case report

Erythema induratum: What is the role of *Mycobacterium tuberculosis*?

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Erythema induratum (EI) was first described by Bazin in 1861, who attributed the condition to tuberculosis (TB).[1,2] In 1901, Whitfield hypothesized that there were two forms of EI, one of which was related to TB.[3] EI is a tuberculid, characterized by chronic or recurrent tender subcutaneous nodules, which sometimes ulcerate. The lesions typically are located on the lower extremities of adult women.[1,4,5] Most individuals with EI have a positive tuberculin skin test, but rarely have evidence of active TB.[4,8]

EI lesions appear histopathologically as a granulomatous lobular panniculitis and vasculitis, with the affected artery lying in the septum of subcutaneous fat.[4,8-11] Several authors were able to demonstrate *Mycobacterium tuberculosis* DNA by polymerase chain reaction (PCR) in tissue biopsy from EI lesions, which leads to the belief among investigators that *M. tuberculosis* has a role in EI lesions.[9-13] We report two cases of EI and their therapeutic response and review the literature on EI.

CASES

The first case was a 63-year-old Saudi female who presented with a 3-week history of painful left lower limb erythema. There was neither a history of TB nor a family history of TB. On examination, she was had a well-defined 3 × 6 cm indurated ulcer at the medial aspect of the left leg close to the heel. The erythrocyte sedimentation rate (ESR) before treatment was 120 mm/hr and the PPD test was positive. Biopsy showed a chronic, active ulcer associated with focal granulomatous changes, with the inflammation extending to the subcutaneous adipose tissue associated with fat necrosis and thrombotic occlusion of blood vessels. The biopsy result was consistent with EI. Culture for *M. tuberculosis* and PCR were negative. The patient was treated with anti-TB medications (isoniazid, rifampicin, pyrazinamide and ethambutol) for 2 months and then isoniazid and rifampicin for 4 months. During this period, she showed a dramatic clinical response with gradual decline in the ESR to 39 mm/hr.

The second case was a 35-year-old Saudi female who presented with a one-month history of painful multiple erythemas in both lower limbs. There was no previous history of TB and no family history of TB. On examination she had 9 multiple indurated, painful nodules, variable in size, 7 lesions in the left lower limb and 2 lesions in the right lower limb (Figure 1). ESR was 112 mm/hr and the PPD skin test was positive. A biopsy for this patient showed lobular panniculaitis, with inflammatory changes seen in the subcutaneous fat and in the interface between the reticular dermis and subcutaneous fat, where there was prominent venulitis in the reticular dermis. In addition, granulomatous inflammation was identified in the panniculus and in the reticular dermis. The biopsy result was consistent with EI. *M. tuberculosis* culture and PCR were negative. She was treated with anti-TB medications (isoniazid, rifampicin, pyrazinamide and ethambutol) for 2 months and then isoniazid and rifampicin for 4 months. She had an excellent clinical response (Figure 2) with a decline in the ESR to 30 mm/hr.

DISCUSSION

EI was described initially by Bazin in 1861.[1,2] Audry, however, challenged the hypothesis that EI has any relation with *M. tuberculosis* in 1898.[14] Whitfield reached the conclusion that there are two forms of EI, one of which was related to *M. tuberculosis*, in 1901.[1,3] Montgomery and colleagues described 72 patients with EI, and most of the patients (85%) were females. A PPD test done on 25 patients was positive in 84%.[15]

Many authors have shown that EI can respond successfully to anti-TB therapy.[16-18] Degitz and colleagues demonstrated that *M. tuberculosis* DNA can be found in the EI lesion by the use of PCR, in 1993. They were able to demonstrate *M. tuberculosis* DNA in skin biopsies using PCR in 5 of 7 patients with EI.[19] Several authors have shown that EI lesions can be associated with other types of active TB like tuberculous lymph-

