A 36-year-old Man with Bowel Obstruction

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Case Presentation
A 36-year-old man presented to the emergency department of a tertiary care hospital because of an eight hour history of nausea and vomiting. He had previously been in good health. He reported eight episodes of emesis and five episodes of diarrhea. The diarrhea had resolved several hours prior and the man was not passing flatus. There had been no blood or mucus in his vomitus or stools. He also complained of abdominal swelling and new-onset crampy abdominal pain. The pain was intermittent but worsening and improved upon vomiting. The man denied any recent history of cough, chest pain, shortness of breath, fever, chills, night sweats, weight loss, or myalgia.

The triad of vomiting, diarrhea, and abdominal pain most often reflects infectious gastroenteritis or ingestion of medications or toxins. A detailed dietary and medication history should be taken, and the patient should be asked about recent contact with people with similar symptoms. Life-threatening causes of acute abdominal pain must be borne in mind. Bowel obstruction is a distinct possibility in a patient with abdominal distension, colicky pain relieved by vomiting, and no passage of flatus.

After a bout of bloody diarrhea seventeen years ago, the patient had been tentatively diagnosed with ulcerative colitis. However, a colonoscopy had failed to support this diagnosis and there had been no bloody diarrhea at any subsequent time. There was no other significant medical or surgical history. The patient had no allergies, took no medications, and did not smoke tobacco or consume alcohol. He had not eaten any unusual foodstuffs recently and had no sick contacts. Family history was noncontributory. The patient was born in India and had lived there until six years ago when he moved to New York. For the past six months he had lived in Toronto and worked as an engineer. He had had no other travel history. There was no active outbreak of viral gastroenteritis in the community at the time of presentation.

No features of the past medical history specifically supported the diagnoses of infectious gastroenteritis or toxin ingestion. However, the lack of such features does not rule out these conditions. During his thirty years in India, the patient could have been exposed to a number of pathogens that are rare or unknown in Canada, but few of these could remain dormant for six years. Similarly, it is unlikely that inflammatory bowel disease would have stayed in remission for so long.

On examination in the emergency department, the patient was a young man in no apparent distress. He was 178 cm tall and weighed 65.5 kg, giving a body mass index of 21. His temperature was 36.4°C, his heart rate 100 beats per minute and regular, his respiratory rate 16 breaths per minute, his blood pressure 147/100 mmHg, and his oxygen saturation 98% on room air. He had no pallor or jaundice and no cervical, axillary, or inguinal lymphadenopathy. The jugular venous pulsation was 3 cm above the sternal angle, and the rest of the cardiovascular examination was normal. Respiratory examination revealed symmetrically decreased air entry to the lung bases. The fingers were clubbed. The abdomen was distended and diffusely tender. Bowel sounds were absent and percussion was normal. There were no peritoneal findings or palpable masses or hemias, and no organomegaly or ascites was noted. Digital rectal examination showed no mass or blood. Examination of the nervous, locomotor, and integumentary systems was unremarkable.

Tachycardia at 100 beats per minute in the absence of hypovolemia supports an infectious process. Abdominal distension suggests ascites or bowel obstruction. No other findings specifically support either diagnosis, but the physical examination is not particularly sensitive for ruling them out. Abdominal radiography and ultrasound would help distinguish between the two. The absence of bowel sounds suggests adynamic ileus.

The finding of clubbing in this patient is surprising and requires explanation. Diagnoses which might unify this finding with the patient’s presenting symptoms include inflammatory bowel disease, celiac disease, and hepatic cirrhosis. However, a patient with one of these diseases would not be expected to develop clubbing until after a long period of symptomatic disease. Clubbing may also be congenital and benign, or it may be a sign of a second disease process unrelated to the presenting illness. Extra-abdominal causes of clubbing include neoplastic or suppurrative intrathoracic disease, cardiovascular disease, pulmonary fibrosis, and thyroid acropachy.¹
The white blood cell count was 15.94, with 88% neutrophils, 5% lymphocytes, 5% monocytes, and 2% bands. The hemoglobin level, mean corpuscular volume, platelet count, coagulation profile, electrolyte panel, liver profile, and serum glucose, creatinine, and creatine kinase were normal. The blood urea nitrogen was mildly depressed at 2.6 mmol/L, and the serum amylase was elevated at 193.

