

# Metastatic tuberculous abscess caused by *Mycobacterium bovis* presenting as subcutaneous nodules in a woman with rheumatoid arthritis

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## ABSTRACT

A metastatic tuberculous abscess is a rare condition that should be considered in the differential diagnoses of subcutaneous nodules in immunosuppressed patients. A 71-year-old woman with rheumatoid arthritis developed disseminated tuberculosis due to *Mycobacterium bovis*. After taking a vertebral biopsy, subcutaneous nodules appeared on the extremities. Initial histopathological and microbiological studies performed on the skin biopsy did not identify the mycobacterium. An aspirate obtained from a cold abscess was cultured and studied with a positive polymerase chain reaction; cultures grew *M. bovis* and treatment for disseminated tuberculosis was initiated. Two months later, the fevers recurred, and new skin nodules appeared. A repeated skin biopsy failed to identify the agent, yet it again grew from the material obtained from an aspirated abscess. Diagnostic tests should be exhausted in order to identify the organism successfully. This case suggested that recurrent hematogenous dissemination may originate after the manipulation of deep foci and present as a metastatic tuberculous abscess.

**Key words:** *Mycobacterium bovis*; Cutaneous tuberculosis; Vertebral tuberculosis; Metastatic tuberculous abscess; Immunosuppression

## INTRODUCTION

Tuberculosis is an infection caused by a mycobacterium from the *Mycobacterium tuberculosis* complex; the most frequently identified agent is *M. tuberculosis*. Cutaneous tuberculosis is a rare manifestation, representing 1% to 1.5% of cases of extrapulmonary tuberculosis. Its etiological agents include *M. tuberculosis*, *M. bovis*, and the attenuated form of the Calmette–Guérin bacillus (BCG vaccine) [1].

Infection by *M. bovis* may be acquired through the inhalation or ingestion of contaminated products, especially unpasteurized dairy products. Hematogenous transmission may present with cervical

lymphadenopathy, intestinal involvement, and skin manifestations [1]. A previous series from a Mexican referral center reported that up to 26.2% of cases of tuberculosis were due to *M. bovis*; 5.2% of the patients had bone, joint, skin, and soft tissue involvement [2].

## CASE REPORT

A 71-year-old woman was admitted for a diagnostic workup due to a fever, weight loss, and lumbar pain. She had a history of rheumatoid arthritis treated with methotrexate (15 mg weekly) and prednisone (5 mg daily). An interferon-gamma release assay (IGRA) was negative, and no pulmonary infiltrates were identified. A PET CT scan revealed a hypermetabolic

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lytic lumbar vertebral lesion, from which a bone biopsy was obtained. A polymerase chain reaction (PCR, GeneXpert MTB/RIF) was positive and a tissue culture isolated *M. bovis*. Treatment began with rifampin, isoniazid, pyrazinamide, and ethambutol. One week after the bone biopsy, she developed multiple subcutaneous, asymptomatic, violaceous nodules, 1 cm in size, on the left arm and hand (Fig. 1). A skin biopsy revealed a granulomatous process with central necrosis, yet Ziehl–Neelsen staining did not find microorganisms (Fig 2a - 2d). Tissue culture and PCR tests yielded negative results. After two days, new fluctuant nodules appeared on the arms and legs (Fig. 3). One of these cold abscesses was drained, and the aspirate was sent again for culture and PCR. The GeneXpert MTB/RIF test was positive, and cultures grew *M. bovis*. The diagnosis of a metastatic tuberculous abscess (MTA) was established and the treatment was continued. Two months later, the fevers recurred, and new skin nodules appeared. A repeated skin biopsy and tissue culture failed to identify the agent, yet it grew from the purulent aspirated of the abscess. No antibiotic resistance was documented, and the treatment was continued. Over the following months, the patient developed neurologic symptoms attributed to central nervous system dissemination, and her overall condition worsened. Unfortunately, she died six months after the initial diagnosis.

