

Oral Manifestations of Tuberculosis: Step towards Early Diagnosis

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ABSTRACT

Tuberculosis, as known universally, is a chronic infectious disease that can affect any part of the body including mouth. It usually affects the lungs, TB bacilli can spread hematogenously to other parts of the body and this also includes mandible or maxilla. It can occur in the mouth involving the tongue with very unusual features and forms. So oral lesions, although rare, are very important for early diagnosis and interception of primary tuberculosis.

Keywords: Bacille Calmette Guerin (BCG), Secondary lesions, Inoculation

INTRODUCTION

Tuberculosis is a chronic granulomatous disease caused by various strains of mycobacteria, usually *Mycobacterium Tuberculosis* in humans [1]. Robert Koch, a German physician, discovered the Tuberculosis bacillus in 1882 [2]. It has been a worldwide major health problem for centuries. Although the disease's prevalence reduced decades ago, it still has extremely high prevalence in Asian countries. India accounts for nearly one third of global burden of tuberculosis. It may take any form clinically, but with decline in number, these tuberculosis lesions of oral cavity have become so rare that they are frequently overlooked in the differential diagnosis of oral lesions [3,4].

Although, oral manifestations of tuberculosis has a rare occurrence, but it has been considered to account for 0.1-5% of all TB infections. These lesions are usually secondarily inoculated with infected sputum or due to hematogenous spread.

Nowadays, oral manifestations of TB are re-appearing alongside many forgotten extrapulmonary infections as a consequence of the outbreak and emergence of drug-resistant TB and of the emergence of acquired immune-deficiency syndrome [5].

This review is an attempt to assess the need of the hour to early diagnose manifestations and symptoms of TB in the oral cavity as documented in the earlier archives published till date. It won't be an exaggeration if it is said that dental identification of the tuberculosis lesions have the potential of serving as an important aid in the first line of control for this dangerous, and often fatal, disease.

BACKGROUND

History of Tuberculosis goes back to some 15,000 to 20,000 years ago. It has been found in relics from ancient Egypt, China and India. Archeologists have detected spinal tuberculosis as Pott's disease in Egyptian mummies [6]. It was known as King's evil. In the 18th century, it reached its peak prevalence of, as much as, 900 deaths per 100,000 and was termed as white plague. It was considered as a stigma in the society and even compared to a 'devouring dragon' in some parts of Europe.

After Robert Koch demonstrated the causative organism in 1882, Edward Livingston Trudeau in 1884 started the concept of isolating these patients from the society, treating them with rest and nutrition [6]. In the year 1904, National Tuberculosis Association (American Lung Association) came into being [6].

Later, Bacillus Calmette Guerin was invented by Albert Calmette and Camille Guerin in Lille, France in 1908. But it was first used in humans in 1921.

Thus, it made a revolution and now this vaccine is counted in WHO's list of most essential medication for basic health system.

In spite of the fact that, the incidence of tuberculosis is towards a downfall in today's times, complete eradication of this disease seems difficult due to concomitant infections of HIV and developing extensively resistant strains causing Tuberculosis.

GLOBAL BURDEN OF THE DISEASE AND PREVALENCE

According the most recent report of WHO (2013), nearly 8.6 million people around the world became infected with TB disease. There were around 1.3 million TB-related deaths worldwide.

An estimated 1.1 million (13%) of the 8.6 million people who developed TB in 2012 were HIV-positive. About 75% of these cases were in the African Region.

HIV-1-associated TB is reaching epidemic proportions in many African countries. The prevalence and incidence of TB is similar in both HIV-positive and HIV-negative individuals, but the risk of active TB were elevated only for seropositive subjects. Increasing problems with TB may well continue because of the continuing emergence of MDR strains of M. TB, which is a major threat, particularly with HIV- and AIDS-infected patients, among whom, mortality rates are high.

Globally in 2012, an estimated 4.5 lacs people developed MDR-TB (Multi-drug resistant Tuberculosis) and there were estimated 1.7 lacs deaths from MDR-TB.

The majority of cases worldwide in 2012 were in the South-East Asia (29%), Africa (27%) and Western Pacific (19%) regions. India and China alone accounted for 26% and 12% of total cases, respectively [7].

Tuberculosis oral lesions have a relatively rare occurrence. The incidence has been reported as less than 0.5-1% amongst all the Tuberculosis patients, according to various studies.