Leukocytosis and neutrophilia support the diagnosis of bacterial gastroenteritis. Elevated serum amylase is a sensitive but nonspecific test for pancreatitis, as amylase may also be increased in hypertriglyceridemia, macroamylasemia, renal failure, and inflammatory processes involving the salivary glands or any abdominal organ. In a patient with no clinical features of pancreatitis, this test result is of limited value. Imaging should be performed at this stage to evaluate for bowel obstruction or ascites.

Radiographs of the abdomen demonstrated multiple dilated loops of small bowel with air-fluid levels. The colon was nearly empty of stool. There was no gross free intraperitoneal air.

Small bowel obstruction (SBO) may be caused by extrinsic, intrinsic, or intraluminal pathology (Table 1). Adhesions, hernia, and neoplasms account for over 90% of cases of SBO; however, in a 36-year-old man with no surgical history and no palpable hernias, other etiologies become more likely. The presence of tachycardia and leukocytosis raises the possibility of strangulating obstruction, although the patient is not febrile. Computed tomography of the abdomen with oral and intravenous contrast should be performed to elucidate the etiology and grade of the obstruction.

Computed tomography of the abdomen and pelvis revealed a high-grade distal small bowel obstruction at the level of the ileocecal junction. The cecal wall was eccentrically thickened in this area (Figure 1, white arrow) with collapse of the distal part of the colon. Regional pericolic fat stranding and pericecal nodes measuring up to 9 mm in diameter were noted. The terminal ileum and appendix appeared normal. A small amount of ascites was noted.

Cecal wall thickening with enlarged regional lymph nodes suggests a neoplastic, inflammatory, or infectious process. A differential diagnosis is given in Table 2. However, the primary concern with this patient at this time is not diagnosis but rather treatment. High-grade small bowel obstruction of unclear etiology in a patient with no previous abdominal surgery requires urgent laparotomy.

On laparotomy, a large amount of ascites was found. The cecum, appendix, and proximal ascending colon were mobilized and found to be quite bulky and nodular with enlarged lymph nodes in the associated omentum. The abdominal contents were otherwise normal. A right hemicolectomy with primary anastomosis was performed and the resected segment sent to the pathology lab in formalin. Hemostasis was achieved and the abdomen closed. The patient tolerated the procedure well and was safely extubated to the recovery room.

Ascites supports a diagnosis of tuberculosis (TB) or malignancy with peritoneal carcinomatosis. The ascitic fluid should be sent for cell count and differential, chemistry, cytology, and culture and sensitivity. The normal appearance of the peritoneum makes tuberculosis the leading diagnosis. A detailed history should be taken once the patient recovers from surgery. This history should include TB exposure, the results of diagnostic tests, and dates of BCG administration if any.

Upon further questioning it was found that the patient's chest radiograph upon immigrating to Canada had been abnormal and a Mantoux skin test had showed 20 mm of induration. The details of the chest radiograph were unavailable. Three sputum cultures and a half months before his presentation were negative. The patient's general practitioner had recommended TB prophylaxis the week before the patient presented to hospital. The patient was unsure whether he had ever received BCG vaccination.
Tuberculosis prophylaxis is recommended in all persons with over 15 mm of induration on a Mantoux skin test. In a person from a high-incidence population, the threshold is lowered to 10 mm; and in someone with an abnormal X-ray, to 5 mm. Sputum cultures are only 50-60% sensitive for pulmonary TB and should be less sensitive for extrapulmonary disease. A tentative diagnosis of cecal tuberculosis is warranted pending additional tests.

On the first postoperative day, the patient's temperature rose to 39.2°C. Chest radiography the following day revealed new lower lobe infiltrates and bilateral small pleural effusions but no other abnormalities. Cultures of sputum, blood, and urine showed no growth. Sputum staining was negative for mycobacteria.

Fever and pulmonary infiltrates on the first postoperative day likely represent atelectasis. As before, the absence of evidence of mycobacteria in sputum does not rule out extrapulmonary tuberculosis. The same is true for the blood and urine cultures. The diagnosis rests on pathological examination of the surgically resected cecum.

