe (Langhans type).<sup>4</sup>

Even though granulomatous inflammation of the oral soft and hard tissues is not frequent, it can be difficult to diagnose when it does occur because of the vast range of potential etiologic illnesses and the generally similar appearance of the individual lesions.

Orofacial granulomatosis treatment is not consistently successful and may not always be necessary, while the majority of patients do need some form of medical attention. This article highlighted the growing importance of oral pathologists in providing the definitive recognition of this dreadful illness by recognizing specific histological characteristics along with its causes to deliver adequate management which is much challenging.

<b>Etiological Classification of Infectious Granulomatous Diseases</b>			
<b>(a) Bacteria</b>	<b>(b) Fungal</b>	<b>(c) Spirochetal</b>	<b>(d) Parasitic</b>
Tuberculosis Leprosy Non-tuberculous mycobacterial infections Actinomycosis Klebsiella Anthrax	Histoplasmosis Blastomycosis Mucormycosis Aspergillosis Candidiasis Cryptococcosis Rhinosporidiosis	Syphilis	Leishmaniasis Myiasis Toxoplasmosis

## **PATHOPHYSIOLOGY**



**Figure 1:** Pathophysiology of granulomatous diseases.

## **SOME INFECTIOUS GRANULOMATOUS DISEASES**

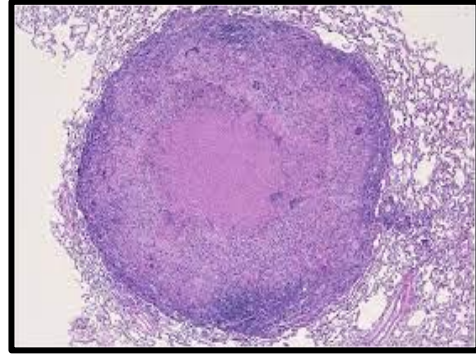
### **(1) Tuberculosis**

Tuberculosis is a potentially fatal infectious which is globally emerging with increased prevalence in Asian nations that affects not only the lungs but also numerous aspects of the oral cavity, including the tongue and gingiva.

The commonest bacteria of this chronic infection is *Mycobacterium tuberculae* associated specially in patients with human immunodeficiency virus infection producing variety of oral manifestations of this illness. Often spreading as a consequence of hematogenous spread or contaminated sputum. Clinically, a chronic tubercular ulcer typically exhibiting irregular, yellowish and indolent with inverted boundaries and less commonly, nodular or granular presentation. **(Figure 2)** Microscopic observation of an excisional biopsy is used to provide a confirmatory diagnosis along with smear microscopy, culture and a tuberculin skin test as an adjuvant.<sup>5</sup>**(Figure 3)**



**Figure 2:** Tubercular ulcer.



**Figure 3:** Microscopic view of Tuberculosis. (4X magnification, H & E)

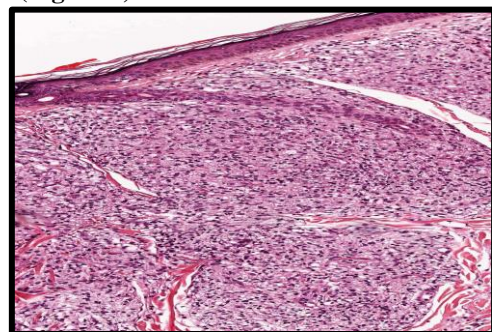
Typical tuberculous ulcer is an irregular lesion with ragged, undermined edges, minimal induration, and often with yellowish granular base. Typically, microscopical hallmark shows epithelioid cells with distinct slipper-shaped nuclei, multinucleated cells of the Langhans type and lymphocytic invasion encircling a characteristic caseating granuloma with a core of necrosis.<sup>6</sup>

**(2) Leprosy (Hansen's Disease)**

It is a chronic infectious condition that prefers air cooled sites and affects up to 60% of the oral cavity. However, the causative bacterium is *M. leprae* and demonstrates a variety of clinical characteristics because of complicated interplay between the invading pathogen and the host's immune system. Bacillary dissemination is mainly through airborne droplet and resulting in cutaneous lesion as erythematous coalesce form of papules which on progression appreciates as a matt-like appearance. (Figure 4) In terms of histopathology, it is identical to tuberculous but specialized lepra cells, which are vacuolated macrophages that are interspersed throughout the site and frequently contain the bacilli, are a variably exist with langhans type giant cells.<sup>7</sup> (Figure 5)



**Figure 4:** Lepromatous lesion of hard palate.



**Figure 5:** Microscopic view mycobacterium lepromatosis infection.

**(3) Non-tuberculous mycobacterial infections**

Oral granulomatous lesions can also be demonstrated by non-tuberculosis mycobacterial diseases. Usually associated with *M. kansasii*, *M. scrofulaceum*, *M. avium-intracellulare* etc and the victims are frequently infected children. However, presented as ocular ulceration followed by significant scrofula which is altogether unilateral involvement. The presumptive diagnosis will be provided by acid fast staining of the sample for bacilli.<sup>8</sup> (Figure 6)



**Figure 6:** Photograph showing lesions associated with nontuberculous mycobacterial infections.

#### **(4) Actinomycosis**

*Actinomyces israelii* is a common organism leads this form of unusual invasive bacterial, suppurative illness that primarily colonize in atmosphere containing at least 5% CO<sub>2</sub> & require organic nitrogen for growth. In majority of the cases they are incriminated in the oral cavity, gastro-intestinal and genital tracts that most of the time mimic the malignancy processes. **(Figure 7)** Therefore, the cornerstone of diagnosis is generally culture along with its characteristic microscopic features.<sup>9</sup>

