A 39-year-old female immigrant with chronic diarrhea

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A 39-year-old female immigrant from Yemen presented with several months' history of diarrhea. The stool was loose in consistency and brown in colour. There was no blood or mucus noted. She reported a dull periumbilical abdominal pain, poor appetite and weight loss but had not experienced any fever, nausea or vomiting. The patient immigrated to the United States after she was married, 18 years previously. She reported a negative tuberculin skin test at the time of intake.

On physical examination, she was cachectic but afebrile, with a normal heart rate and blood pressure. Chest auscultation revealed clear lung fields and regular heart sounds. The abdomen was soft, not tender and without organomegaly. She had no skin rash and no lymphadenopathy.

Laboratory test results revealed a hemoglobin level of 85 g/L and a white blood cell count of 9.4×10^9 cells/L without eosinophilia. Her blood chemistry, including kidney and liver function tests, were within normal limits. Stool microscopy for ova and parasites and stool culture were unrevealing. An abdominal computed tomography scan showed segmental thickening in the right colon (Figure 1A). Colonoscopy was performed and tissue biopsies were obtained. Hematoxylin and eosin-stained slides are shown in Figures 1B and 1C.

What is your diagnosis?

DIAGNOSIS

The colon biopsy showed granulomatous inflammation composed of epithelioid histiocytes and multinucleated giant cells, and acid-fast bacilli staining showed mycobacteria (Figures 1B and 1C). She was diagnosed with segmental tuberculosis (TB) of the colon. She had no evidence of lung disease. The patient was started empirically on rifampin (RIF), isoniazid (INH), ethambutol and pyrazinamide. The tissue culture grew *Mycobacterium tuberculosis* that was susceptible to all of the above anti-TB medications. She finished a seven-month course without significant side effects. She was symptom free at one-year follow-up.

DISCUSSION

TB causes significant morbidity and mortality worldwide (1). Immigration and the HIV epidemic led to resurgence of this infection (1). Poverty, malnutrition, overcrowding and HIV coinfection facilitates the spread of this ailment (2). The incidence of TB has been declining in the United States and other Western countries (1,3). In 2012, the incidence of TB in the United States was 3.2 per 100,000 population, a significantly lower number compared with its incidence in 1993, which was 9.7 per 100,000 population. Despite this decline, the number of extrapulmonary TB cases have been increasing; the expanding immigrant populations, HIV and improved diagnostic tools partially explain this (3,4).

Extrapulmonary TB accounts for 20% of diagnosed TB cases in immunocompetent individuals and up to 50% of TB cases in immunocompromised hosts (5). Gastrointestinal (GI) TB is the sixth most frequent form of extrapulmonary TB, after lymphatic, genitourinary, bone and joint, miliary and meningeal TB (6). It can affect any part of the GI tract, with ileocecal involvement being the most common. GI TB infection is acquired following one of four mechanisms: swallowing infected sputum, hematogenous spread from active pulmonary or miliary TB, ingestion of contaminated milk or food, and contiguous spread from adjacent organs (7). Only 15% of patients with GI TB show evidence of pulmonary disease (7).

Isolated segmental TB of the colon is rare and accounts for <10% of GI TB (7). It is subacute in presentation, with symptoms developing over weeks to months. Patients often complain of nonspecific abdominal pain (the most common symptom, occurring in 80% to 90% of cases), fever, weight loss, night sweats and diarrhea (8). Physical examination may reveal cachexia, right lower abdominal mass – in cases of ileocecal involvement – and ascites.

Routine blood tests may reveal chronic anemia and high erythrocyte sedimentation rate; however, the white blood cell count is usually normal. Tuberculin skin test (TST) and interferon-gamma release assay (IGRA) may be positive, but neither can differentiate between active and latent TB infection. In meta-analyses, TST sensitivity and specificity were reported to be 71% and 97%, respectively (9). In two small studies investigating intestinal TB, reported TST sensitivity was 64% and 86% (10,11). The reported sensitivity of IGRA in the diagnosis of extrapulmonary TB is between 71% and 93% and the specificity ranged between 56% and 89%, based on the prevalence of TB in the study population (12,13). IGRA has not specifically been studied in intestinal TB, but was useful in the diagnosis described in two case reports (14). In intestinal TB, stool studies are nonspecific (2).

Contrast-enhanced computed tomography of the abdomen and pelvis is the imaging modality of choice in diagnosing colonic TB (15). Imaging may reveal one or more of the following: enlarged lymph nodes, asymmetric bowel wall thickening or an inflammatory mass, strictures, ascites and, rarely, pancolitis.

The definitive diagnosis of colonic TB hinges on the combination of consistent histology and positive mycobacterial culture of biopsy material obtained by colonoscopy. Colonoscopic findings of colonic TB show one of three forms: ulcerative, hypertrophic or ulcerohypertrophic, or fibrinous (7). For optimal diagnostic yield, at least four to six deep endoscopic biopsies should be obtained from the ulcer base and its margins (16). Of note, acid-fast bacilli are identified in a minority (<33%) of biopsy specimens (17). Culture of biopsy material remains the gold standard but is slow. Polymerase chain reaction testing of biopsy specimens can facilitate the diagnosis and results can be reported within 48 h; however, this is not widely available (9,18). The role of Xpert MTB/RIF (Cepheid, USA), a polymerase chain reaction assay, in the diagnosis of extrapulmonary TB was evaluated in 1476 extrapulmonary specimens (19). The assay showed an overall sensitivity and specificity of 81.3% and 99.8%, respectively. For biopsies, urine, pus and cerebrospinal fluid, the sensitivity exceeded 85%; meanwhile, it was slightly <80% for gastric aspirates and <50% for ascites and other cavitary fluid samples.