**Clinical Diagnosis**

**Cecal tuberculosis**

**Abdominal Tuberculosis**

**Epidemiology, Etiology, and Clinical Features**

Tuberculosis is a granulomatous infectious disease caused by Mycobacterium tuberculosis. It may affect almost any organ, but the most common site of infection is the lung. Although the incidence of extrapulmonary tuberculosis has not decreased as rapidly as that of pulmonary TB, extrapulmonary disease remains an uncommon manifestation of tuberculosis in the Western Hemisphere, occurring in 15% of cases in the absence of HIV infection. Pleural, skeletal, central nervous system, genitourinary, and gastrointestinal sites are the most prevalent. Foci of extrapulmonary tuberculosis are thought to arise through three mechanisms: (1) the spread of infectious pulmonary secretions via the respiratory and gastrointestinal tracts, (2) contiguous spread, and (3) lympho-hematogenous dissemination. These modes of spread can occur either at the time of primary infection or, occasionally though less commonly, from chronic established pulmonary or extrapulmonary foci. However in the absence of immunosuppression, the latter is very uncommon.

Abdominal tuberculosis is uncommon in Europe and America but is encountered with increasing frequency by hospitals that serve growing immigrant populations. The clinical presentation tends to be non-specific, with abdominal pains and general complaints. As with our patient, the differential diagnosis will often include an obstructive process secondary to either inflammatory bowel disease, malignancy, or some other infection. Prompt diagnosis allows an early start to quadruple anti-TB therapy, with advantages for the patient and savings to the health system.

Before the advent of effective chemotherapy for tuberculosis, over 70% of patients with advanced pulmonary disease developed gastrointestinal disease. The proposed mechanism of spread in this case involves the swallowing of infected expectorated secretions. The disease has been located anywhere in the gut including the esophagus, stomach, and small and large intestines and can involve any gastrointestinal-associated organ: that is, the spleen, liver, and pancreas.

The most common site of gastrointestinal involvement is the ileocecal region, possibly because of the increased physiological status, increased rate of fluid and electrolyte absorption, minimal digestive activity, and abundance of lymphoid tissue at this site. It has been shown that the M cells associated with Peyer's patches can phagocytose BCG bacilli. In a case series including 196 patients with gastrointestinal tuberculosis, the ileum was involved in 102 and the cecum in 100 patients. The frequency of gastrointestinal involvement declines as one proceeds both proximally and distally from the ileocecal region, although any area from the mouth to the anus may be involved. Peritoneal involvement may occur because of spread from lymph nodes or intestinal lesions or from tubercular salpingitis in women. Lymph nodal and peritoneal tuberculosis may occur without gastrointestinal involvement in about one third of abdominal cases. Early in the development of this disease, mesenteric adenitis is thought to represent an early form of tuberculosis, specifically lymphocytic infiltration. This presentation has been seen predominantly in Asians and young women, and usually occurs in individuals from countries where the prevalence of tuberculosis is high. Pancreatic involvement is extremely rare; when tuberculosis is isolated in the pancreas, it may mimic pancreatic carcinoma. It has been reported that pancreatic involvement occurs in 5% cases of miliary tuberculosis. Pancreatic TB presents with various symptoms including weight loss, fever, abdominal pain and obstructive jaundice. Imaging methods usually reveal a pancreatic mass in affected patients. Considering these manifestations, pancreatic TB should be kept in mind in the differential diagnosis of solitary masses in the pancreas, especially in young people in countries where TB is common.

Abdominal masses, pain, and an obstructive presentation are common in gastrointestinal TB, and concern that an underlying malignancy is the cause is frequently an issue. Indeed, obstruction is the most common complication of GI tuberculosis, occurring in 30% of cases. Perforations and fistulae are encountered less frequently than obstruction. The reported incidence of enteric perforation ranges from 1 to 15%.

Given the prevalence of abdominal tuberculosis among new immigrants from endemic parts of the world, it has been noted that a significant delay from the time of immigration to presentation with symptoms is common. In an interesting series of 22 immigrants to London from Africa and the Indian subcontinent with peritoneal tuberculosis, the mean delay was 5.2 years (range 1 to 12 years), suggesting that the patient’s vulnerability to this disease is brought into the new country and persists for many years. Our patient’s presentation six years after emigration from India was quite typical in this regard.
Radiography and computed tomography (CT) are the most frequently used imaging modalities in the diagnosis of gastrointestinal tuberculosis.\textsuperscript{20}

Chest X-ray
Evidence of tuberculosis in a chest X-ray supports the diagnosis but a normal chest X-ray does not rule it out. A study of abdominal tuberculosis found evidence of active or healed lesions on chest X-ray in 22 of 70 cases (46\%).\textsuperscript{21} Chest radiographs were more likely (80\%) to be positive in patients with acute complications. However, another series found the chest X-ray to be positive in only 25 per cent of patients.\textsuperscript{22} Hence, about 75 per cent of abdominal cases do not have evidence of concomitant pulmonary disease.