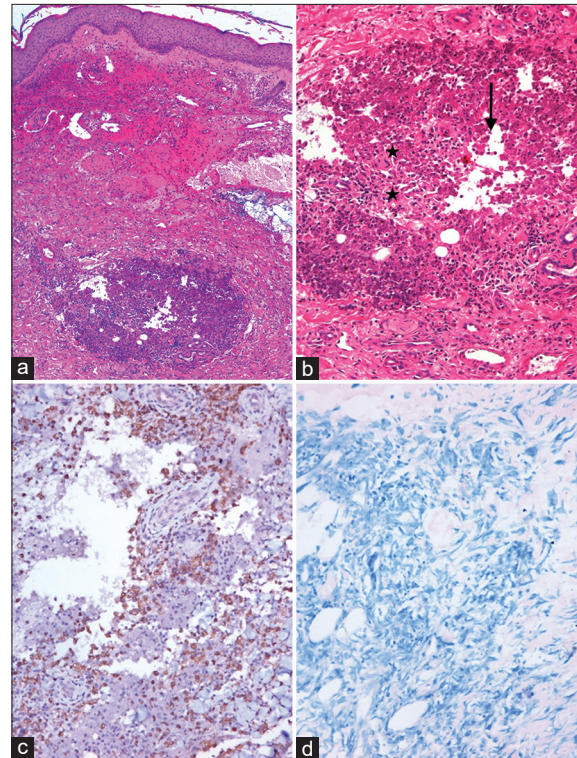
## DISCUSSION

MTA, also known as tuberculous gumma, is due to the hematogenous spread of the mycobacterium from an endogenous infectious source. It represents between 1% and 2% of all forms of cutaneous tuberculosis.



**Figure 1:** Subcutaneous erythematous and violaceous nodules on the back of the left hand.

In the absence of regional lymphadenopathy, single or multiple asymptomatic subcutaneous nodules represent the most common cutaneous finding. The term *cold abscess* describes a fluctuating nodule with no increase in local temperature [3]. Histopathologically, MTA presents a suppurative granulomatous dermatitis with central caseous necrosis [4].



**Figure 2:** a) Extravasated erythrocytes observed in the superficial dermis and granuloma in the deep dermis (H&E; 4×). b) The granuloma consisting of epithelioid macrophages (\*) and showing necrosis in its central portion (arrow) (H&E; 10×). c) Immunohistochemistry for CD68 showing the presence of abundant histiocytes in the lesion. d) Directed search for acid-fast bacilli by Ziehl–Neelsen staining returning negative.



**Figure 3:** Presence of gumma in the upper left extremity.

Although infrequent, MTA commonly occurs in the setting of immunosuppression. Most descriptions involve individuals living with HIV, yet there are some reports in which immunosuppression was due to medical treatment, such as in rheumatoid arthritis [5] and systemic lupus erythematosus [6]. MTA development associated with osteomyelitis is rare, yet reports describe cases caused by *M. tuberculosis* [7]. The reviewed literature did not reveal cases of MTA accompanied by osteomyelitis due to *M. bovis*.

A relevant finding in our case was the development of MTA after taking a bone biopsy, which suggests that the procedure could have prompted the hematogenous spread. Documenting MTA should always drive physicians to search for an internal infectious source.

The prevalence of *M. bovis* in humans is underestimated or ignored in most developing countries, such as Mexico and Latin America [1]. Jaka Moreno et al. described five cases of lupus vulgaris in the setting of infection by *M. bovis* [8].

The gold standard for diagnosis is the isolation of the mycobacterium in tissue samples. However, the sensitivity of culture and special stains for extrapulmonary forms is lower when compared to pulmonary tuberculosis, which makes the diagnosis difficult. PCR has increased sensitivity (24.5–100%) and specificity (73.7–100%) for the diagnosis of cutaneous tuberculosis. Cutaneous tuberculosis constitutes a diagnostic challenge given the low sensitivity of the laboratory and histopathological tests and the paucibacillary nature. Based on previous studies, it has been shown that DNA polymerase chain reaction (PCR) has greater sensitivity for the diagnosis of cutaneous tuberculosis (24%) than culture (16%) [9]. Both tests could have a higher diagnostic performance in multibacillary samples, such as abscesses, when compared to samples obtained from skin tissue, which are typically paucibacillary [10].

Treatment should be directed according to a sensitivity study, yet it generally consists of a scheme based on rifampin, isoniazid, pyrazinamide, and ethambutol [3].

## CONCLUSION

MTA is one of the least common skin manifestations of cutaneous tuberculosis and should be considered in the differential diagnosis when immunosuppressed patients develop subcutaneous nodules and cold

abscesses. The possibility that taking a bone biopsy initiated a hematogenous spread cannot be excluded in our case. Likewise, despite adequate treatment and mycobacterial susceptibility, recurrent MTA may develop in immunosuppressed hosts.

## Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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