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Clinical Manifestation of Oral Tuberculosis in HIV Patient: A Review Article

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ABSTRACT

Introduction: Tuberculosis (TB) is a disease that has become a global problem. the incidence of TB cases decreased by 9% from 2015 to 2019. In general, TB disease is divided into 2, namely latent TB and active TB. Latent TB indicates the presence of Mycobacterium Tuberculosis bacteria but is in an inactive/inactive phase, but in this type of TB there is a 10% chance that these bacteria will be active. Meanwhile, active TB shows active bacterial activity so that it can infect other hosts.

Objective: This literature study is to determine the clinical manifestations of tuberculosis in the oral cavity in HIV patients.

Discussion: Mycobacterium tuberculosis is slowly replicating intracellular pathogen in macrophages that elicits a T cell immune response mediated by antigen-specific CD4+ and CD8+ T cells. This immune response may eliminate the Mycobacterium tuberculosis, but more frequently Mycobacterium tuberculosis persists in a latent form, constituting a reservoir of inactive Mycobacterium tuberculosis that under certain circumstances may become active. TB may occur at any stage of HIV disease and, as in the case presented here, may be the first indicator of HIV infection. HIV-seropositive subjects and particularly those HIV-seropositive subjects with low CD4+ T cell counts more frequently have extrapulmonary TB than do HIV-seropositive subjects or HIV-seropositive subjects with high CD4+ T cell counts.

Conclusion: Patients who suffer from HIV may be associated with the tuberculosis infection. The TB infection may be known from the oral manifestation in HIV patients.

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Introduction

Tuberculosis (TB) is a disease that has become a global problem. This disease has a higher mortality rate when compared to HIV. Tuberculosis is a disease caused by the bacterium Mycobacterium tuberculosis. This bacterium has the ability to develop gene mutations so that it can be resistant to several antibiotics [1]. Tuberculosis has been detected in various countries in the world, the World Health Organization (WHO) states that, in the world, TB cases reached around 10 million people in 2019. According to the most recent report of WHO (2013), there were around 1.3 million TB-related deaths in worldwide. An estimated 1.1 million (13%) of the 8.6 million people who developed TB in 2012 were HIV-positive. 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 was elevated only for seropositive subjects. Increasing problems with TB may well continue because of the continuing emergence of MDR strains of mycobacterium tuberculosis, which is a major threat, particularly with HIV- and AIDS-infected patients, among whom, mortality rates are high. Meanwhile in Indonesia, the number of new TB cases reached 420,994 cases in 2017 [2]. Men are 3 times more likely to experience TB than women, this is not only happening in Indonesia but also in other countries. Men tend to be more at risk because they have a smoking habit and are more likely to be non-adherent in taking medication. WHO also stated that the incidence of TB cases decreased by 9% from 2015 to 2019 [3].

Tuberculosis infection is a chronic infectious disease that can spread through droplets and aerosol droplets, besides that this

disease can also be spread through unsterile equipment that is used or has been contaminated by people who have been infected with TB. The risk of infection is more common in people with low economic levels. This disease initially infects the lungs. However, this disease can manifest in other parts of the body such as the intestines, meninges, bones, joints, lymph nodes, skin, mouth and other body tissues. The oral cavity is one of the regions that can be affected by TB infection. Several studies mention the presence of manifestations in the oral cavity due to TB infection, but until now these manifestations are still rarely found [4].

Some individuals infected with TB can have oral manifestations. However, these clinical symptoms are not always found. This is because the infection that occurs depends on systemic factors such as a poor immune system or a high level of virulence of the microorganism. In addition, there are other factors that also affect clinical symptoms in the oral cavity in individuals infected with TB, namely the presence or absence of local trauma in the oral cavity, pre-existing dental and oral diseases and oral hygiene [5].

Oral TB lesions may be either primary or secondary in occurrence. Primary lesions are often seen in younger patients, and presents as single ulcer with the enlargement of regional lymph node. The secondary lesions of oral TB lesions are descripted as single, indurated, irregular. Oral TB may occur at any region on the oral mucosa. Tongue is most commonly affected in oral mucosa. 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. The oral lesions may be present in a variety of forms, such as ulcers, nodules, tuberculomas, and periapical granulomas. Establishing a diagnosis based on clinical symptoms in the oral cavity in individuals infected with TB can be used as a marker of the presence of the infection. Individuals who have been infected with HIV and other immunocompromized conditions are at risk for infection with TB. Therefore, clinical examination of oral manifestations can be used to identify the presence of tuberculosis infection in HIV patients [6].

Tuberculosis Pathogenesis

Tuberculosis is an infectious disease caused by the bacterium *Mycobacterium tuberculosis* which can spread through the air. This disease can infect the entire body, but is most commonly found in the lungs. *Mycobacterium tuberculosis* that is in *droplets* from people infected with TB then coughs, sneezes and talks or sings then is carried by the air [7,8].