Abdominal X-ray
Plain abdomen radiography may show enteroliths, features of obstruction (i.e. dilated bowel loops with multiple air fluid levels, as in our patient), ascites, perforation, or intussusception. In addition, there may be findings of calcified lymph nodes, calcified granulomas, and hepatosplenomegaly.

Small Bowel Barium Series
Features which may be seen include accelerated intestinal transit; hypersegmentation of the barium column ("chicken intestine"); precipitation, flocculation and dilution of the barium; stiffened and thickened folds; luminal stenosis with smooth but stiff contours ("hour glass stenosis"); multiple strictures with segmental dilatation of bowel loops; and fixity and matting of bowel loops.

Computed Tomography (CT)
Ileocecal tuberculosis is usually hyperplastic and well evaluated on CT scan. In early disease there is slight symmetric circumferential thickening of cecum and terminal ileum. Later the ileocecal valve and adjacent medial wall of the cecum is asymmetrically thickened. In more advanced disease, such as in this patient, gross wall thickening, adherent loops, large regional nodes, and/or mesenteric thickening can together form a soft tissue mass centered on the ileocecal junction. CT scan can also pick up ulceration or nodularity within the terminal ileum, along with narrowing and proximal dilatation. Other areas of small and large bowel involvement manifest as circumferential wall thickening, narrowing of the lumen, and ulceration. In the colon, involvement around the hepatic flexure is common. Complications of perforation, abscess, and obstruction are also seen.

Tubercular ascitic fluid is of high attenuation value (25-45 Hounsfield units) due to its high protein content. Strands, fine septa, and debris within the fluid are characteristic, but are better appreciated on ultrasonography. Thickened peritoneum and enhancing peritoneal nodules may be seen.\textsuperscript{23}

Mesenteric disease on CT scan is seen as a patchy or diffuse increase in density, strands within the mesentery, and a stellate appearance. Lymph nodes may be interspersed. Omental thickening is well seen, often as an omental cake appearance. A fibrous wall developing from long standing inflammation can cover the omentum and is called an omental line. Omental lines are less common in malignant infiltration.

Caseating lymph nodes are seen as having hypodense centers and peripheral lymph nodes are characteristically involved, reflecting the lymphatic drainage of the small bowel. The retroperitoneal nodes (i.e. the paraaortic and pericaval) are relatively spared, and are almost never seen in isolation, unlike in lymphoma.\textsuperscript{24}

Pathology
Mycobacterial infection in the abdomen may be caused by multiple species besides \textit{M. tuberculosis}. \textit{M. bovis} can be a causative agent, but is uncommon with the routine pasteurization of milk in developed countries. \textit{M. avium} and \textit{M. intracellulare} have no virulence in normal hosts, but cause disseminated infections in 15-24\% of patients with AIDS.\textsuperscript{25} Acid-fast stains (Ziehl-Neelsen or Kinyoun's acid-fast staining) will identify the infectious agent as slender, red, rod-shaped bacilli approximately 2.4 µm in length and 0.2 – 0.5 µm in width. Auramine staining of the organisms and visualization under fluorescence microscopy is a more sensitive technique.

Classic gastrointestinal TB lesions are circumferential ulcerations resulting in stricture of the small intestine from cicatricial healing.\textsuperscript{25} Occlusive arterial changes may produce ischemia and also contribute to the development of strictures.\textsuperscript{26} Microscopically, the inflammation produced by TB infection is granulomatous. Epithelioid macrophages, giant cells, lymphocytes, plasma cells, neutrophils, and fibroblasts are present in the lesion. Characteristic caseating necrosis may be seen towards the center of the lesion, particularly if the lesion is located in the mesenteric lymph nodes.\textsuperscript{27} Mesenteric lymph nodes may be enlarged and matted and may caseate. Characteristic granulomata may be seen only in these lymph nodes, especially in patients who have undertaken extensive antitubercular therapy.\textsuperscript{28} The presence of granulomata in the intestine without granulomatous lymph node involvement is rare.\textsuperscript{29}

