

Papulonecrotic tuberculid and Poncet disease: A case of multisystem delayed-type hypersensitivity in a patient with *Mycobacterium tuberculosis* infection



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INTRODUCTION

It is well known that the clinical manifestations of *Mycobacterium tuberculosis* (TB) are as much a function of host immune conditions as of direct infection by the organism. In rare cases, patients will have localized immune phenomena without laboratory isolation of the organism. Examples of such phenomena include tuberculids and Poncet disease. Tuberculids represent a cutaneous immune reaction in patients with strong cell-mediated immunity against *M tuberculosis*.¹ Poncet disease is an immune-mediated oligoarthritis associated with TB.² We present an unusual case of concurrent papulonecrotic tuberculid and Poncet disease, representing multisystem *M tuberculosis*—induced delayed-type hypersensitivity reactions.

CASE REPORT

A 42-year old Indian man, who had lived in the United States for several years, presented to the dermatology clinic with a history of recurrent erythematous, papular rash on the bilateral dorsal and palmar hands and in the groin. This waxing and waning cutaneous eruption occurred concurrently with recurrent flares of oligoarthritis, malaise, and gastrointestinal upset.

Four years prior, the patient underwent a thorough rheumatologic and gastrointestinal evaluation for the same symptoms; however, there was no dermatologic evaluation to further

Abbreviations used:

IGRA: interferon gamma release assay
TB: tuberculosis

characterize the rash. At that time, an elevated erythrocyte sedimentation rate (40 mm/h; normal, ≤ 15 mm/h) and C-reactive protein (4.42 mg/dL; normal, ≤ 0.60 mg/dL) supported an inflammatory process. However, there was only weak antinuclear antibody positivity (1:40 speckled and nucleolar pattern), and the following additional studies were all within normal limits: anti–double-stranded DNA antibody (12 IU/mL; normal, <100 IU/mL), extracted nuclear antigen antibodies (negative; normal, <100 AU/mL), cyclic citrullinated peptide antibody (0.0 U/mL; normal, ≤ 5.0 U/mL), and rheumatoid factor (<20 IU/mL; normal, <20 IU/mL). Therefore, laboratory tests failed to show evidence of autoimmune disease. Upper and lower endoscopy found gastropathy and biopsy found *Helicobacter pylori*. The patient was treated with amoxicillin and clarithromycin twice a day for 14 days with temporary resolution of his symptoms.

After a 3-year asymptomatic period, the patient had recurrence of oligoarthritis, rash, and diarrhea. Specifically, the patient presented to the rheumatology department and reported pain in the bilateral ankles and right knee. Physical examination found active synovitis in the right ankle with x-ray

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Fig 1. Papulonecrotic tuberculid. **A**, The patient presented with scattered hyperpigmented scaling macules and indurated papules on the bilateral dorsal and palmar hands. Crusted lesions were also present. Biopsy sites outlined with dashed lines. **B**, Nearly complete resolution after treatment with isoniazid, rifampin, pyrazinamide, and ethambutol.

imaging confirming the presence of soft tissue swelling in the same joint. Again, inflammatory markers were found to be elevated (CRP = 5.49 mg/dL and ESR = 57 mm/h) but autoantibodies were unremarkable (antinuclear antibody, 1:160 nucleolar; anti-double-stranded DNA antibody, 82 IU/mL, anti-Smith antibody, 9 AU/mL, anti-ribonucleoprotein antibody, 30 AU/mL, anti-Ro antibody, 14 AU/mL, Anti-La antibody, 25 AU/mL, cyclic citrullinated peptide antibody, 1.2 U/mL, and rheumatoid factor, <20 IU/mL). Given his previous improvement with antibiotics, empiric treatment for rash and diarrhea with amoxicillin/clavulanic acid twice daily and clindamycin 3 times daily for 10 days was prescribed; this treatment did mitigate his symptoms, suggesting an underlying infectious etiology.

Given the lack of clear diagnosis for his symptoms and the recurrent nature, he was referred to the dermatology department for evaluation of his cutaneous lesions. On examination, he had scattered hyperpigmented scaling macules and indurated papules on the bilateral dorsal and palmar hands. A few of these lesions exhibited a central crust, suggesting possible underlying inflammation and necrosis (Fig 1, A). Punch biopsies of the left dorsal

and palmar hands both found epidermal ulceration associated with necrotizing granulomatous inflammation involving the dermis and superficial subcutaneous tissue as well as a perivascular lymphocytic infiltrate (Fig 2). Bacterial, fungal, and mycobacterial stains were negative. Additionally, fresh tissue culture of a skin lesion was negative for mycobacterium. An interferon- γ release assay (IGRA) was positive. Taken together, the clinical, laboratory, and pathologic findings suggested a diagnosis of a cutaneous papulonecrotic tuberculid.

