

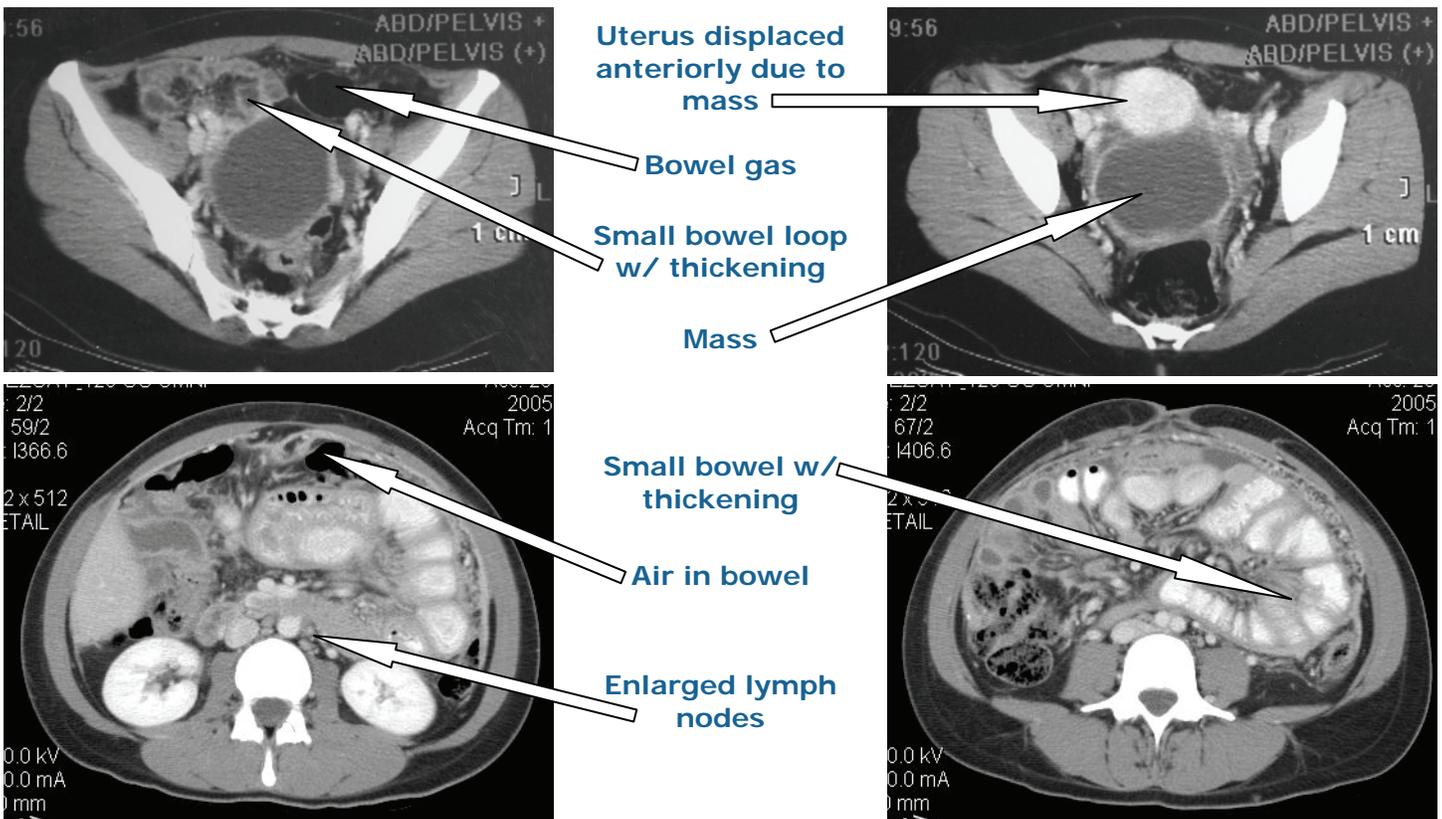
Case Presentation

Patient History

A 27-year old Hispanic female was admitted to hospital with a fever of 104°, a two week history of abdominal swelling, decreased appetite and body aches. She was anemic with a hemoglobin of 10.4; liver functions were within normal limits, an erythrocytic sedimentation rate (ESR) was 70 (normal ≤ 20) and a CA125 (ovarian cancer marker) was 438 (Normal < 21). A CT scan of the chest, abdomen and pelvis revealed large bilateral pleural effusions and multiple intra-thoracic nodes (pericardial, cardiophrenic angle, and para esophageal); the largest measuring 1.2 x 0.8cm. Ascites, omental caking, and thickening of the mesenteric vessels were present in the abdomen. Multiple nodes were also present (paraortic, aortocaval and iliac). Large bilateral ovarian masses with lobular contours were noted as well as concentric thickening of the distal sigmoid and proximal rectum. A tuberculin skin test (TST) was negative and three sputums were smear negative for AFB.

A diagnostic laparoscopy revealed approximately 1000cc of serosanguineous ascitic fluid. The abdominal and pelvic cavities were inflamed and there were areas in the pelvis consistent with phlegmon. Bowel to bowel adhesions and shortening of the mesentery were present. The

CT scans of patient's abdominal/pelvic region



ovaries were not visualized due to the adhesions and the peritoneal inflammation. Frozen section of an abdominal node revealed granulomatous inflammation.

The patient had had two abdominal surgeries during the previous year to address symptoms of abdominal pain. The initial surgery was a laparoscopic cholecystectomy. Six months later she presented with pain and pelvic fluid and underwent a laparoscopic appendectomy. Adhesions were present around the appendix and site of the prior gall bladder procedure. Cytology was negative for malignancy and granuloma were noted in the appendix.

