Unusual presentation of more common disease/injury

Multiple, large granulomas in a patient with extensive intestinal tuberculosis

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Summary

A 42-year-old patient presented with low-grade fever, pain of the right iliac fossa, constipation and tendency to vomit. Clinical examination revealed abdominal wall rigidity and rebound tenderness of the right iliac fossa. The patient was operated immediately because of an acute abdomen and the probable diagnosis of ruptured appendicitis. In laparotomy, terminal ileum, ileocaecal valve and the entire ascending colon, up to the right colic flexure, were occupied and distorted by multiple, large masses. In addition, many enlarged lymph nodes were scattered in the mesentery and the mesocolon. A right hemicolectomy was performed. Pathological examination of biopsy specimens revealed findings compatible with tuberculosis. The patient was started on empirical anti-tuberculosis treatment with a four-drug regimen. He was discharged 10 days later with marked improvement. Six months after surgery, the patient remains in very good condition without any symptoms.

BACKGROUND

Intestinal tuberculosis (ITB) is an uncommon manifestation of extrapulmonary tuberculosis (TB) in developed countries, affecting mainly immigrants or immunocompromised patients. Any part of the gastrointestinal system may be affected, especially the ileum, ascending and transverse colon. It may be classified in the ulcerative form with multiple ulcers, the hypertrophic form with scarring, fibrosis and mass-like appearance mimicking carcinoma and the ulcerohypertrophic form with mixed features (60%, 10% and 30% of cases, respectively). Patients may present with abdominal pain, weight loss, night sweats, low-grade fever, palpable mass, malabsorption or altered bowel habits. Diagnosis of ITB may be a real challenge as no diagnostic test is sensitive enough and these patients usually have a normal chest x-ray with no signs of previous TB. Treatment consists of a combined antibiotics regimen or surgical intervention in case of complications, such as perforation, haemorrhage, ileus or acute abdomen.

A rare case of a patient with multiple, large granulomas occupying the terminal ileum and the ascending colon is described below, with his consent.

CASE PRESENTATION

A 42-year-old man, from Pakistan, resident of our country's rural area for the last 5 years, presented with low-grade fever (up to 37.5°C) in the last 2 weeks, loss of weight (20 kg in 3 months), gradually deteriorating pain of the right iliac fossa, constipation and tendency to vomit. His medical history was clear, without any comorbidity that could cause immunosuppression. Clinical examination revealed abdominal wall rigidity and rebound tenderness of the right iliac fossa.

INVESTIGATIONS

Chest x-ray showed a small (<1 cm) nodule of the right upper lobe while abdominal x-ray showed dilatation of the right colon and few, small air-fluid levels of terminal ileum. An abdominal ultrasound found enlarged lymph nodes without abdominal fluid. Laboratory investigation showed: white blood cell count, 12.160/μl (neutrophils:68%); Hb, 12.4g/dl; platelets, 610 000/μl; erythrocyte sedimentation rate, 45/1h and C reactive protein: 8.3mg/dl (normal value <0.5). The rest of the laboratory findings (liver and kidney function tests, urine, creatine phosphokinase, amylase and electrolytes) were normal. HIV antibodies were negative.

DIFFERENTIAL DIAGNOSIS

The aforementioned symptoms are not specific enough for an accurate diagnosis. Many diseases may present with these clinical features. Differential diagnosis includes infections (*Yersinia* or *Salmonella* with acute manifestation and positive cultures), appendicitis, neoplasms (positive biopsy), bowel ischaemia (elderly patients), vasculitides (Henoch-Schönlein purpura, Behçet's disease, polyarteritis nodosa or systemic lupus erythematosus with more systemic manifestations), eosinophilic enteritis (eosinophilic infiltration), chronic granulomatous colitis (pigmented macrophages with lipofuscin deposits), sarcoidosis (rare manifestation of generalised disease), drug-related enteritis (mainly non-steroidal anti-inflammatory drugs) ITB and most importantly inflammatory bowel disease, especially Crohn's disease (CD).

TREATMENT

The patient was operated on immediately because of an acute abdomen and the probable diagnosis of ruptured appendicitis. In laparotomy, it was found that the

terminal ileum, ileocaecal valve and the entire ascending colon, up to the right colic flexure, were occupied and distorted by multiple, large masses, an appearance compatible with extended colon carcinoma (figure 1). In addition, many enlarged lymph nodes were scattered in the mesentery and the mesocolon. A right hemicolectomy was performed and multiple biopsies were sent for analysis. A combined drug regimen was started (ampicillin/sulbactam 1.5 g×4 with metronidazole 500 mg×3).