Transmission occurs through inhalation of droplet nuclei that pass through the mouth or nasal cavity, upper respiratory tract, bronchi and finally reach the pulmonary alveoli. After Mycobacterium Tuberculosis or tubercle bacilli reach the alveoli, then they are digested by alveolar macrophages resulting in damage or inhibition of most of the tubercle bacilli that are inhaled. A small proportion of these residues then multiply within the macrophages and are released when the macrophages die. The live released tubercle bacilli spread through the bloodstream or lymphatics to all parts of the body's tissues or organs other than areas highly susceptible to TB infection such as the lungs, larynx, lymph nodes, spine, bones or kidneys. In about 2 to 8 weeks, an immune response is triggered that allows the white blood cells to destroy most of the tubercle bacilli. Encapsulation by white blood cells produces a barrier around the tubercle bacilli which then forms a granuloma [6].

When in the *barrier* area, the tubercle bacilli are said to be under control and thus form a state of latent tuberculosis infection (LTBI). People at this stage do not show symptoms of TB, cannot spread the infection and so are not considered TB cases. On the other hand, if the immune system fails to control the tubercle bacilli, a rapid multiplication of the bacilli can occur and lead to the progression from LTBI to TB cases. Time to progress to TB may be immediately after LTBI or be longer after many years. TB cases are highly contagious and can spread to other people [8].

Diagnosis

Pulmonary TB was defined as pulmonary parenchymal tuberculosis. Primary pulmonary TB is different from post-primary pulmonary TB, which is the most common manifestation of TB in adults. The most common clinical symptoms of pulmonary TB include chronic cough, phlegm production, decreased appetite, weight loss, fever, night sweats and hemoptosis. A person with clinical symptoms like these should be suspected of having TB. If the individual is known to have been in contact with infectious TB, then they may have TB. In countries with a high prevalence of TB, primary pulmonary disease usually occurs in childhood, but where TB is less endemic, it is quite common in adults as well. It is characterized by localized granulomatous inflammation, usually in the region of the periphery of the lung (Ghon focus), and may be accompanied by involvement of ipsilateral lymph nodes, called the Ghon complex. The infection is usually asymptomatic but may present as an acute lower respiratory tract infection. The most important clue to the diagnosis is a history of close contact with an infectious TB patient. The diagnosis is suspected when a tuberculin skin test or blood test with an Interferon-G Release Assay (IGRA) turns positive, usually 3-8 weeks after infection. *Chest* radiography may show a Ghon focus/complex [9,10].

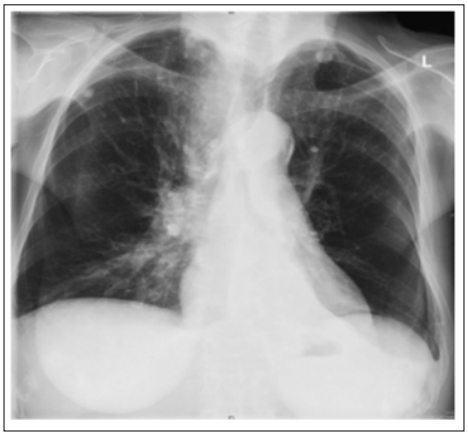

Figure 1: Gambaran radiografi toraks yang menunjukkan kompleks Ghon [9].

Postprimary pulmonary TB is a common manifestation of TB in adults around 60%-80%). This can occur years after exposure to an individual with infectious TB and can be triggered by a malfunction in the individual's immune system. Men are affected more often than women. The most common symptoms of active disease are fever, anorexia or decreased appetite, weight loss, night sweats, anemia, and a persistent cough (that is, lasting for 14 days) usually producing purulent sputum and/or blood. Occasionally, patients complain of localized thoracic pain associated with pleural inflammation. Hoarseness may occur if there is involvement of the larynx. Patients with laryngeal and tracheobronchial TB may have Mycobacterium tuberculosis in the sputum even though the chest X-ray is normal. Although, in general, radiographs will show a possible diagnosis. Following anti-TB treatment the lesions resolved [8,9].

Oral Manifestations of Tuberculosis Infection

Oral TB lesions can be primary or secondary. The primary lesion is rare, is seen in younger patients, and presents as a single, painless ulcer with regional lymph node enlargement. Secondary lesions are common, often associated with pulmonary disease, usually presenting as a single, indurated, irregular, painful ulcer covered with an inflammatory exudate [11,12].