The patient was promptly referred to the local health department. A chest radiograph was normal, and sputum/urine cultures were negative for mycobacteria. The patient was initiated on standard 4-drug therapy for TB (isoniazid, rifampin, pyrazinamide, and ethambutol). Nearly complete resolution of his rash was noted after completion of therapy (Fig 1, B) with the patient also reporting resolution of joint pain. Interestingly, gastrointestinal symptoms continued to wax and wane, and he was given a provisional diagnosis of irritable bowel syndrome.

DISCUSSION

Although immunopathology is a key element of diagnosing TB, in most cases, the organism can be

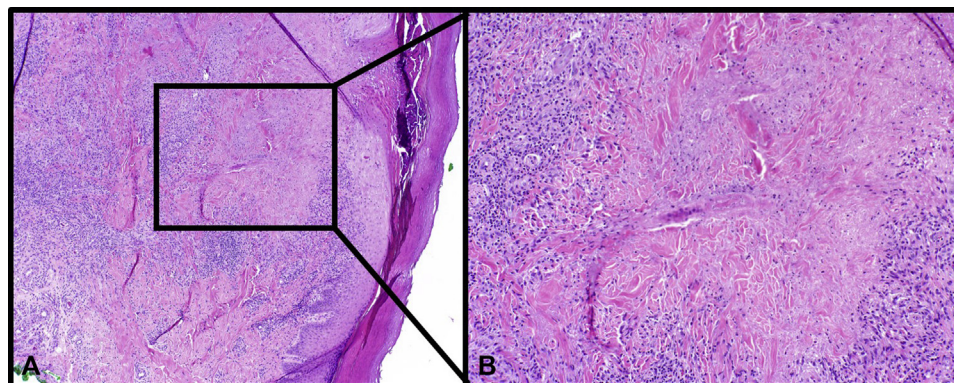


Fig 2. Necrotizing granulomatous inflammation. Punch biopsy of a palmar lesion showed epidermal ulceration associated with necrotizing granulomatous inflammation. There are dermal neutrophils and perivascular infiltrate with lymphocytes and eosinophils. Fite and acid-fast bacilli stains were negative (not shown). (Original magnifications: **A**, $\times 4$; **B**, $\times 10$.)

isolated from the site of pathology. However, rare manifestations of tuberculosis caused by delayed-type hypersensitivity reactions in the absence of *M tuberculosis* organisms at the site of inflammation have been described in the skin (ie, tuberculids) and in the joints (ie, Poncet disease).

Specifically in terms of cutaneous TB hypersensitivity reactions, tuberculids are commonly defined by the following criteria: (1) positive tuberculin skin test or IGRA, (2) additional foci of TB infection, (3) histopathologic evidence of granulomatous inflammation, and (4) disappearance of lesions with antituberculous therapy.¹ Tuberculids are a paucibacillary form of cutaneous tuberculosis, with the absence of bacilli on biopsy being characteristic.³ Papulonecrotic tuberculid was previously described as the most common tuberculid¹ but seems to be rarer according to recent series of patients with cutaneous tuberculosis in Brazil and China, accounting for less than 10% of cutaneous tuberculosis cases in both.^{4,5} In a review of 12 Indian patients with papulonecrotic tuberculid, common clinical findings included symmetric papulonodular lesions on the extremities that may ulcerate and scar.⁶ Although mycobacterial culture of these lesions is negative, *M tuberculosis* DNA has been detected with polymerase chain reaction in about 50% of biopsies.⁷

In addition to tuberculids, Poncet disease is also a rare, immune-mediated, paucibacillary manifestation of TB. Recently proposed diagnostic criteria define Poncet disease as the presence of inflammatory, nonerosive, nondeforming arthritis; the exclusion of other causes of inflammatory arthritis; and the presence of both major criteria: concurrent diagnosis of extra-articular tuberculosis and complete response to antitubercular therapy.⁸ In the absence of both major criteria, Poncet disease

is less likely but can still be considered if minor criteria, such as positive tuberculin skin test, presence of associated hypersensitivity phenomenon, or absence of sacroiliac and axial involvement are met.⁸ Poncet disease is considered a form of reactive arthritis caused by cross-reactivity between *M tuberculosis* antigens and host cartilage.² Interestingly, patients with reactive arthritis caused by common urogenital and gastrointestinal pathogens often present with cutaneous manifestations, suggesting a shared pathologic mechanism.

Our patient presented with recurrent indurated papules on the hands and groin that were mitigated by antibiotic therapy. He experienced concurrent inflammatory arthritis that also improved with antibiotic therapy. Skin biopsy result was consistent with necrotizing granulomatous inflammation and an IGRA was positive. This patient meets the proposed criteria for both papulonecrotic tuberculid and Poncet disease, with both being temporally related and resolving with antituberculous therapy. Interestingly, before the diagnosis, the patient's symptoms seemed to improve with amoxicillin/clavulanate, which has known antituberculous activity.⁹ To our knowledge, this is only the second report (first in the United States) of concurrent papulonecrotic tuberculid and Poncet disease in an immunocompetent patient.¹⁰

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