

Tubercle Rods and Its Compatriot, Crohn's: Lessons to Learn

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Abstract

Objectives: To illustrate the two closely-related challenging disease entities and the deleterious impacts of disseminated tuberculosis, together with some important literature reviews regarding the diagnosis and its sequelae.

Case: Patient is a 22-year-old male with initial presentation of chronic diarrhea and constitutional symptoms, diagnosed as intestinal Crohn's disease. Symptoms persisted despite starting him on immunosuppressive agent (mesalazine 2.0g once daily) during the second presentation. At the same time, chronic cough was reported. Physical examination showed bibasal crepitations with expiratory rhonchi on lung examination, with unremarkable abdominal examination. Investigations revealed normocytic normochromic anemia with raised inflammatory markers (C-reactive protein 13.12 mg/L, erythrocyte sedimentation rate 63 mm/hour) and coagulopathy. Subsequent chest and abdominal

radiography were suggestive of a possibility of disseminated tuberculosis involving lung and bowel. His condition deteriorated rapidly despite starting on anti-tuberculous agents and the patient expired due to refractory respiratory failure from acute respiratory distress syndrome.

Conclusion: Diagnosing and differentiating inflammatory bowel disease with bowel tuberculosis could be challenging. Let us always bear in mind about this constant threat of tuberculosis with combination and vigilant approaches to any presentations. The aims are to clinch the diagnosis early and to treat this communicable disease promptly.

Keywords: tuberculosis, Crohn's disease, immunosuppressive agent, ventilation

Introduction

Crohn's disease and bowel tuberculosis often present identically, especially with mural involvement. Diagnostic approach could be challenging in this group of patients. Any unrecognized case at early stage of presentation could have deleterious implications. Here is a case presentation of a young gentleman with disseminated tuberculosis which was thought to be Crohn's disease at first presentation.

Case Report:

Patient is a 22-year-old man presented initially to our centre with chronic diarrhea of two months duration (three to four times per day), Bristol stool of 6 to 7 with mucus, no blood. There was constitutional symptom of weight loss 6.0 kg in five months. But family history was not significant. Clinically there was no lymphadenopathy. Peripheral blood revealed normocytic normochromic anemia with monocytosis (absolute count of 13.6), but normal total

white and platelet count. Renal profile was normal. Thyroid function was normal. He was then admitted to surgical ward and colonoscopic biopsy showed chronic active colitis with ulcer and granulation tissue. There were only two specimen available for analysis (i.e. from distal ascending colon and distal transverse colon). No granuloma and negative acid fast bacilli was reported from the histopathological specimen examination. He was then subsequently referred to gastroenterology team as outpatient.

Subsequent review in the clinic (three months after discharge) diagnosed as Crohn's disease and commenced on mesalazine 2.0g once daily with the Crohn's Disease Activity Index at that time 145 (<150, good prognosis). Next review was planned in six weeks time (keep in view repeat scope or add on azathioprine).

Three weeks later, he came to our centre again with symptomatic anemia (lethargic and reduced effort tolerance for one week), and the diarrhea was persistent with no history of prolonged fever. History revisited revealed chronic cough for the past three to four months (around two to three months following the initial gastrointestinal presentations). He defaulted mesalazine for one week because the patient did not feel well. Physical reviews showed pallor and no jaundice. Blood pressure was 114

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/ 70 mmHg, pulse rate was 107 per minute, temperature 36.5°C, Oxygen saturation of 99% under room air, capillary blood sugar 6.5 (normal range: 4.1 to 6.1 mmol/L). There were bibasal crepitations with expiratory rhonchi on chest examination. Cardiovascular examination and abdominal examination were unremarkable. Per rectal examination revealed brownish stool.

Blood investigations showed haemoglobin dropped from 10 g/dL to 8.2 g/dL (2 gm) within a month (normal hemoglobin range: 13 to 17 g/dL), C-reactive protein 13.12 mg/L (1-3 mg/L), erythrocyte sedimentation rate 63 mm/hour (< 20 mm/hour), sodium 122 mmol/L (135-145 mmol/L), potassium 3.1 mmol/L (3.5- 5 mmol/L), urea 5.7 mmol/L (3.2 -7.4 mmol/L), creatinine 65.3 umol/L (70-104 umol/L), albumin 11 g/L (35-50 g/L). Coagulopathy was present with INR 2.06, APTT 46.6 s (30.16-44.29 s), and PT 22.7 s (11.6-14.1 s) (but platelet count normal: 206). Chest radiography revealed consolidations bilateral upper zones:-