Saliva is considered to have a significant role which explains the paucity of oral lesions, despite the large numbers of bacilli present in sputum contacting the oral mucosa in a typical case of pulmonary tuberculosis. Other attributing factors to relative resistance of oral cavity for TB are presence of saprophytes, resistance of striated muscles to bacterial invasion, and thickness of protective epithelial covering. It is believed that the organisms enter the mucosa through small breaches in the surface epithelium which makes it a favourite site for colonization of bacteria. Local factor that may facilitate the invasion of oral mucosa includes poor oral hygiene, leukoplakia, local trauma, and irritation by clove chewing, etc. Self-inoculation by the

patient usually results from infected sputum or by hematogenous or lymphatic dissemination [8-10].

Conditions that predispose to the disease include crowded urban living, drug abuse, poor health and hygiene, poverty. Viral infections like HIV with or without the development of AIDS, cause immunosuppression which has lately emerged as a very significant risk factor for development of TB [11].

ORAL MANIFESTATIONS OF TUBERCULOSIS

Oral TB lesions may be either primary or secondary in occurrence. Primary lesions are uncommon, seen in younger patients, and present as single painless ulcer with regional lymph node enlargement. The secondary lesions are common, often associated with pulmonary disease, usually present as single, indurated, irregular, painful ulcer covered by inflammatory exudates in patients of any age group but relatively more common in middle-aged and elderly patients [8,12].

Oral TB may occur at any location on the oral mucosa, but the tongue is most commonly affected. Other sites include the palate, lips, buccal mucosa, gingiva, palatine tonsil, and floor of the mouth. Salivary glands, tonsils, and uvula are also frequently involved. Primary oral TB can be present as painless ulcers of long duration and enlargement of the regional lymph nodes [13].

The oral lesions may be present in a variety of forms, such as ulcers, nodules, tuberculomas, and periapical granulomas [8,13,14].

The oral manifestations of TB can also be in the form of superficial ulcers, patches, indurated soft tissue lesions, or even lesions within the jaw that may be in the form of TB osteomyelitis or simple bony radiolucency [14,15]. Of all these oral lesions, the ulcerative form is the most common [15,16]. It is often painful, with no caseation of the dependant lymph nodes.

Oral lesions of TB are nonspecific in their clinical presentation and often are overlooked in differential diagnosis, especially when oral lesions are present before systemic symptoms become apparent.

Primary gingival involvement is more common in children and adolescents than adults. It usually presents as a single painless indolent ulcer, which progressively extends from the gingival margin to the depths of the adjacent vestibule and is often associated with enlarged cervical lymph nodes. They may be single or multiple, painful or painless and usually appear as irregular, well-circumscribed ulcer with surrounding erythema without induration and satellite lesions are commonly found [17].

When oral TB occurs as a primary lesion, an ulcer is the most common manifestation usually developing along the lateral margins of the tongue which rest against rough, sharp, or broken teeth or at the site of other irritants. Patients with oral tubercular lesions often have a history of preexisting trauma. Any area of chronic irritation or inflammation may favor localization of the *Mycobacterium* associated with the disease [18]. Deep tubercular ulcers of the tongue are typical in appearance with a thick mucous material at the base. These tongue lesions are characterized by severe unremitting and progressive pain that profoundly interferes with proper nutrition and rest. Classically, tubercular ulcers of the tongue may involve the tip, lateral margins, dorsum, the midline, and base of the tongue. They are irregular, pale, and indolent with inverted margins and granulations on the floor with sloughing tissue [19].

With the increasing number of TB cases, unusual forms of the disease in the oral cavity are more likely to occur and be misdiagnosed. Although rare, doctors and dentists should be aware of the oral lesions of TB and consider them in the differential diagnosis of suspicious oral ulcers. TB of the oral cavity frequently simulates cancerous lesions and others like traumatic ulcers, aphthous ulcers, actinomycosis, syphilitic ulcer, or Wegener's granuloma. The traumatic ulcer, which occurs in areas of chronic irritation from either sharp cusps or prosthesis, is acute in presentation and exquisitely

tender. Also, the source of irritation is usually evident on examination. The chronic indurated ulcer has to be carefully distinguished from a carcinoma, as with other TB lesions of head and neck, they can resemble each other and frequently coexist.

ROLE OF AN ORAL PATHOLOGIST

Clinicians find it difficult to differentiate oral TB from other conditions on the basis of clinical signs and symptoms alone. While evaluating a chronic, indurated ulcer, clinicians should consider differential diagnosis of infectious process such as primary syphilis, deep fungal diseases and noninfectious processes such as chronic traumatic ulcer and squamous cell carcinoma. If there is no systemic involvement, one should go for excisional biopsy for tissue diagnosis and bacteriological examination with culture for a definitive diagnosis. The efficiency of demonstration of acid fast bacilli in histological specimens is low, as there is relative scarcity of tubercle bacilli in oral biopsies.

