A Case of Generalized, Superinfected Dermatitis and Inguinal Mycobacterium Lymphadenitis – TB or not TB?

Dear Editor,

Eczema is an inflammatory dermatitis mediated by cellular immunity, with an etiology in which environmental, immunological, and genetic factors are involved. Skin inflammation through proinflammatory cytokines creates a favorable environment for microbial antigens and optimal conditions for infection (1). In case of underlying immunosuppression, inflammatory features of dermatitis and superimposed infections are more severe. The presence of minor trauma of the skin in the form of fissures can favor both easier inoculation of some bacterial germs, leading to a dermatitis superinfection, and/or the transcutaneous inoculation of atypical mycobacteria, with a possibility of developing localized types of tuberculous lymphadenitis (TLA). TLA, the localized type of systemic tuberculosis (TB) infection, is the most common form of extra-pulmonary TB in developing countries (2), while lymphadenitis due to atypical mycobacteria is a localized disease, more frequently seen in developed countries (3,4). In tuberculosis, the transmission of *Mycobacterium tuberculosis* is airborne, while in atypical mycobacterium lymphadenitis transmission can be both airborne or by ingestion or inoculation (5). In both forms of TB, lymphadenopathy evolves towards abscess and presents fibrotic scars or calcifications upon healing (6). A positive diagnosis involves a clinical and epidemiological investigation, a purified protein derivative (PPD) skin test, ultrasound, and CT / MRI of lymph node masses. A lymph node biopsy is used to confirm the diagnosis of TB and PCR, while positive culture confirms the etiology of TB lymphadenitis. The differential diagnosis of TLA is difficult: neoplastic, bacterial, or viral and fungal infections, sarcoidosis, Castleman's disease, drug reactions, etc. (5). TB-induced immunosuppression may favor the development of fungal and bacterial infections, sometimes severe and poorly responsive to treatment. On the other hand, immunosuppressive conditions increase the risk of extra-pulmonary TB (2).

A 40-year old woman who had experienced recurrent episodes of dermatitis over the previous 7 years was hospitalized with fever, malaise, and a disseminated erythematous and crusted, exudative, and flexural itching rash (Figure 1). There were fetid, purulent secretions at the conjunctival, auricular, genital, and umbilical areas. The clinical exam also revealed lymphadenopathy syndrome (large, painful submandibular, cervical, and axillar bilateral lymph nodes; an indurated, painful, and adherent left inguinal lymph node of 5-6 cm).

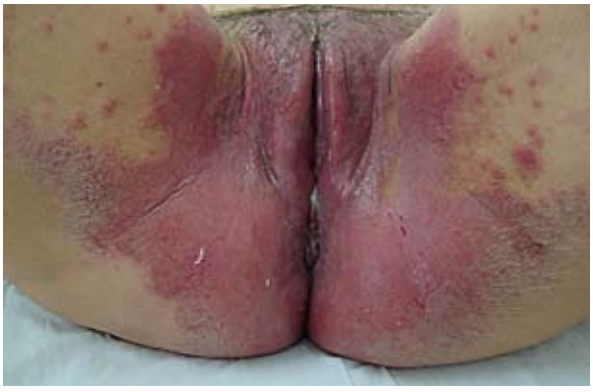

Figure 1. Clinical manifestations of the skin lesions on the groin and perineum at first referral.

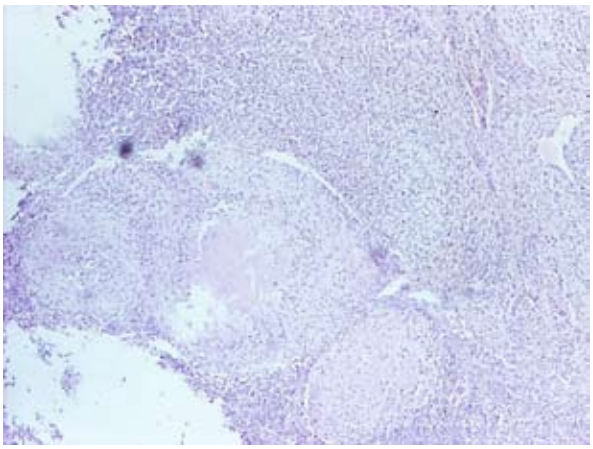

Figure 2. Histopathological features of tuberculous lymphadenitis (hematoxylin and eosin ×100).