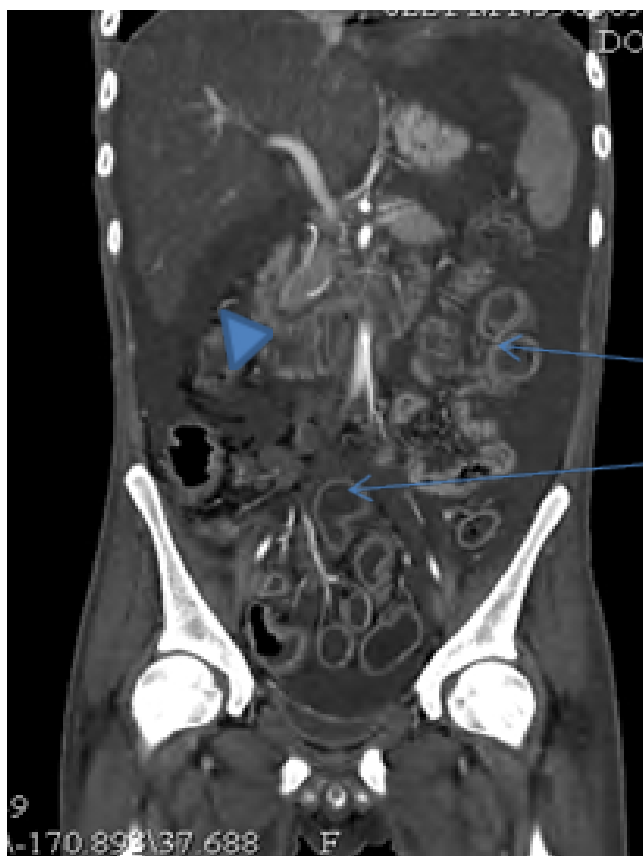


Figure 1: CT abdomen- necrotic mesenteric nodes (arrows), with thickened bowel wall (arrowhead)

Two pints packed cells were transfused and intravenous ceftriaxone 2.0g once daily was initiated to cover for intra-abdominal sepsis. Meanwhile, mesalazine was continued. One pair of intravenous parentroviite as well as peripheral total parenteral nutrition was administered in view of hypoalbuminemia and vitamin K was given to correct the coagulopathy. Computed Tomographic Angiography was arranged during current admission in view of melenic episode four days after admission. However, no active bowel luminal bleed was identified. But tree-in-bud appearance noted from lung window in the Computed Tomographic Angiography, together with mildly thickened terminal ileum and ascending colon. Multiple necrotic mesenteric nodes were also present. Left adrenal gland appeared bulky, suspicious of TB infiltration.

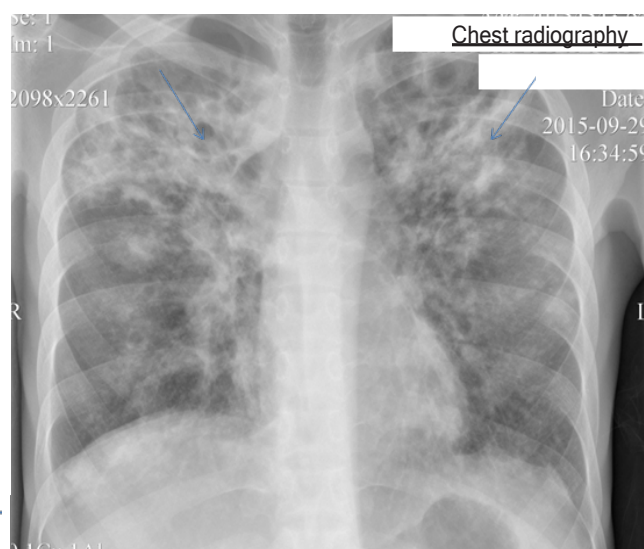


Figure 2: Chest radiography depicting bilateral upper zone consolidations (arrows)

Intravenous hydrocortisone was started with one cycle of disseminated intravascular coagulation regime given. Bridging anti-tuberculous agents (iv streptomycin 540 mg once daily, ethambutol 600 mg once daily, ciprofloxacin 500 mg twice daily, pyridoxine 10 mg once daily) were started in view of transaminitis (alanine aminotransferase = 83 U/L; normal range = 0-55 U/L). However, his condition continued to deteriorate as he developed pulmonary haemorrhage with on-going coagulopathy, culminating in acute respiratory distress syndrome. Mechanical ventilation was instituted but the progression of respiratory failure was too rapid to be salvaged. He succumbed after six days of hospitalization. Acid fast bacilli smear from the tracheal aspirate was negative (no TB culture and sensitivity was sent).

