Crohn’s Disease or Tuberculosis?

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A Nepali-born migrant was diagnosed with intestinal tuberculosis (TB) after being initially considered for Crohn’s disease. Differentiating the two diseases is challenging but important owing to variation in treatment, the potential for dissemination of TB under immunosuppression for Crohn’s disease, and emergent Australian migration from TB endemic countries.

Clinical Record

A 23-year-old Nepalese man was referred for assessment of a 2-month history of postprandial abdominal pain, diarrhea, and 7 kg loss of weight. There was no associated history of fevers, diaphoresis, cough, or dyspnea. His symptoms were refractory to antacids (Mylanta, Johnson & Johnson Pty Ltd) and pantoprazole (Somac, Nycomed). He immigrated to Australia 8 months prior, had no previous medical or family history or allergies, and physical examination was unremarkable.

Laboratory results revealed microcytic hypochromic anemia (hemoglobin concentration 112 g/L, normal 130–180 g/L; mean cell volume 74 fL, normal 80–100 fL; and mean cell hemoglobin 24 pg, normal, 27–32 pg), thrombocytosis (platelet concentration 521 × 10^9 L^-1, normal 150–450 × 10^9 L^-1), raised erythrocyte sedimentation rate (76 mm/h, normal 1–10 mm/h), and C-reactive protein (56 mg/L, normal < 5 mg/L) suggesting an inflammatory process (albeit a normal white cell count and differential), normal renal function and electrolytes, an isolated raised alkaline phosphatase (205 U/L, normal 35–110 U/L) on liver function panel, and a positive quantiFERON gold [tuberculosis (TB) antigen 1.50 IU/mL, normal < 0.35 IU/mL and mitogen 5.44 IU/mL, normal > 0.50 IU/mL]. Subsequent amebic and schistosoma serology were negative.

Contrast enhanced chest, abdominal, and pelvic computed tomography (CT) revealed a calcified granuloma within the left lower lung lobe with left hilar and subcarinal foci of calcification, marked right colonic wall thickening with surrounding inflammation (Figure 1), prominent regional lymphadenopathy with one showing nodal calcification, and terminal ileal thickening.

Gastroscopy revealed a 5 cm area of mucosal inflammation in the posterior wall of the antrum and prepyloric region with a cobble stone appearance, small ulcerations, and scant mucopurulent exudates. Similar changes were noted in the pyloric channel and proximal duodenum. Multiple antral and pyloric biopsies were obtained. Colonoscopy revealed a cobblestone mucosa in the ascending colon that was associated with inflammation, mucopurulent exudate, and multiple large ulcers. The cecum revealed similar inflammatory and ulcerative changes, and a fistulous opening but the terminal ileum appeared normal. Similarly, multiple biopsies of the terminal ileum and ascending colon were obtained for histopathology, polymerase chain reaction (PCR), microscopy, and culture for Mycobacterium tuberculosis (MTB).

Histopathological examination of gastric mucosal biopsies showed severe Helicobacter pylori-associated gastritis, whereas a nonspecific chronic inflammatory cell infiltrate was noted in colonic mucosal biopsies. The changes were not suggestive of either Crohn’s disease or mycobacterial infection. Terminal ileal biopsies did not reveal any histological abnormalities. Microscopy and PCR of right colon biopsies were negative for MTB. However, 3 weeks later cultures of ascending colonic
biopsy specimens grew MTB that was subsequently shown to be sensitive to isoniazid and rifampicin.

The patient was treated with combination of esomeprazole, amoxicillin, and clarithromycin (Nexium, Amoxil, Klacid, Astrazeneca) for Helicobacter pylori eradication, and antituberculous therapy with isoniazid (Fawns & McAllan), rifampicin (Rifadin, Sanofi-Aventis), pyrazinamide, and ethambutol (Myambutol, Sigma Pharmaceuticals) was initiated after culture results returned positive. The patient experienced resolution of his symptoms after commencing treatment for MTB.