According to various studies only a small percentage (7.8%) of histopathology specimens stain positive for acid fast bacilli. Therefore, a negative result does not rule out completely the possibility of TB. Another concern is the occurrence of mycobacterial infection as a part of AIDS. The low counts of lymphocytes and atypical non-caseating epithelioid granuloma seen in the histology of this case indicated an immunocompromised state. Histologically, an immunocompromised patient may not show granuloma or caseation. This poses a potential problem in diagnosing tuberculosis. Though the patient in the case presented here tested negative for rapid assay, HIV infection cannot be completely ruled out.

Further confirmatory investigation with western blot to rule out AIDS could not be performed due to lack of patient cooperation.

A radiological examination of chest and a Mantoux skin test are mandatory to rule out systemic TB.

A biopsy of an oral lesion is confirmatory but in majority of the cases, a single biopsy may not suffice because the granulomatous changes may not be evident in early lesions. The lesion is eventually disclosed by repeat biopsies. The differential diagnosis is made with the identification of a caseating granuloma with associated epithelioid cells and giant cells of the Langerhans type during histological evaluation of biopsied tissue. Deeper biopsies are always advocated for ulcers of the tongue; a superficial biopsy may not reveal the aetiology due to epithelial hyperplasia.

Fine-needle aspiration cytology is a highly specific and sensitive tool for identifying parotitis and/or TB in major salivary glands [20].

The history reported by the patient and the clinical and radiological examination play an important part in the diagnosis of TB. However, laboratory confirmation and thorough histopathological examination is most essential for the diagnosis, with culture of microorganisms taken as the absolute proof of the disease.

TREATMENT

The treatment of oral tuberculosis lesions is the same as the systemic tuberculosis. Currently, the most effective regimens require a combination of four drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) administered daily for the first two months, followed by an additional four months with only two drugs (isoniazid and rifampicin) [14]. The complexity of this regimen prompted the World Health Organization (WHO) to launch a new global strategy for TB control known as "directly observed therapy, short course" (DOTS) in 1997. The central component of this strategy is direct observation, by trained personnel, which both ensures patient compliance with the drug regimen and reduces the likelihood of drug resistance. However, this strategy also increases the cost of treatment and makes TB therapy more inconvenient.

Control of Tuberculosis is difficult because of two primary factors: persistence and resistance. In spite of the fact that, antibiotics are

available, *M. tuberculosis* is highly persistent, possibly because the bacterium induces chronic inflammation that sequesters it within the tissues, protecting it against drug exposure [21]. Thus, drug treatment must be extended to fully destroy the bacterium and prevent relapse.

Drug resistance is the result of genetic mutations that cause a heritable loss of drug susceptibility. Although resistance to a single drug does not render therapy ineffective, multidrug-resistant strains make TB much more costly and difficult to treat [21]. For this reason, the need for newer and more effective drugs that achieve multiple goals in improving TB control is imperative [22].

There are two types of resistance usually observed in the context of TB; MDR (multidrug resistant TB), XDR (Extensively drug resistant)

MDR-TB is defined as *Mycobacterium tuberculosis* (*M. tuberculosis*) resistant to the most potent first-line anti-TB medications, isoniazid and rifampicin, while XDR-TB has additional multidrug resistance to the most active second-line agents, injectable drugs (aminoglycosides and/or cyclic polypeptides-capreomycin, kanamycin and amikacin) and fluoroquinolones.

Clearly, the need of the hour is to expand the range of the treatment by either enhancing the application of existing agents or introducing new drugs.

Potential new agents should reduce treatment duration, have an acceptable tolerability profile, be active against MDR/XDR TB, be of use in HIV-infected patients with TB, and be active against latent TB.

Numerous novel drugs have been introduced in the market in recent times which promise to be a better alternative like Nitroimidazoles group (PA 824, OPC 67683), Diarylquinolines (TMC 207 or Bedaquiline or J compound) [23], Oxazolidinones (PNU-100480 and AZD5847), SQ109, Phenothiazines (Thioridazine), LL3858 for effective treatment of TB [24].

PRECAUTIONS FOR DENTAL HEALTH CARE PROFESSIONAL

Clinical Dental Practice has a potential for transmission of various infections from patient to Dentist, patient to patient as well as Dentist to patient due to close proximity to the nasal and oral cavities of the patient.

