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***Mycobacterium chelonae* Bacteremia After First Dose of Infliximab for Ulcerative Colitis**

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To the Editor

Tumor necrosis factor (TNF) plays a critical role in controlling *Mycobacterium tuberculosis*, as well as nontuberculous mycobacterial infections (1). While there are several reports of cutaneous mycobacterial infections, particularly *M. marinum*, in IBD patients receiving anti-TNF therapy, to our knowledge no case of disseminated *Mycobacterium chelonae* related to TNF antagonists has been reported.

A 72 year-old woman with ulcerative colitis was hospitalized with worsening colitis and transferred to our tertiary care center after she failed to respond to more than a week of intravenous steroids. Stool cultures were negative, and flexible sigmoidoscopy confirmed severely active chronic colitis.

Preparations were made to initiate anti-TNF therapy, and a purified-protein derivative (PPD) tuberculin skin test and T-SPOT.TB (interferon-gamma release) were negative. She received an initial dose of infliximab 5 mg/kg, and over the next several days experienced significant improvement. One day prior to discharge she developed an erythematous rash on the right hand (Figure 1A), raising a concern for medication reaction. Dermatology was consulted and obtained a skin biopsy.

Twenty-four hours later, the preliminary report of the skin biopsy revealed florid acid-fast bacilli (AFB). The biopsy showed a dense subcutaneous inflammatory infiltrate, consisting of confluent sheets of neutrophils (Figure 1B, C) with abundant karyorrhexis (fragments of nuclear debris from apoptotic cells) (Figure 1D). The main differential diagnosis for these histopathologic findings is infection and neutrophilic panniculitides such as early erythema nodosum, erythema induratum, or Sweet's syndrome (3). Special stains for organisms (acid-

fast and Fite) showed innumerable positive rod-shaped organisms consistent with *Mycobacterium* species (Figure 1E).

She was also found to have *Klebsiella pneumonia* bacteremia and *C. difficile* infection, and was started on imipenem, clarithromycin and amikacin and oral vancomycin. Because she continued to have severe disease, and could no longer receive aggressive immunosuppression due to multiple concurrent infections, she underwent proctocolectomy and ileostomy. Thirty-four days after the initial biopsy of her rash, molecular identification of the AFB revealed *M. chelonae*, and conventional blood cultures, which had been preliminarily positive for AFB, also revealed *M. chelonae* after 28 days. She was continued on antibiotics and has done well after her colectomy.

M. chelonae is a highly drug-resistant mycobacterium that is widely distributed in the environment (4). It most commonly causes cellulitis and abscesses, and may present as nodules in the dermis and subcutaneous fat, which can clinically mimic erythema nodosum in patients with IBD. Pathology shows a marked inflammatory infiltrate within the dermis or subcutaneous tissue, which ranges from neutrophilic to histiocytic and granulomatous (5–8). Organisms are almost always identified on acid-fast or Fite stains (5, 6), and may be numerous as in the present case.

Assessment of TB status is standard prior to initiating anti-TNF therapy. Conventional PPD testing utilizes a mixture of more than 100 different mycobacterial peptides and has poor specificity for *M. tuberculosis*, as both BCG vaccination and exposure to nontuberculous mycobacteria produce a positive result. Newer interferon-gamma (IFN- γ) release assays have improved specificity compared to PPD (10). In this assay, peripheral monocytes from patients are cultured with TB antigens in plates coated with anti-IFN- γ antibodies. *M. tuberculosis*-specific T cells, if present, release IFN- γ , which is captured by the plate-bound antibodies and spots are visualized by ELISA (11). Current IFN- γ release assays utilize the ESAT-6, CFP-10 and TB7.7 peptides, which are expressed by *M. tuberculosis* but absent from BCG vaccine strains and most atypical mycobacteria (11, 12). This assay therefore does not provide information about past or current nontuberculous mycobacterial infections. A high degree of clinical vigilance for atypical mycobacteria becomes increasingly important as we more precisely target specific aspects of innate and adaptive immunity in the treatment of IBD.

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Study Highlights

What is current knowledge

- All immunosuppressive drugs increase the risk for opportunistic infections
- TNF is critical for controlling mycobacterial infections
- PPD skin testing utilizes a heterogeneous mixture of mycobacterial proteins

What is new

- IFN- γ release assays (T-SPOT.*TB* and QuantiFERON-TB Gold) have improved specificity for *M. tuberculosis* but do not assess past or present status of nontuberculous mycobacterial infections
- A high degree of clinical vigilance for atypical mycobacterial infections is required in patients receiving anti-TNF therapy.

FIGURE 1. Clinical appearance and histopathological features of cutaneous *M. chelonae* infection

A) Several days after the first infliximab infusion for treatment of ulcerative colitis, there was the rapid onset of an erythematous rash involving the dorsum of the right hand overlying the 1st-3rd metacarpophalangeal joints. B) Pathology of a punch biopsy of the skin shows a dense inflammatory infiltrate within the subcutaneous fibroadipose tissue (asterisk) (Hematoxylin & Eosin, 20X magnification, scale bar=500 μ m). C) The inflammatory infiltrate consists of confluent sheets of neutrophils (suppurative panniculitis) (Hematoxylin & Eosin, 100X magnification, scale bar=100 μ m). D) There is abundant karyorrhexis (apoptotic nuclear debris) (Hematoxylin & Eosin, 400X magnification, scale bar=25 μ m). E) The infiltrate contains innumerable acid-fast bacilli consistent with *Mycobacterium* species (acid-fast stain, 400X magnification, scale bar=25 μ m).