CONCISE COMMUNICATION

*Mycobacterium tuberculosis* found at both skin lesions and Mantoux testing site in a patient with erythema induratum of Bazin

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ABSTRACT

*Mycobacterium tuberculosis* is very rarely found in erythema induratum of Bazin; recently, we found an unusual case with positive acid-fast bacilli and polymerase chain reaction for detecting *M. tuberculosis* in both skin lesions of the extremities and the site of Mantoux test.

Key words: erythema induratum of Bazin, erythematous macules, Mantoux testing, tuberculosis, Ziehl–Neelsen staining.

INTRODUCTION

Erythema induratum of Bazin (EIB) is believed to be a kind of tuberculid. As a hypersensitive reaction to *Mycobacterium tuberculosis*, the acid-fast bacillus is usually absent in the skin lesions of the disorder. The tuberculin skin test (Mantoux test) is to detect the cutaneous immune response to the purified protein derivate from *M. tuberculosis* (PPD) in patients with either tuberculosis or tuberculids. The acid-fast bacillus is usually negative in the test skin sites. Here, we report an unusual case with positive acid-fast bacilli in both the original skin lesions and the skin site of Mantoux test.

CASE REPORT

A 65-year-old woman presented with erythematous rashes on her lower legs that had been present for 3 years and then exacerbated 3 weeks prior. She had been diagnosed with erythema nodosum and failed prednisone therapy, and her skin lesion had been on and off during the past 3 years and mainly recurrent in spring or autumn, with poor responses to anti-inflammation drugs. Physical examination revealed several tender, linearly arranged, brownish erythematous nodules or plaques on the extremities of the patient (Fig. 1a). The general examination ruled out active tuberculosis at any other sites of her body. Blood chemistry showed a slightly elevated platelet count (124 × 10^9/L), elevated level of alanine transaminase (93 U/L) and aspartate aminotransferase (80 U/L). White blood cell count, C-reactive protein, erythrocyte sedimentation rate, immunoglobulins and complements were within normal range. The test results for rheumatoid factor, anti-streptolysin O and antinuclear antibodies were negative. Neither hepatitis virus nor HIV was detected. Chest X-ray and electrocardiogram examination did not show any abnormalities. Tuberculin skin test (Mantoux test) was strongly positive (Fig. 1b). The T-SPOT.TB (HealthDigit, Shanghai, China) test showed a positive result. Histopathology of the skin specimens from the lower leg revealed granulomatous inflammation consisting of Langerhans giant cells, epithelioid cells and necrotic adipose cells (Fig. 2a,b). Ziehl–Neelsen staining for acid-fast bacilli was

Figure 1. Clinical pictures of the extremities and the site of Mantoux test. (a) Brownish red patches and nodules at the extremities of the patient. (b) Positive results of tuberculin skin test. (c,d) Erythematous nodule at the site of Mantoux test.
positive (Fig. 2c). Meantime, a polymerase chain reaction test for detecting \textit{M. tuberculosis} was positive (primer sequences: forward, CCGTAAACACCGTAGTT; reverse, CCTACTACGAC-CACATCA). The bacterial culture was not conducted due to limited laboratory conditions. A diagnosis of EIB was made, and isoniazid, rifampicin and ethambutol combination therapy was prescribed. A silymarin tablet was given as well, but we did not prescribe any corticosteroids. During the first month of the treatment, a large crusted indurated erythematous patch was found at the site of the former Mantoux test, with tenderness (Fig. 1c,d). Then, a biopsy at this site was performed and the histopathological study revealed multiple granuloma in the dermis and subcutaneous fat tissues composed of Langerhans giant cells and epithelioid cells, with a positive result of acid-fast staining again (Fig. 3). Furthermore, a polymerase chain reaction test for detecting \textit{M. tuberculosis} was also performed and showed a positive result, too. After 2 months more, a good response to antiphthisic treatment was observed. All of the skin lesions including those at the site of the PPD test had dramatically subsided and the serum level of alanine transaminase and aspartate aminotransferase turned to normal. The patient is still in follow up.

**DISCUSSION**

Erythema induratum of Bazin was first described by Ernest Bazin in 1861 and characterized by recurrent, painful nodules or plaques on the calves of the lower legs. The histopathology of EIB consisted of granulomas containing Langerhans giant cells and focal areas of fat necrosis at the dermis and subcutaneous adipose tissues.\(^1,2\) The pathogenesis of EIB remains poorly understood and its relation to tuberculosis is still controversial. Most authors currently consider EIB a multifactorial disorder with many different causes, tuberculosis being one of them, which was thought to be a hypersensitive immune response to \textit{M. tuberculosis}.\(^2,3\) Multidrug antituberculosis therapy is helpful in the latter situation.\(^4\)

In this case, the typical skin lesions with a recurrent pattern, the characteristic histopathological features and the excellent therapeutic outcomes of antituberculosis treatment supported the diagnosis of EIB. To our knowledge, there is no previous report about the positive findings of \textit{M. tuberculosis} at the location of Mantoux testing.\(^3\) It is negative in other patients receiving Mantoux test in our ordinary clinical practice, according to our serial observations.

It is very interesting that the Ziehl–Neelsen staining for acid-fast bacilli showed positive in both skin lesions of EIB and the site of Mantoux test which were confirmed by positive polymerase chain reaction testing. To the best of our knowledge, this is the first case in the published work. We excluded the possibility of reagent contamination because the other patients receiving Mantoux test using the same batch of reagent and a series of observations on the subjects confirmed that. We speculate that such a phenomenon represents an isoform skin reaction (Koebner reaction) in EIB. Or, at least, it is one of the possible explanations.

The pathogenesis of Koebner reaction remains unclear.\(^5,6\) It is believed to be associated with some inflammatory factors (e.g. tumor necrosis factor-\(\alpha\), interleukin [IL]-1, IL-6, Hsp70, Hsp72, Hsp90 and intercellular adhesion molecule-1), and caused by immune-mediated mechanisms, although it is not

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enough to explain its roles in the present case and in the other latent tuberculosis infections.

However, in the present case, we found a positive Ziehl–Neelsen staining for acid-fast bacilli in EIB lesions, and we also found a positive Ziehl–Neelsen staining for acid-fast bacilli in Mantoux testing, which deserves further studies to explore the real reasons of them and the details of the etiopathogenesis of tuberculids including EIB.

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