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Microbial cultures isolated multiple multi-drug-resistant bacteria (SAH-MRSA, *Acinetobacter baumannii*, *Enterococcus faecalis*, *E. coli*, *Enterobacter*) and *Candida albicans* in the oral cavity and conjunctival, auricular, nasal, umbilical, and genital areas. The skin biopsy confirmed the diagnosis of dermatitis. PPD skin test was 21 mm. Other tests (HIV and syphilis serology, blood culture, chest X-ray) were negative.

Systemic treatment with vancomycin, metronidazole, fluconazole, local antiseptic compresses, and topical corticosteroid ointments was initiated. 2 days after starting the treatment with vancomycin, Redman syndrome occurred (headache, dyspnea, colicky pains, myalgia, rush, fever (39 °C), hypotension (80/40 mmHg), and tachycardia (100 bpm)). This syndrome resolved upon discontinuation of Vancomycin. Further treatment with imipenem/cilastatinand linezolid for 14 days lead to a favorable response with amelioration of the symptoms.

Biopsy of the submandibular lymph node raised the suspicion of Castleman's disease; however, due to the overall incomplete clinical picture (no night sweats, no weight reduction, lack of hepatosplenomegaly and peripheral neuropathy), we decided to perform a biopsy of an inguinal lymph node. The histopathological aspect suggested TLA (lymphoid hyperplasia predominantly diffuse, reactive, presenting tuberculous follicles with central caseous necrosis) (Figure 2).

A combination of specific antituberculous drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) for 6 months resolved the lymphadenopathy syndrome with no further recurrence of eczema and skin infections.

Certain delayed hypersensitivity mechanisms are involved both in dermatitis and in TB. CD4 lymphocytes are the primary mediators of anti-TB immunity, while proinflammatory cytokines mediate the activation of macrophages involved in controlling bacillary growth (1). In cases of superinfected dermatitis, microbial exotoxins penetrate the skin barrier more easily due to inflammation. Released cytokines (IL-1, TNF, and IL12) favor the expression of E-selectin on endothelial vascular growth factor and on skin lymphocyte antigen expression, with amplification of initial skin inflammation and creating favorable conditions for microbial colonization and infection (7). The common denominator in dermatitis and TB are the circulating immune complexes (up to 56% of TB cases), which are formed by the interaction between an antibody and bacterial antigen (8), which was in this case evidenced by increased levels of IgA and IgG.

In our case, the frequent recurrences of infected dermatitis with multiple multi-drug-resistant germs that were poorly responsive to treatment and displayed a severe evolution towards generalization as well as the lymphadenopathy and the persistence of a biological inflammatory syndrome indicated that another immunosuppressive cause could be involved. Isolated bacterial and fungal germs changed the immune status of the patient. The risk of mycobacterium infection was increased by the environment they created and the patient's underlying skin inflammation. The diagnosis of TB lymphadenitis was established by the histopathologist, but in the absence of PCR we could not determine whether the TB infection was caused by *Mycobacterium tuberculosis* or by atypical mycobacteria. Given that there was no evidence of other sites of TB infection, we conjectured that inoculation of mycobacterium took place at the skin lesion and that an atypical mycobacterium might have contributed to the etiology of the TLA. In our case, the anti-tuberculous drugs and skin infection treatment with follow-up of the side-effects led to complete remission of mycobacterium lymphadenitis, dermatitis, and infectious processes, without relapses.

In conclusion, in the present case chronic dermatitis alongside infection with multi-drug-resistant germs led to an immunosuppressive status which, when associated with the presence of multiple skin ports of entry, allowed a mycobacterial infection at the inguinal lymph node level. Inguinal TLA induced severe dermatitis and difficulties in diagnosis and treatment.

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