Discussion

Disseminated tuberculosis has long been known to be associated with high mortality rate. It has been reported to be differing between 25% to 30%.¹ It could involve any organs (like gut, adrenal and lung in this case). Several factors have been contemplated to have been contributing to development of such condition, for instance, immunosuppressive agents (mesalazine) as in this relevant context. There was a reported case of lung sequelae resembling TB following treatment with such therapy 10 years ago.² However, to date, there is no precise recognizable mechanism of action yet for this particular 5-aminosalicylate based therapy.³

The second part of discussion here is about the tuberculosis as a great mimicry, masquerading as a different disease entity. Inflammatory bowel disease, lymphoma, lung tumour, and vasculitis/autoimmune diseases are among the countless diseases that the tuberculosis could imitate. Numerous case reports in the past have described on tuberculosis mimicking Crohn's disease that has posed challenges upon diagnosis and treatment.^{4,5,6} The fact that the diarrhea persistent in this case and the presence of necrotic mesenteric lymph nodes with thickened bowels could well represent that this could be a case of abdominal tuberculosis even from the beginning, and later on became disseminated. Every effort and vigilant care should be exercised to look hard for the differential diagnosis of tuberculosis (abdomen in this case) before commencing definitive treatment. In this case perhaps combination of radio-graphical examinations at initial stage (eg. Chest radiography/Computed Tomography scan) to explore systemic involvement could aid in further delineating the underlying culprit lesions. A number of differentiating features have been put forward. First, the duration of illness, which appears to be shorter in tuberculosis versus Crohn's disease.⁷ Secondly, the endoscopic features, the major component, assist to a great extent, to the diagnosis of gut tuberculosis as opposed to Crohn's. (Table I)⁸

Table I: Endoscopic features of intestinal TB and Crohn's disease

	BOWEL TUBERCULOSIS	CROHN'S
ENDOSCOPIC FEATURES	circumferential ulcer	longitudinal ulcer
	abnormal surrounding mucosa (inflamed/nodular)	normal surrounding mucosa
	aphthous ulcer uncommon	aphthous ulcer
	hyperemic nodules	cobblestoning
	pseudopolyps	multiple skip lesions
	hypertrophic mucosa	anorectal lesion
	strictures (also present in Crohn's)	stricture
	destruction of ileocecal valve and/or cecum	ileocecal valve preserved

Apart from that, the histopathological finding in this patient may not be representative. The biopsy taken may not be deep enough (i.e. submucosa) to yield the acid fast bacilli/ chronic granulomatous tissues in order to rule out safely the existence of tuberculosis, rather than Crohn's. Thus, high index of suspicion is required even from the initial colonoscopic procedure itself. Furthermore, the fact that only two specimens available for analysis (i.e. from distal ascending colon and distal transverse colon) probably was not reliable in terms of Crohn's disease. As advocated by European Crohn's and Colitis Organisation, multiple biopsies from five sites around the colon (including the rectum) and the ileum are required to clinch the diagnosis.⁹

The third issue here is about the smear negative pulmonary tuberculosis (tracheal aspirate negative for acid fast bacilli). Bear in mind that more than half of cases of disseminated tuberculosis can have negative tuberculosis test. The spread of tubercle bacilli into the bloodstream could have contributed to it being undetectable in the sputum smear. Furthermore, the sensitivity of the smear microscopy has been reported to be relatively low (around 20 to 60%), especially lower among those co-infected with retroviral disease and children.¹⁰

Hence, high level of clinical suspicion is important for prompt treatment especially in this endemic area to avoid respiratory failure. Once the tuberculosis is advanced, ventilation may be compromised and becomes challenging. This patient developed acute respiratory distress syndrome from on-going pulmonary haemorrhage due to disseminated tuberculosis. Elevated death rate of between 70 to 100% has been reported among tuberculosis patients with ensuing acute respiratory distress syndrome.¹¹ Possible explanation in this case is flooded airspace with blood compromised gas exchange with resultant respiratory failure and death. Other poor prognostic factors in this case include coagulopathy and septic shock. Nonetheless, there was reported case of successful treatment of such sequel with prolonged extracorporeal membrane oxygenation,¹² and latest, the potential use of prone ventilation (PROSEVA study).¹³ In this case, however, the progression was too rapid for the institution of such therapy.

Conclusion

Anti-tuberculous therapy will need to be considered early in highly suspicious cases, especially in Malaysia as a tuberculosis-endemic country. A combination of detailed clinical history, radio-graphical investigation, endoscopic evaluation and histopathological specimen examination for any chronic abdominal presentation should always be carried out with tuberculosis in mind. Once aforementioned deadly acid fast bacilli invade systemically, prognosis is guarded.

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