Tuberculous granulomata are initially formed in the mucosa and result from necrosis of Peyer's patches. These granulomata are present just beneath the ulcer bed in the submucosal layer. They are of variable size and become confluent with the progression of disease. Tuberculous granulomata are relatively superficial and usually do not penetrate beyond the muscularis.\textsuperscript{30} However, in long-standing lesions there may be variable degrees of fibrosis of the bowel wall, which extends from submucosa into the muscularis.\textsuperscript{31} Many sections may also show only non-specific chronic inflammation and no granulomata. Colonic mucosa can be inflamed with hyperemia and edema. Extensive fibrosis may lead to bowel wall thickening and pseudotumoral mass lesions. Nodular tubercular masses may be present on the serosal surface. Aphthous ulcers may also be present in the colon.\textsuperscript{32}

On gross pathological examination, the involved bowel can be
classified into 3 categories. The ulcerative form is seen in approximately 60% of patients. Multiple superficial ulcers are largely confined to the epithelial surface with the long axis of the ulcers perpendicular to the long axis of the bowel. This is considered a highly active form of the disease. The hypertrophic form consists of thickening of the bowel wall with nodular masses of variable size on the serosal surface with scarring and fibrosis. Both the ulcerative and hypertrophic forms are localized to the small intestine. Colonic and ileocecal lesions are most often of the ulcerohypertrophic classification, which is a combination of both ulcerative and hypertrophic forms, as in our patient. In this form, the ileocecal angle is often distorted and obtuse. Both sides of the ileocecal valve are usually involved leading to valve incompetence in GITB.

**Diagnosis of Tuberculosis**

Arriving at the diagnosis of tuberculosis can be a challenge. Patients may present with nonspecific systemic symptoms; consequently, tuberculosis must be included in the differential diagnosis of any patient who presents with non-specific symptoms, especially if the patient is at high risk for TB. (i.e. previously documented history, HIV infection, or residence in an endemic area).

**History**

The classic symptoms of pulmonary tuberculosis include a productive, prolonged cough (duration of more than 3 weeks), chest pain, and hemoptysis. Systemic symptoms of TB can include fever, chills, night sweats, reduced exercise tolerance, loss of appetite, and concomitant weight loss. Pulmonary tuberculosis should only be considered in patients who present with these symptoms. The symptoms of extrapulmonary tuberculosis depend on the site affected, e.g. back pain in spinal TB and hematuria in renal TB. Extrapulmonary tuberculosis should be considered in the differential diagnosis of ill persons who have systemic symptoms and especially in those who are at high risk for TB.

It is important to ask patients suspected of having tuberculosis about their history of TB exposure and infection. Clinicians may also contact the local health department for information about whether a patient has received TB treatment. If a regimen was inadequate or if the patient did not adhere to therapy, tuberculosis may recur and may be drug resistant. It is also important to consider demographic factors (country of origin, age, ethnic or racial group, occupation) that may increase the patient's risk for exposure to TB. Our patient immigrated from South Asia, which is an endemic area, thus placing him at increased risk for TB exposure. In addition, clinicians should determine whether the patient has medical conditions, especially HIV infection, that increase the risk for tuberculosis. Patients who have risk factors for HIV infection but who do not know their current HIV status should be referred for HIV counseling and testing.

**Physical Examination**

Physical examination is an essential part of the evaluation of any patient. It cannot be used to confirm or rule out tuberculosis, but it can provide valuable information about the patient's overall condition and other factors that may affect how TB is treated.

**Mantoux Skin Test**

The Mantoux tuberculin skin test is useful for detecting infection in the absence of active disease. Some persons may have a false-negative reaction to the tuberculin skin test if they are tested too soon after being exposed to TB. In general, it takes 2 to 10 weeks after infection for a person to develop an immune response to tuberculosis. Classically, the tuberculin immune response is a delayed-type hypersensitivity reaction (DTH). This reaction is mediated through the CD4+ subset of T-cells, and the induration that develops on the skin is a nodule composed of these lymphocytes and macrophages. Persons who have recently been exposed to a patient with active TB and who have a negative reaction to the tuberculin skin test should be retested 10 weeks after the last time of exposure. Importantly, children younger than 6 months of age may have a false-negative reaction to the tuberculin skin test because their immune systems are not yet fully developed. It is important to note that a negative reaction to the tuberculin test does not exclude the diagnosis of TB, especially for patients with severe illness or HIV infection.