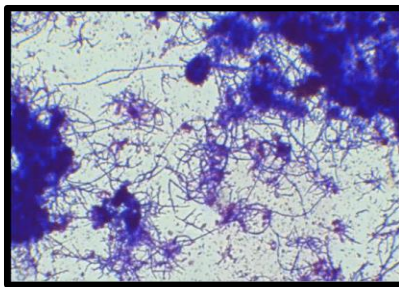
After invasion, the typical hallmark of this disease that is appreciated microscopically is yellow sulphur granules depicted as basophilic masses exhibiting eosinophilic terminal clubs when stained with H & E. **(Figure 8)** Also, the host calcium phosphate mineralizes the masses of filaments, which expand in spore-like ways and have a "sunburst radiation" or fiery image. At the end of these filaments are club shaped extensions or rossets established by the adherence of infiltrating neutrophils and a core of necrosis. **(Figure 9)** These inflammatory areas are frequently surrounded by the peripheral fibrous connective tissue capsule.<sup>10</sup>



**Figure 7:** Photograph showing bony sequestra bilaterally.



**Figure 8:** Microphotograph showing actinomycetes colonies.



**Figure 9:** Actinomycetes microorganism after gram staining.

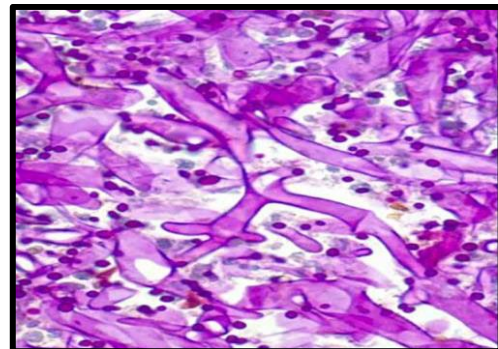
**(5) Mucormycosis**

Mucormycosis is a rare, frequently aggressive, devastating angio-invasive infection which is life-threatening condition that poses a serious risk of death and high morbidity and mortality typically affects people with immune system issues. It is often referred to as the 'Black fungus' because its produced decomposition of tissue result in eschar which gives the appearance of coloured black which is a misnomer till now.<sup>11</sup>(**Figure 10**)

Mucorales genera often produce typical ribbon-like hyphae with usually no or few septation characterized by non-pigmented, pale-staining, with branching at right-angle, unlike those of *Aspergillus* species or other hyaline moulds, which are generally 3-5 μm broad, septate, and create acute-angle branching.<sup>12,13</sup>(**Figure 11**)



**Figure 10:** Clinical photograph presenting eyelid swelling, axial proptosis with eyelid necrosis.



**Figure 11:** Microphotograph showing non-septate fungal hyphae with branching (Periodic acid Schiff stain)

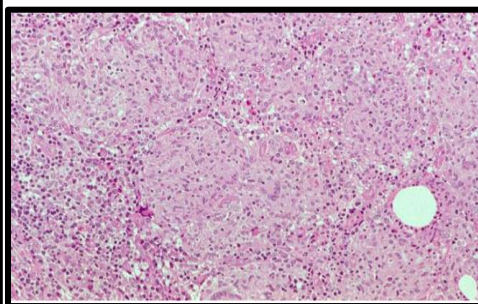
**(6) Syphilis**

It is highly contagious infection, usually associated with the bacteria well-known as *Treponema pallidum*.<sup>14</sup> The following groups of individuals that have an strengthen the risk include sex without a protective method (condom) or sex with multiple people and HIV. The symptoms of syphilis change as it progresses through distinct phases-<sup>15</sup>(**Figure 12**) (**Figure 13**) Clinical stages of syphilis present different feature- (**Table 2**)

<b>Clinical Stage of Syphilis</b>		
<b>Primary stage</b>	<b>Secondary stage</b>	<b>Tertiary stage</b>
I One or multiple painless chancres II Oral cavity is the most common extra genital site III Regional lymphadenopathy bilaterally IV Chancres last for 3-4 weeks to heal.	I Diffuse, painless, maculopapular Cutaneous rash II Oral cavity -commonly seen on tongue, lip, buccal mucosa and palate. III Lues Maligna – Prodromal symptoms of fever, headache, and myalgia, followed by formation of necrotic ulcerations.	I Less significant, but more characteristic, are scattered foci of Granulomatous inflammation II Active site of Granulomatous inflammation is known as GUMMA.



**Figure 12:** Clinical photograph of primary syphilis.



**Figure 13:** Microphotograph of enlarged node with multifocally replaced by granuloma. (10X magnification, H & E)

**CONCLUSION**

The prevalent of granulomatous infections remain unrecognized due to lack of their specific symptoms. The specific origin of the illness is still an unknown. As potential reasons, infectious agents, genetic components, and allergic or hypersensitive reactions have all been put forth.

Also, it is influenced by several pathogenic processes for which there is no familiar trigger. So, comprehensive clinical, microscopic and laboratory examination of these isolated granulomas is critically important for giving the appropriate management. Thereby minimizing the morbidity in the afflicted persons.

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