**Discussion**

Gastrointestinal TB is not infrequent and is reportedly the sixth commonest extrapulmonary site of infection, accounting for 3%–5% of all extrapulmonary disease. Although common in countries of high TB endemicity, the incidence of gastrointestinal TB in Australia is poorly documented.

Gastrointestinal TB follows the swallowing of infected sputum, ingestion of contaminated milk or foods, hematogenous seeding from active pulmonary or miliary TB, or local spread from adjacent organs. The small bowel and colon, in particular the terminal ileum, cecum, and ascending colon are commonly affected sites. Clinical manifestations in intestinal TB are often nonspecific and the clinical course can vary widely from an acute to chronic illness. Nonspecific chronic abdominal pain is the commonest complaint, present in 80%–90% of patients while fever, night sweats, and weight loss may also be present. Other gastrointestinal symptoms including diarrhea, constipation, per-rectal bleeding, and palpable right iliac fossa mass are varied. Small bowel obstruction and colonic perforation have also been reported.

Showing the presence of MTB and granulomatous inflammation on histopathological examination, PCR and culture of mucosal biopsy specimens makes a definitive diagnosis of intestinal TB and is more useful than routine cultures alone.

**CT** is useful in assessing intraluminal and extraluminal pathology, like bowel wall and mesenteric thickening, and abdominal lymphadenopathy which can have features of hypoattenuation, peripheral rim enhancement, or calcification. Chest X-ray is nondiagnostic as <50% of patients with intestinal TB have evidence of pulmonary disease. Colonoscopic findings are diverse and include macroscopic inflammatory changes, circumferential ulcerations, strictures, nodules, pseudopolyps, fibrous bands, fistulas, and deformed ileocecal valves.

The differential diagnoses of intestinal TB include Crohn’s disease, lymphoma, adenocarcinoma, and other infective causes like amebiasis, actinomycosis, and Yersinia enterocolitica enteritis. In patients from countries of high MTB endemicity, the challenge lies in distinguishing intestinal TB from Crohn’s disease as both diseases have overlapping clinical, radiological, endoscopic, and histopathological features. Treatment is distinctly different and immunosuppressive therapies used for Crohn’s disease may have disastrous effects in intestinal TB by predisposing to the development of disseminated TB.

Clinically, both can be present in an insidious manner with chronic abdominal and systemic symptoms. However, a previous or family history of TB, history of chronic immunosuppression, and an origin from a country of high TB endemicity are all suggestive of TB rather than Crohn’s disease. Fistulizing disease is one of the hallmarks of Crohn’s disease but this is also well described in intestinal TB. Histologically, both Crohn’s disease and intestinal TB are characterized by granulomatous inflammation but multiple large confluent caseating granulomas which may be submucosal and associated with disproportionate submucosal inflammation, caseous necrosis, and ulcers lined with epithelioid histiocytes are more commonly seen in intestinal TB. Once a definitive or presumptive diagnosis has been made of TB, treatment with standard regime antituberculous drugs is highly effective.

Our case illustrates the importance of considering intestinal TB as a significant differential to Crohn’s disease, especially in patients with high-risk demographics. The overlapping clinical features and lack of rapid and specific diagnostic tests highlight the diagnostic challenge posed by intestinal TB.

The current TB incidence in Nepal is 163/100,000 which contrasts markedly to Australia’s 6.4/100,000 highlighting the burden of disease that is transferable with the advent of rising migration from countries of high TB endemicity. It is therefore more likely that local clinicians will face the diagnostic dilemma of differentiating intestinal TB from Crohn’s disease. The importance of this is further emphasized by the significant differences in treatment of the two diseases.
and the potentially dire consequences that may ensue in misdiagnosing intestinal TB for Crohn’s disease.

Declaration of Interests

The authors state they have no conflicts of interest to declare.

References