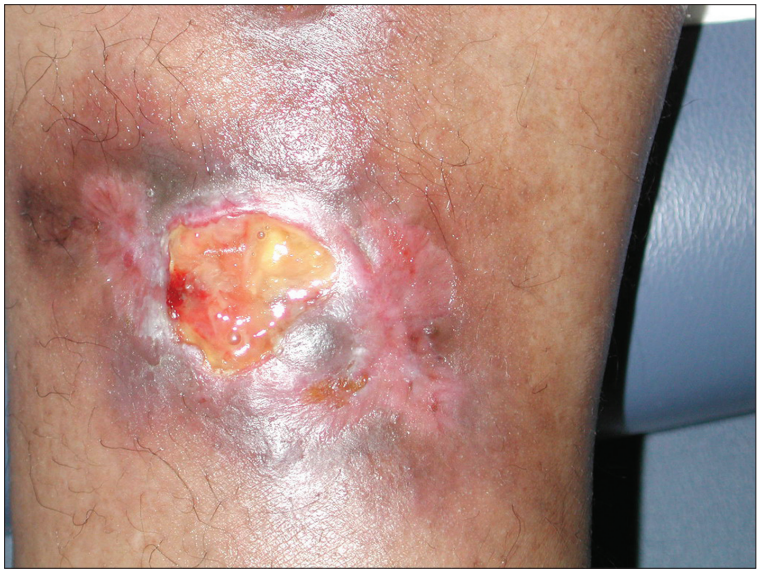

Figure 1. Ulcerated erythema induratum on presentation.

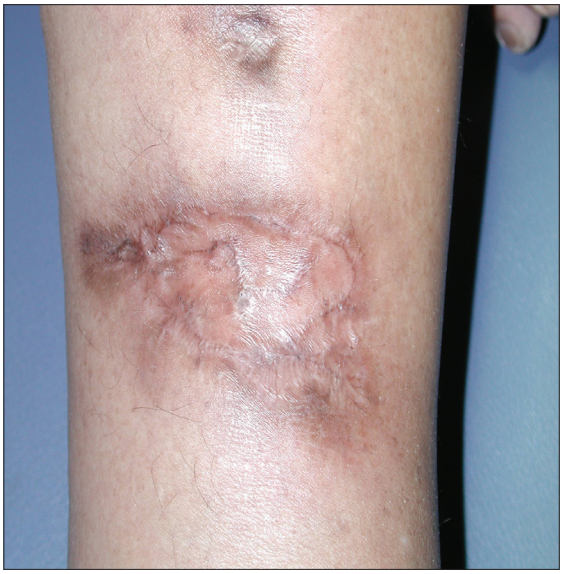

Figure 2. Healed erythema induratum after 6 weeks of therapy.

adenitis,[6,20] pulmonary tuberculosis,[21] renal tuberculosis,[22] endometrial tuberculosis,[23] and tuberculosis of the nasopharynx.[24]

A review of the medical literature shows that EI lesions can present as a primary lesion[1,4,5,8,15,18,19] or a secondary skin disease to other active tuberculosis.[20-24] Distler and colleagues reported a case with panniculitis for 30 years,[25] and Ollert and colleagues reported two cases of chronic EI for 10 years.[8] All of these cases have responded successfully to anti-TB therapy. Both of our cases who had chronic EI lesions diagnosed histologically have successfully responded to 6 months of anti-TB therapy. However, both of our cases did not have caseating granuloma on the histopathology of their skin biopsy and we were not able to diagnose a tuberculous origin of their lesions microbiologically. Also, *M. tuberculosis* DNA was negative on the PCR in both cases.

Most of the published studies support the use of *M. tuberculosis*-DNA PCR on skin biopsy of EI lesions,[9] but a few investigators have not found PCR to be a useful test in cutaneous TB.[13] We believe that the recent molecular biology evidence that *M. tuberculosis* DNA is present in a majority of EI lesions together with the successful response to anti-TB therapy supports the hypothesis that most cases of EI are due to a paucibacillary *M. tuberculosis*-DNA infection of the skin.

We recommend that EI patients be given a trial of anti-TB therapy (for example, isoniazid 300 mg by mouth once daily, rifampicin 600 mg by mouth once daily, pyrazinamide 1.5 g. by mouth once daily, and ethambutol 800 mg by mouth once daily for the first 2 months, then continue isoniazid and rifampicin for another 4 months) while waiting for *M. tuberculosis*-DNA PCR results, or evaluating the response to therapy in 4 weeks.

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