Thus, a barrier should be created to prevent the transmission of infections and to make the clinical procedures safe from the threat of cross infections.

A detailed history of TB should prompt the dental practitioner to discern whether the person is an active case under treatment, active case without treatment or previously infected but currently disease free. The non-treated active cases pose maximum risk to the dental healthcare personnel [25].

Dental healthcare professionals are at the constant risk of getting exposed to TB by the means of splatter, aerosols or infected blood. Dental treatment for those with active Tuberculosis should be limited to urgent and essential procedures.

As numerous serious diseases are air-borne, blood-borne or can spread through the contact of other body fluids, and it is impossible to know which certain patients are infected, so it is pertinent to avoid direct contact with blood, body fluids and mucous membranes. High standards of operatory disinfection and instrument sterilization should be maintained.

For known active tuberculosis patients, TB isolation rooms which are appropriately equipped room with effective air evacuation, negatively pressured relative to the corridors, with air either exhausted to the outside or HEPA-filtered if recirculation is necessary, with high volume suction are indicated for carrying out any procedure to minimize aerosol generation. Portable suction should be avoided as they recirculate air.

Rubber dams can be used to minimize aerosol contact however, if coughing occurs rubber dam should not be used.

Maintenance of proper hand hygiene, personal protective equipment (eye shields, face masks, headcaps, gloves and surgical gowns) and proper sterilization procedures should be followed. Standard surgical face masks do not protect against TB transmission; dental healthcare personnel should use particulate face masks. Masks should be changed at regular intervals, inter-appointments (between patients) and intra-appointments (during patient treatment) if it becomes wet.

Any contaminated item is a potential exposure source, so by taking care to limit contamination to the greatest extent possible, dental team members limit the risk of exposure to infectious materials and in turn, the potential for disease transmission.

Reusable facial protective equipment (protective eyewear or face shields) should be cleaned and disinfected between patients. Handpieces and other oral instruments should be cleaned and autoclaved regularly.

Gloves should be worn while exposing and handling radiographs, handling and transporting biopsy specimens, prosthesis.

The goal of the dental infection-control program is to provide a safe working environment that reduces the risk of both healthcare-associated infections among patients and occupational exposures among dental team members [26].

DISCUSSION

A large number of dentists and consultants in otolaryngology in India have limited experience with the tuberculosis of the upper aero digestive tract since its oral lesions are non-specific in its clinical presentation and are often ignored in the differential diagnosis. This is very common in cases where oral lesions are present before the systemic symptoms become apparent [27].

Oral tubercular lesions can be either, primary or, secondary to pulmonary tuberculosis, with secondary lesions being more common. Most common sites for these lesions are tongue, gingiva, floor of the mouth, buccal mucosa. Dorsum of the tongue is most favourable site with these lesions appearing as a stellate ulcer. It can also present on the tongue as macroglossia, around upper aero digestive tract as parotitis, intra-osseous lesions, preauricular swelling and trismus, tracheitis and laryngitis [28].

The diagnosis of these lesions usually becomes difficult as other lesions like aphthous ulcer, traumatic ulcer, syphilitic ulcer or squamous cell carcinoma are expected in the first thought, in our differential diagnosis before inclusion of tuberculosis, leading to misdiagnosis [28]. Even on histological examination, we see a granulomatous lesion we ought to consider other entities like sarcoid, Crohn's disease, cat scratch disease, foreign body reaction, tertiary syphilis, and Melkersson Rosenthal syndrome.

Regardless of the fact that, laboratory investigations have the prime role which provide the certain evidence and confirms the disease.

Confirmatory diagnosis of tuberculosis is the presence of Acid Fast bacilli in the specimen or can also be confirmed by culture of tuberculosis bacilli [29]. Sputum culture and radiographic evidence are other supportive modes of confirmatory diagnosis.

A protocol of taking multiple deeper biopsies can also eventually make the job easier. Mandatory steps should be followed to rule out systemic TB like a chest x-ray and a Mantoux skin test.

Administration of standard antitubercular therapy, with antibiotics such as isoniazide, rifampicin, pyrazinamide, and ethambutol for six months, is essential for the complete eradication of tubercular lesions.

CONCLUSION

We conclude by stating that incidence of oral lesions in tuberculosis cases is very less, so each and every persistent and atypical oral lesion must be examined carefully to intercept and prevent the disease early. Intercepting the disease early will increase the morbidity and mortality of the patients.

So it becomes the duty of the dentist to include tuberculosis in differential diagnosis of suspicious oral lesions to avoid the needless delay in the treatment of this disease.

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