Her mother had recurrent ovarian carcinoma and there was a distant family history of tuberculosis. She had visited Mexico frequently as a child but not recently.

She was identified as a TB suspect and was started on treatment with isoniazid (INH), rifampin (RIF), pyrazinamide (PZA) and ethambutol (EMB). She was subsequently discharged home to directly observed therapy (DOT). Her fever improved over the initial weeks of therapy and the ascites resolved. Two months later, the lab reported PZA resistance and identified her isolate as *Mycobacterium bovis*. Treatment with INH and RIF for 9 – 12 months was planned.

The patient completed 12 months of therapy for disseminated *Mycobacterium bovis* infection. At the end of therapy, a repeat CT scan showed a decrease in the pelvic fluid collection and mild thickening of the distal ileal mucosa. Multiple sub centimeter retroperitoneal and mesenteric lymph nodes were again seen but were stable. Repeat lab tests revealed CEA antigen, CA 125, ESR, and hemoglobin to be within normal ranges. She will be followed because of the extensive initial disease and the persistent abnormal CT findings. Repeat scans and laboratory tests will be done at 3 and 6 months post therapy.

Medical Issues

Tuberculosis (*Mycobacterium tuberculosis* and *bovis*) can infect the gastrointestinal tract after ingested organisms penetrate normal mucosa. This can occur in one of four ways:

1. swallowing of infected sputum coughed up from active pulmonary disease
2. hematogenous or lymphatic spread from a distant foci
3. direct extension from a contiguous site
4. ingestion of *M. bovis* infected milk products

Few patients present with intestinal TB and concurrent active pulmonary disease (20-30%) but almost 50% of smear-positive cavitating pulmonary TB patients have TB enteritis with a correlation between the severity of lung disease and intestinal involvement.

The most common region to be infected in the gastrointestinal tract is the ileocecal (80-90%) demonstrating wall thickening, ulcers, and stricture formation. The second site is the colon with segmental involvement, especially on the right side with ulcerative colitis and pseudo-polyps usually seen. Rarely, the esophagus and stomach are infected.

Most patients are young adults. The peak incidence is between the ages of 20 and 40. Females are somewhat more commonly affected than males. Diagnosis may be very difficult and less than 50% of cases are correctly diagnosed. Treatment, if started early enough, is usually successful; immunocompromised patients or misdiagnosed end-stage disseminated infections have a poor prognosis. Follow-up issues or risks for successfully treated patients include adhesions, obstructions and blockages. Female patients may suffer infertility. *M. bovis* – infected patients are always resistant to PZA and must receive at least 9 months of therapy.

Teaching Points

- Delays in diagnosis of gastrointestinal TB (GI TB) - whether caused by *M. tuberculosis* OR *M. bovis* - are due to many factors:
 - Patients usually present with non-specific symptoms of weight loss, abdominal pain, anorexia and/or ascites. Nausea or vomiting may be present, especially with an obstruction. The symptoms mimic a host of other conditions which must be ruled out.

Teaching Points continued

Type of Symptom	Percent with Symptom
Pain	90%
Abdominal Tenderness	80%
Weight Loss	70%
Nausea / Vomiting	60%
Fever	36%
Constipation	35%
Diarrhea	25%

- Patients may have non-specific laboratory findings; anemia, normal WBC count, elevated ESR, CEA, CA125, and liver enzymes. An alkaline phosphatase elevated out of proportion to other liver enzymes is suggestive of infiltrative disease of the liver.
- The TST can be variable; it is usually negative in patients presenting with primary intestinal TB or disseminated disease. A positive TST does not always indicate active disease and a negative TST does not exclude disease.
- GI TB is difficult to diagnose for many reasons:
 - Chest x-rays indicating pulmonary TB infection are positive in less than 1/3 of cases. Barium studies are helpful in 66% of patients while ultrasound and CT scans are useful for detecting peritoneal, hepatic, splenic and nodal involvement.
 - Pathology usually indicates inflammation and fibrosis of the bowel wall and the regional lymph nodes. Patients can have mucosal ulcerations; as the disease progresses ulcerations become confluent and can lead to bowel wall thickening, fibrosis and pseudo-tumoral mass lesions. Strictures and fistulae formation can occur.
 - Biopsies from areas of involvement show caseating granuloma with the presence of epithelioid cells, Langhan's giant cells and occasionally positive AFB smears (negative smears do not rule out infection).
 - Stool cultures may be positive for *Mycobacterium* sp. and should be also be ordered to rule out *Yersinia*, *actinomyces* and *amebiasis*.
 - Patients will need to have malignancies ruled out including ovarian and colon cancer. Other GI pathologies such as appendicitis, cholecystitis, and Crohn's disease need to be considered in the differential diagnosis. In the case of Crohn's disease, TB disease MUST be ruled out prior to initiating TNF α blocker therapy.
- The most common sites for TB disease within the gastrointestinal tract are:
 - Primary: ileocecal region – 44-93%
 - Secondary: ascending colon
 - Others in descending order: jejunum, appendix, duodenum, stomach, esophagus, sigmoid colon and the rectum
- Treatment - as with other forms of TB disease, GI TB responds well to the standard antitubercular therapy when started early in the disease. Surgery is reserved for management of complications. Treatment should be initiated while waiting for culture results; improvements are usually seen within 2 weeks depending on the severity of symptoms.
- GI TB is more often found in immunocompromised patients, either due to HIV, chronic renal disease, diabetes or immunosuppressive drug therapy. It may present with pulmonary TB (20-30% of patients only) but it is more commonly the primary organ system involved.

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- Primary gastrointestinal tuberculosis due to *M. bovis* should be considered when there has been a history of drinking non-pasteurized milk from areas where *M. bovis* is present in cattle herds such as along US Mexican border.

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