**Radiology**

A posteroanterior view of the chest is the standard radiograph needed for the detection and description of chest abnormalities. In some instances, other views (e.g. lateral, lordotic) or additional studies (e.g. CT) may be necessary. In pulmonary tuberculosis, radiographic abnormalities often occur in the apical and posterior segments of the upper lobe or in the superior segments of the lower lobe. However, lesions may appear anywhere in the lungs and may differ in size, shape, density, and cavitation, especially in HIV-infected and other immunosuppressed persons. Abnormalities on chest radiographs may be suggestive of, but are never diagnostic of TB. However, chest radiographs may be used to rule out the possibility of pulmonary TB in a person who has a positive reaction to the tuberculin skin test and no symptoms of disease.

In HIV-infected persons with pulmonary tuberculosis, the chest radiograph may have an unusual appearance. For example, TB may cause infiltrates without cavities in any lung zone, or it may cause mediastinal or hilar lymphadenopathy. In HIV-infected persons, almost any abnormality on a chest radiograph may indicate tuberculosis. In fact, the radiograph of an HIV-infected person with TB disease may even appear entirely normal.

**Diagnostic Microbiology**

Persons suspected of having pulmonary or laryngeal tuberculosis should have at least three sputum specimens examined by smear and culture. A health care worker should coach and directly supervise the patient at least the first time sputum is collected. It is best to obtain a series of three early morning specimens collected on different days. Patients should be properly instructed how to produce a good specimen. They should be informed that sputum is the material brought up from the lungs and that mucus from the nose and throat and saliva are not good specimens. Coaching patients individually on how to expectorate can facilitate sputum collection. Unsupervised patients are seldom successful in pro-
viding an adequate specimen, especially the first time. The amount of coaching required on later visits will depend on individual patient needs.

Bronchoscropy can be done if the patient cannot cough up sputum and there is reasonable suspicion of TB. Bronchial washings, brushings, and biopsy specimens may be obtained, depending on the diagnostic possibilities and findings. Sputum collected after bronchoscopy may also be useful for a diagnosis. Gastric aspiration can also be used to obtain swallowed sputum specimens, but it is uncomfortable and invasive. It is, however, the best way to obtain specimens from infants and some young children who cannot produce sputum even with aerosol inhalation. During specimen collection, patients produce an aerosol that may be hazardous to health care workers or other patients in close proximity. For this reason, precautionary measures for infection control must be followed during sputum induction, bronchoscopy, and other common diagnostic procedures.

Because tuberculosis can occur in almost any anatomical site, a variety of clinical specimens other than sputum (e.g., urine, cerebrospinal fluid, pleural fluid, pus, or biopsy specimens) may be submitted for examination when nonpulmonary mycobacterial disease is suspected. Tissue specimens for the culture of M. tuberculosis should be placed in a saline solution, not in formalin, and should be delivered to the laboratory promptly. Our patient underwent extensive fluid evaluation, all of which was negative.

Laboratory Examination

Detection of acid-fast bacilli (AFB) in stained smears examined microscopically may provide the first bacteriologic clue of TB. Fluorescent staining with Auramine O is the preferred staining method because it is faster and more sensitive than the traditional methods in which Ziehl-Neelsen or Kinyoun stains are used. Smear examination is an easy and quick procedure; results should be available within 24 hours of specimen collection. However, smear examination permits only the presumptive diagnosis of TB because the AFB on a smear may be mycobacteria other than M. tuberculosis. Furthermore, many TB patients have negative AFB smears. A positive culture for M. tuberculosis confirms a diagnosis of TB; however, TB may also be diagnosed on the basis of clinical signs and symptoms in the absence of a positive culture. Generally it is on this basis that empiric anti-TB therapy is initiated. Culture examinations should be done on all specimens, regardless of AFB smear results. When a liquid medium is inoculated for growth (using the BACTEC radiometric system) and rapid methods are used for species identification, culture results should be available within 10 to 14 days of specimen collection. If a solid medium and conventional biochemical tests are used, the isolation of the organism can take 6 to 12 weeks.