OUTCOME AND FOLLOW-UP

The patient remained afebrile on the second postoperative day. Blood and stool cultures were repeatedly negative. Pathological examination of biopsy specimens revealed extensive granulomatous disease with a plethora of large granulomas infiltrating the mucosa, submucosa and smooth muscles accompanied by many ulcers of the mucosa. The granulomas were confluent, with central necrosis and presence of Langerhans' giant cells. Similar granulomas were found in the terminal ileum and the ileocaecal valve as well as in the infiltrated lymph nodes. No cancer cells were detected in the specimens. These findings were compatible with TB despite negative staining (Ziehl-Neelsen, Fite) for acid-fast bacilli (AFB). Tuberculin skin test was positive (16 mm). The patient was started on

empirical anti-TB treatment with a four-drug regimen: rifampicin 600 mg/day, isoniazid 300 mg/day, pyrazinamide 1.5 mg/day and ethambutol 1 mg/day. The patient was discharged 10 days later with marked improvement. Cultures from biopsy specimens for *Mycobacterium tuberculosis* were negative. Six months after the surgery, the patient remains in very good condition without abdominal symptoms and he regained weight.

DISCUSSION

Intestinal TB is the sixth most prevalent form of extrapulmonary TB. It is common in developing countries but relatively uncommon in western countries, despite the increased incidence on account of concurrent HIV infection and immigration. Symptoms are not specific and ITB usually manifests as ileitis (probably because of the high density of lymphoid tissue aggregated in this region). Diagnosis of ITB is based on detection of AFB in biopsy specimen (low sensitivity, 25–35%), positive cultures for *M tuberculosis* (delayed diagnosis after 4–8 weeks, positive in 30% of patients), PCR for TB (modest sensitivity 40–75%) and Quantiferon-TB Gold.¹ The latter is a new test without cross-reaction to BCG or non-tuberculous mycobacteria and useful in monitoring the clinical response to treatment but unable to differentiate active from latent infection. Nevertheless, its diagnostic role in ITB still remains unclear.² On the other hand, anti-*Saccharomyces cerevisiae* antibody test, which is considered as specific for CD, was found positive in 50% of patients with ITB.

The low sensitivity of the aforementioned tests causes many difficulties in diagnosis of ITB, especially contrary to CD. Both of them are chronic granulomatous diseases sharing common clinical, endoscopic, radiological and histopathological findings. Many articles have attempted to identify findings that are highly suggestive for each disease.³ CD generally has a longer duration (usually >12 months), presents with diarrhoeas, haematochezia, perianal complications, fistula or malabsorption, relapses after surgery and a family history is common. In endoscopy, the typical finding is a cobblestone appearance with aphthoid or longitudinal deep, fissuring ulcers. CD usually involves ileum with typical sparing of the ileocaecal valve. CT reveals increased opacification of the bowel wall, the combing and abrupt tapering of the inflamed wall. In biopsy, CD is characterised by small (<200 µm), infrequent (<5), poorly organised granulomas which are located mainly in the mucosa and rarely in the submucosa or other sites.⁴

On the other hand, TB may present with a shorter duration of symptoms and high fever in the absence of any intra-abdominal abscess or perianal disease. Endoscopic findings include colitis (39% of patients), transversely placed ulcers, hypertrophic lesions resembling tumours (7%), characteristic involvement of the ileocaecal valve and stenosis with partial intestinal obstruction (54%). Perforation and fistulas are found in 19% of cases. In CT, the ileocaecal wall appears asymmetrically thickened with concurrent presence of enlarged regional lymph nodes, ascites and mesenteric thickening that may form a soft tissue mass. In histopathology, a score with eight parameters was recently suggested to differentiate ITB from CD (at least four of them): size (>400 µm) and number (>5 in one segment) of granulomas, Langerhans' giant

Figure 1 A right hemicolectomy was performed on the patient where the terminal ileum, ileocaecal valve and the entire ascending colon, up to the right colic flexure, were occupied and distorted by multiple, large tuberculous granulomas.

cells, caseating necrosis, confluent or discrete granulomas, ulcers with bands of epithelioid histiocytes and perigranulomatous lymphoid cuffs.⁵ Granulomas are typically found in abundance in the submucosa and regional lymph nodes which are commonly found in ITB.

Therefore, differentiation of ITB from CD is crucial for treatment determination. Our patient had most of the typical features of ITB. Duration of the symptoms was short without bloody stools or diarrhoeas. In laparotomy, multiple, large masses were scattered in the terminal ileum, ileocaecal valve and ascending colon with enlarged regional lymph nodes. Pathological examination of biopsy specimens revealed diffuse infiltration of the colon wall, ileocaecal valve and lymph nodes by large granulomas with histopathological findings compatible with ITB. The most reliable criterion for correct diagnosis is a good response to treatment. The patient responded very well to antituberculous treatment with complete remission of symptoms, confirming the diagnosis of ITB in such an extreme case with tumour-like, multiple granulomas.

Learning points

- ▶ Intestinal tuberculosis is an uncommon manifestation of extrapulmonary tuberculosis in developed countries.
- ▶ Diagnosis is not always feasible as no diagnostic test is sensitive enough, though highly specific, for the disease.
- ▶ The most reliable criterion for correct diagnosis is a good response to anti-TB treatment.
- ▶ Treatment consists of a combined antibiotics regimen or surgical intervention in case of complications.

Competing interests None.

Patient consent Obtained.

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