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Mycobacterium bovis enterocolitis in an immunocompromised host

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Gastrointestinal tuberculosis (ITB) is an uncommon but well described form of extrapulmonary tuberculosis. Presentation can include fever, abdominal pain, and enterocolitis (1,2). In countries where tuberculosis (TB) is uncommon, other forms of enterocolitis, particularly Crohn disease, are more likely (1,2).

We report an immunosuppressed Mexican teenager in the U.S. who developed enterocolitis and was diagnosed with *Mycobacterium bovis* (*M. bovis*) ITB .

Case Report

A 16-year-old Mexican girl with systemic lupus erythematosus (SLE) presented with 3 months of fever, anorexia, weight loss, fatigue, and abdominal pain. She reported frequent diarrhea without melena or hematochezia, as well as night sweats, palpitations, and dizziness with standing.

Her medications included mycophenolate mofetil, benazepril, aspirin, prednisone, hydroxychloroquine, and lansoprazole. Her SLE was well controlled and the mycophenolate mofetil dose was decreased just prior to symptom onset. Family history revealed an aunt with SLE, an uncle with active pulmonary TB, and a sister with history of a positive tuberculin purified protein derivative (PPD) test. The patient was born in Mexico, and had

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received the Bacille Calmette-Guerin (BCG) vaccine. She immigrated to California six years earlier and had never returned to Mexico. Her diet included Mexican soft cheeses.

On admission, she appeared fatigued and pale. Her temperature ranged from 34-39°C, her heart rate 150 beats/min, and other vital signs were normal. She had a normal respiratory exam and a soft, non-distended abdomen that was tender to palpation in the right upper quadrant. The remainder of the exam was normal. Laboratory tests included: hemoglobin 6.8 g/dL (normal 12.0 - 15.5 g/dL), white blood count $6.1 \times 10^9/L$ (normal $4.5 - 13.2 \times 10^9/L$), ESR >100 mm/hr (normal 0-15 mm/hr), and CRP 66 mg/L (normal < 6.3 mg/L). C3 and C4 were normal. The fecal occult blood test was positive.

Hectic fever and diarrhea continued. An abdominal ultrasound was done and was normal. Tests for HIV, CMV and cryptosporidium were negative, and a PPD showed 34mm of induration. Abdominal and pelvic computed tomography (CT) showed inflammation of the distal ileum, proximal transverse colon and cecum (Figure 1).

Upper and lower endoscopy showed friability throughout the colon and blood and exudate in the cecum (Figure 2A). Histology from the cecum and proximal transverse colon showed active inflammation with ulceration and multiple well-formed granulomas (Figure 2B). A Kinyoun stain demonstrated acid-fast bacilli (AFB) (Figure 2C). Rifampin, pyrazinamide, ethambutol, and isoniazid were started. Polymerase chain reaction (PCR) of *Mycobacterium tuberculosis* (*M. tuberculosis*) complex in the cecal biopsy using the IS 61101 locus was negative; however symptoms resolved with anti-tuberculosis therapy.

After seven weeks, tissue cultures from the endoscopic biopsy grew acid fast organisms identified as *M. tuberculosis* complex and further speciated to *M. bovis*. Ethambutol and pyrazinamide were discontinued. She was treated with isoniazid and rifampin for 9 months and was symptom free. Her infection was attributed to ingestion of contaminated Mexican soft cheese.

Discussion

This case describes a teenager with SLE who developed primary *M. bovis* enterocolitis.

Tuberculosis (TB) is largely a disease of developing countries, and rates of TB in the U.S. are among the lowest worldwide (3). In 2012, the Centers for Disease Control (CDC) reported 3.2 cases per 100,000 people, with disease burden highest in immigrants from developing countries and lowest in children under fourteen (4).

ITB is rare in the U.S., with no specific cases reported by the CDC in 2012 (4). However, historically, ITB in U.S. children has occurred more frequently in Hispanic children and is more commonly caused by *M. bovis* than *M. tuberculosis* (5-6).

The presenting symptoms of ITB are those of enterocolitis, including abdominal pain and bloody diarrhea (1,2). Symptoms overlap with those of Crohn disease, a more common childhood illness of the developed world (1). Crohn disease and ITB are differentiated by evidence of mycobacteria in tissue or complete resolution of symptoms after anti-TB

medication (1·2). Since culture can take several weeks, patients are often treated for TB rather than Crohn disease to avoid high dose steroids precipitating disseminated TB (1·2). This is challenging, since multi-drug resistant TB may not respond to anti-TB medications and delay in therapy for Crohn disease can lead to adverse outcomes.

In TB endemic areas, distinguishing between ITB and Crohn disease is a challenging clinical dilemma, driving a clinical trial to develop a scoring algorithm to separate the diseases based on clinical and laboratory findings (7). Without an algorithm currently available, epidemiologic and exposure history are the main clues to diagnosis.

The patient presented in this case report had a recent decrease in immunosuppressive medication and the clinical, radiological and endoscopic findings strongly suggested an idiopathic inflammatory condition. The decision to consider other diagnoses was based on history, laboratory results, the danger of exacerbating infectious colitis with steroids and the rarity of Crohn disease in SLE patients (8).

Supporting ITB, the patient had hectic fever, which is more common in ITB than Crohn disease (1·2). She was Hispanic, born in a developing country, and ate Mexican soft cheeses. The size of the induration from the positive PPD test was striking given the history of autoimmunity and chronic immunosuppression.

This case highlights *M. bovis* intestinal tuberculosis. Presenting symptoms were non-specific and a high index of suspicion based on family and exposure history was critical to diagnosis.

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Figure 1. Imaging findings that support a diagnosis of either Crohn disease or tuberculosis include (A) skip lesions (black arrowheads) and comb sign (white arrows); and (B) asymmetric colonic wall thickening (white arrowheads).

Figure 2.

Photograph of the ascending colon (A) shows diffuse exudate (white arrow) and ulceration (black arrow) throughout the colon. H&E stained section of proximal colon shows well-formed non-necrotizing granuloma consisting of dense collections of macrophages with surrounding granulation tissue (B), Kinyoun stain for AFB shows magenta-colored bacilli in association with granulomas (C).