Oral TB can occur at any location on the oral mucosa, but is most commonly affected by the tongue. Other regions include the palate, lips, buccal mucosa, gingiva, palatine tonsils, and floor of the mouth. The salivary glands and uvula are also frequently affected. Primary oral TB may present as a painless ulcer of long duration and regional lymph node enlargement. Oral lesions can appear in various forms, such as ulcers, nodules, tuberculomas, and periapical granulomas. Oral manifestations of TB can also be in the form of superficial ulcers, patches, swollen soft tissue lesions, or even lesions within the jaws which may be in the form of tuberculous osteomyelitis or simple radiolucency of bone. Of all these oral lesions, the ulcerative form is the most common. When TB of the oral cavity occurs as a primary lesion, ulcer is the most common manifestation which usually develops along the lateral edge of the tongue adjacent to a rough, sharp, or broken tooth or others irritant site. Patients with oral tubercular lesions often have a history of preexisting trauma. Any area of chronic irritation or inflammation may favor the localization of Mycobacterium Tuberculosis. This tongue lesion is characterized by severe pain that does not go away and is progressive which greatly interferes with the patient's nutrition and quality of rest. In general, tubercular ulcers of the tongue can be found on the ventral, lateral margin, dorsum, midline, and base of the tongue. The lesions found tend to be irregular in shape. Oral TB often resembles cancerous and other lesions such as traumatic ulcers, aphthous ulcers, actinomycosis, syphilitic ulcers, or Wegener's granulomas [4,11,12,5].

Figure 2: Ulcers in the oral cavity in primary TB patients [13].

Discussion

Tuberculosis is spread from person to person through the air via droplet nuclei, particles 1 to 5 mm in diameter that contain the M. tuberculosis complex. Droplet nuclei are produced when a person with TB of the lungs or larynx coughs, sneezes, talks, or eats. They can also be produced by aerosol treatment such as dental treatment, sputum induction, aerosolization during bronchoscopy, and by manipulation of lesions or processing of tissue or secretions in a hospital or laboratory. The droplet nuclei are small enough to reach the alveoli within the lungs, where the organism replicates. Although patients with tuberculosis also produce larger particles containing many bacilli, these particles do not serve as effective vehicles for transmission of infection because they do not remain in the air, and if inhaled, do not reach the alveoli. Organisms deposited on intact mucosa or skin do not invade tissues. When large particles are inhaled, they impact the walls of the upper airways, where they are trapped in a blanket of mucus, carried to the oropharynx, and swallowed or expel [11,13].

Mycobacterium tuberculosis is slowly replicating intracellular pathogen in macrophages that elicits a T cell immune response mediated by antigen-specific CD4+ and CD8+ T cells. This immune response may eliminate the Mycobacterium tuberculosis, but more frequently Mycobacterium tuberculosis persists in a latent form, constituting a reservoir of inactive Mycobacterium tuberculosis that under certain circumstances may become active. Only 5%–10% of subjects with latent Mycobacterium tuberculosis infection will develop active TB, but in the remainder the infection will remain inactive and the infected subjects will remain asymptomatic for life. Subjects with immunosuppressing conditions and children with immature immunity are at higher risk of developing active TB than immunocompetent subjects. Infection with HIV is the greatest single risk factor either for the progression of latent infection to active TB or for acquisition of new Mycobacterium tuberculosis infection [11,14].

TB may occur at any stage of HIV disease and, as in the case presented here, may be the first indicator of HIV infection. TB may also sometimes present as an immune reconstitution inflammatory syndrome shortly after HAART has brought about a decrease in the HIV load with consequential significant elevation of the CD4+ T cell count. HIV-seropositive subjects and particularly those HIV-seropositive subjects with low CD4+ T cell counts more frequently have extrapulmonary TB than do HIV-seropositive subjects or HIV-seropositive subjects with high CD4+ T cell counts. Primary extrapulmonary TB is much less common than secondary extrapulmonary TB, and primary oral TB as the sole manifestation of TB in an HIV-seropositive subject, as in our patient, is rare. The diagnosis of TB in HIV-seropositive subjects is not always straightforward as the clinical signs and symptoms. The diagnosis of primary oral TB in patient was made by biopsy since the clinical features of the oral lesions were nonspecific. On microscopical examination, typical tuberculous granulomas were not evident. The presence of epithelioid cells prompted the Ziehl-Neelsen stain which revealed the acid-fast bacilli. Failure to express well-defined granulomas with giant cells is the result of immune suppression due to HIV coinfection. But it is important to note that HIV-Mycobacterium tuberculosis co-infected subjects are frequently negative to tuberculin skin testing, acid fast bacilli are very scant in their sputum although sputum culture invariably confirms pulmonary TB, and pulmonary TB granulomas are not always present [14].

Conclusion

Patients who suffer from HIV may be associated with the tuberculosis infection. The TB infection may be known from the oral manifestation in HIV patients. Some patients with HIV can be found a single ulcer which can be associated with oral tuberculosis.

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