

## **Dermatological Manifestations Due to Mycobacterium Tuberculosis Infection**

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### **ABSTRACT**

Cutaneous tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis*, especially in its human and bovine varieties, either directly or through its antigenic components, and the clinical pictures it gives rise to depend not only on its pathogenicity, but also on the host's immune response. It is generally accepted that the skin integument is an organ that is not very receptive to Koch's bacillus and that even the latter suffers, when invading it, its virulence is attenuated: the manifestations are less frequent than those observed in other sites, more chronic and with fewer bacilli since the skin is not an ideal environment for this, however, it is not free from presenting affectations that could put the integrity of patients at risk.

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### **INTRODUCTION**

Tuberculosis (TB) is an infectious disease caused by mycobacteria of the *Mycobacterium tuberculosis* complex, mostly *M. tuberculosis* (95% of cases). Other species involved are *M. africanum*, *M. microti*, *M. bovis* and, exceptionally, the derivative of the latter: bacillus Calmette - Guérin or BCG.<sup>1,2</sup>

The main route of transmission is through infectious particles eliminated by the patient when coughing, sneezing or speaking and when they are inhaled by the people around them they reach the lungs, where the main affectation occurs (pulmonary TB) and from there they spread through the lymphohematic route. affecting the lymphatic system, bones, digestive, genitourinary, skin and any other organ of the economy (extra-pulmonary forms). Other routes of transmission are digestive and less frequently by inoculation. Factors such as overcrowding, poor socioeconomic conditions, HIV and other states of immunosuppression predispose to infection.<sup>2,3</sup>

TB is an ancient disease that continues to be a major public health problem in non-developed countries, but even in developed countries after AIDS it has re-emerged with force. The World Health Organization (WHO) estimates that in 2016 there were close to 10,000,000 new cases, 95% in developing countries, being the ninth cause of death.<sup>3</sup>

Cutaneous tuberculosis (TC) is an infrequent chronic infectious disease, representing between 1.5 and 4% of the cases of extrapulmonary tuberculosis, being produced by *Mycobacterium* spp. of the *Mycobacterium tuberculosis* complex.<sup>(4)</sup>

In recent decades, an increase in the number of CT cases has been observed, similar to other forms of tuberculosis, which responds to the growing infection of the Human Immunodeficiency Virus, the appearance of multi-resistant strains of *M. tuberculosis*, and/ or to increasing pharmacological immunosuppression.<sup>(4)</sup>

### **CLINICAL PRESENTATION**

Scrofuloderma is one of the most common forms in all series. It consists of a subcutaneous infection, by direct extension to the skin due to contiguity from an adjacent focus, lymph nodes in most cases, but also bones, joints and even the epididymis; forming nodules that fistulate and form ulcers. When healing they leave hypertrophic cord scars. Other pathologies that may have this appearance are deep mycoses such as paracoccidioidomycosis, actinomycosis, tertiary syphilis with gummy lesions, and even hidradenitis and acne conglobata, which must be excluded with specific studies. Most cases are located in the neck, armpits, and inguinal region, over compromised lymph nodes. In all cases, AFB

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will be observed in the skin by smear or pathological anatomy and in severe cases lung involvement could be found. (4,5)

The gummy form or metastatic abscesses is a form reported as rare. There are series of case reviews that report that of 26 cases only 2 presented this form, however in this series it is presented as being related to hematogenous dissemination from a non-cutaneous primary focus, in a period of profound immunosuppression due to malnutrition, diseases such as AIDS or immunosuppressive drugs.(5,6)

Wart syndrome is a clinical aspect shared by several pathologies, such as chromomycosis, sporotrichosis, leishmaniasis and tuberculosis, mainly. Laboratory tests generally define the diagnosis, mycological being fundamental in the first 2. In leishmaniasis, as time passes, it is usually difficult to visualize the agent, PCR being important, the same as in TB because this form is difficult to visualize in smears and growth in cultures.(6,7)

Verrucous TB represents approximately 8% of extrapulmonary TB and is generally a form of reinfection or exogenous inoculation in a patient with high immunity to the bacillus. However, in 10% of cases there may be tuberculosis in other organs, the pulmonary manifestation being very frequent. (8)

### DIAGNOSIS

Inoculation of tuberculosis from an exogenous source is known as tubercular chancre, the result of the entry of the mycobacterium into the skin or mucosa, through skin lesions of a person who has not been previously infected or who does not have immunity to it. Mycobacterium tuberculosis. It is reported as a sporotrichoid lesion. Verrucous tuberculosis is part of this group.(9)