Nucleic acid probes specific for the genus Mycobacterium, the M. tuberculosis complex, M. avium, and M. intracellulare provide a rapid method of species identification. Once the mycobacteria have been grown in culture, nucleic acid probes can identify the species in 2 to 8 hours. High-performance liquid chromatography (HPLC), which detects differences in the spectrum of mycolic acids in the cell wall, is equally rapid. Polymerase chain reaction (PCR) techniques are being developed that could be performed directly on sputum or other clinical specimens to diagnose TB disease more quickly. However, until the evaluation of this method is completed, PCR should be considered an experimental technique; it is not available for the routine diagnosis of TB. In the future, this technique may become widely available to clinicians.

Follow-up bacteriologic examinations are important for assessing the patient’s infectuousness and response to therapy. At a minimum, specimens should be obtained at monthly intervals until culture conversion to negative. Laboratories should report positive smears and positive cultures within 24 hours by telephone or fax to the primary health care provider. Follow-up results may be reported by mail. It is the responsibility of the primary health care provider to promptly report all suspected or confirmed cases of TB to public health so that a contact investigation can be initiated as quickly as possible.

For all patients, the initial M. tuberculosis isolate should be tested for drug susceptibility. It is crucial to identify drug resistance as early as possible in order to ensure appropriate treatment. Drug susceptibility patterns should be repeated for patients who do not respond adequately or who have positive culture results after two months of therapy. Susceptibility results from laboratories should be promptly forwarded to the health department. Risk factors for drug resistance are given in Table 3.

Table 3
Risk Factors for Drug-resistant TB

| 1. Persons who have a history of treatment with TB drugs |
| 2. Contacts of persons known to have drug-resistant TB |
| 3. Persons born in areas of the world where the prevalence of drug-resistant TB is high (e.g., Asia, Africa, and Latin America) |
| 4. Residents of geographic areas in Canada where the prevalence of isoniazid-resistant TB is documented to be 4% or greater |
| 5. Persons whose smears or cultures remain positive after two months of therapy with TB drugs |

The radiometric BACTEC method, which uses liquid media cultures, is faster than conventional methods for determining susceptibility to first-line TB medications. When BACTEC is used, results can be obtained within 5 days of inoculation; conventional methods, which use solid media for growth, can take as long as 21 days after inoculation.

Restriction fragment length polymorphism (RFLP), a method of DNA fingerprinting, can be used to identify specific strains of M. tuberculosis and thus to track TB transmission during outbreaks. The restriction enzymes used in this technique cut DNA at certain sites to produce fragments. These fragments are separated by size to produce a pattern, or “fingerprint,” that is specific for each strain. Related isolates show the same pattern.
Treatment of Tuberculosis

Treatment of mycobacterial infections remains a challenge. The algorithms followed depend on the species isolated, the drug-sensitivity of the organism, and whether or not the disease recurs. A clinical practice guideline has been produced by the American Thoracic Society in concert with the Centers for Disease Control in the United States. This guideline advocates a total of six months of treatment, the first two with either triple or quadruple therapy (depending on whether the prevalence of drug resistance in the community is less than or greater than 4%) and the last four with isoniazid and rifampin alone. Not surprisingly, treatment options have been more closely studied in pulmonary TB than in exclusively extrapulmonary disease.

Pathological Discussion

Histological examination of the surgically resected cecum demonstrated necrotizing granulomatous inflammation with giant cells (Figure 2, black arrow) extending through the muscularis propria and serosal granulomata. Granulomata were also present in pericolic lymph nodes extending into the proximal appendiceal wall. Adjacent to areas of ulceration, the colonic mucosa showed mild regenerative changes, but there were no signs of chronic colitis. Ziehl-Neelsen stain revealed rare acid-fast bacilli (Figure 3, black arrow). Because the specimen had been preserved in formalin, cultures could not be taken to definitively identify these as M. tuberculosis.

Pathological Diagnosis

Mycobacterial infection of the cecum.

Treatment and Subsequent Course

Quadruple-agent therapy with daily administration of isoniazid 300 mg, rifampin 600 mg, pyrazinamide 1250 mg (20 mg/kg), and ethambutol 1300 mg (20 mg/kg) was initiated. The patient was also given vitamin B6 50 mg daily. Public health was informed of the diagnosis. The rest of the patient’s hospital stay was uneventful. He was discharged home with instructions to follow up with his family doctor and general surgeon as well as the tuberculosis clinic. After two months, pyrazinamide and ethambutol were discontinued. Treatment with isoniazid and rifampin lasted for a total of nine months.

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