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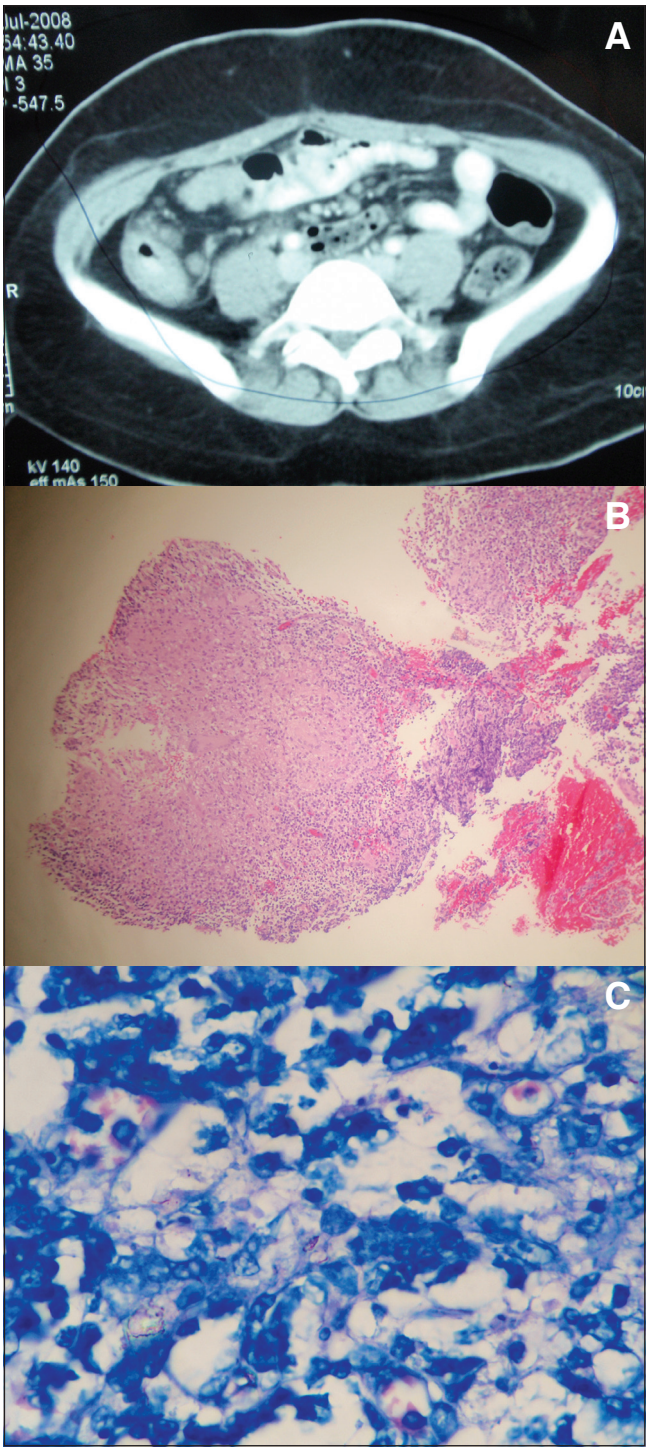

Figure 1) A *Computed tomography section of the abdomen with contrast showing thickened right colonic wall*. **B** *Hematoxylin and eosin-stained section of the colon biopsy showing granulomatous inflammation composed of epithelioid histiocytes and multinucleated giant cells. Original magnification ×100*. **C** *Acid-fast bacillus stain showing mycobacteria. Original magnification ×400*

Despite the above, the diagnosis of TB colitis can remain uncertain (20). For situations in which there is high index of suspicion of TB on clinical grounds, anti-TB therapy is appropriate.

The differential diagnoses of colonic TB include inflammatory bowel disease, carcinoma and amebiasis (2). Ileocecal TB has broader differential diagnoses including lymphoma, appendicular abscess, enteric fever, actinomycosis and yersiniosis (2).

TB colitis treatment consists of RIF, INH, pyrazinamide and ethambutol for two months, followed by four to seven months of RIF and INH (1). Treatment is commonly started empirically based on high clinical suspicion or suggestive preliminary test results. In Western countries and mainly among immigrant populations, multidrug-resistant TB (MDR-TB) and extensive drug-resistant TB are on the rise, making reliable empirical therapeutic recommendations difficult (21). A recent study evaluated the prevalence of MDR-TB among foreign-born persons in Alberta (22). Between 2002 and 2011, MDR-TB prevalence was 2.1%, a sharp increase from the preceding decade, during which the prevalence was 0.56%. Resistant TB strains should be suspected in immigrants from high-risk areas and empirical therapy should, preferably, be based on genotypic drug susceptibility testing. Delaying therapy in stable patients of this group, if they can be quarantined so as not to infect others, to allow for susceptibility-guided therapy as opposed to empirical therapy that may be inadequate (risking failure and the further development of resistance) is a consideration.

Bowel obstruction is the most common complication and may be due to a progressive stricture or adhesions (23). Other potential complications include perforation with secondary peritonitis, gastrointestinal bleed and fistula formation (24,25). TB colitis patients demonstrate clinical improvement within two weeks of therapy commencement. Surgical treatment is reserved for bowel obstruction, bowel perforation and massive bleeding (26).

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