It is distinguished by localized and asymmetric lesions; begins as a painful warty nodule at the site of the lesion, with a purple inflammatory halo, which grows to form a hyperkeratotic, violaceous, erythematous or grayish plaque, the lesion grows slowly and eccentrically to form a plaque of variable size, sometimes annular in shape, which becomes lighter in the center; It frequently drains purulent material with a fetid odor, with a predominance of crusts and exudation, over an inflamed base. There are usually one to three plaques, always close to the main lesion.(10)

In the histology, hyperkeratotic epidermis and pseudoepitheliomatous hyperplasia are observed, in the middle dermis tuberculous granulomas with multinucleated Langhans-type giant cells, epithelioid cells and lymphocytes are observed, as well as areas of caseous necrosis.(10,11)

Rapid diagnostic molecular techniques are applied to clinical samples based on the amplification of *M. tuberculosis* DNA fragments using a polymerase chain reaction (PCR) that can increase diagnostic sensitivity up to 90%.

Other techniques for diagnosing active or latent infection include those known as IGRA (Interferon-Gamma Release Assay) tests, which measure the degree of reaction of a person's immune system to TB bacteria. The most widely used in clinical practice are the ELISpot technique, an acronym for enzymelinked immunospot assay, (T-SPOT®.TB) and the QFT-GIT, a cell-mediated immune response quantification method that consists of detecting in vitro the release of gamma interferon secreted by T leukocytes of the sensitized patient in the presence of specific antigens of *M. tuberculosis*.(12,13)

The diagnosis of TB with dermatological involvement is based on the absolute criteria (microbiological culture) and relative criteria (clinical history, physical examination, tuberculin reaction, active tuberculosis in other organs, bacteriology, histology of the samples obtained and response to treatment) by Robert J. Wilkinson.(14)

The characteristic histopathology of CT is the finding of tuberculoid granuloma, consisting of a collection of central epithelioid cells with Langhans giant cells, surrounded by a border of lymphocytes-monocytes. (13,14)

As the inflammation progresses, the center undergoes caseous necrosis, this lesion being characteristic and distinctive of tuberculosis, although it can also be found in infections such as deep mycosis, syphilis and leprosy. It should be noted that histopathological findings vary according to the patient's immunological status. The greater the host's immune compromise, there will be less formation of tuberculoid granulomas, with greater necrosis and bacilli in the tissue.(14,15)

The definitive diagnosis requires the isolation of the microorganism by culture or PCR sequencing, because the histological findings can be nonspecific, but suggestive, but there is a high frequency of negative cultures, so the diagnosis is established based on the clinical-pathological correlation and response to antifungal treatment.(12,14)

It is important to rule out underlying tuberculosis in patients with this disease because it has been reported in 10% of cases, so it is convenient to study the patient completely.(15)

### TREATMENT

Despite the high probability of skin disorders, the lesions are generally temporary, with a good prognosis and little impact on work activity. However, and less frequently, there are variables related to cutaneous TB, other personal history or side effects of treatments that may have repercussions on the general condition of the worker.(16)

The risk increases significantly in people who are immunosuppressed due to diseases (HIV, transplantation, neoplasia, chemotherapy treatment, chronic renal failure, hemodialysis, silicosis, etc.) or due to immunosuppressive treatments.(17)

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Management of cutaneous TB is done following the same guidelines for TB of other organs, adjusting time and dose, monitoring the appearance of adverse effects. Most of the cases described in the current literature suggest treatment with isoniazid (5 mg/kg/d), rifampicin (10 mg/kg/d), pyrazinamide (25 mg/kg/d), ethambutol (20 mg/kg /d) and always accompanied by vitamin B6 and durations of schemes between 6 and 9 months are suggested depending on the severity of the condition and monitoring of adverse effects to treatment.

### CONCLUSIONS

In recent years there has been an increase in cutaneous TB predisposed by immunosuppression in HIV-positive patients and diagnostic difficulty due to the different forms of the disease and similarity with other etiologies. The manifestations at the cutaneous level can be transmitted via the blood or lymphatics from a primary focus, although in certain cases it can be introduced directly through trauma at the cutaneous or mucosal level.

The clinical history of the patient focused on the epidemiological study as well as drug susceptibility is extremely important, since in most cases of cutaneous TB there is a high bacterial load and drug resistance in HIV-positive patients. For the first contact doctor, it is extremely important to identify the injuries and be able to provide timely treatment or even refer them to the relevant specialist doctor.

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