**CME Article**

**Gastrointestinal tuberculosis**

Chong V H, Lim K S

**ABSTRACT**

Tuberculosis (TB) infection is still common and remains an important cause of morbidity and mortality, particularly in underdeveloped and developing nations. The gastrointestinal (GI) tract is the sixth comonest extrapulmonary site to be affected after lymphatic, genitourinary, bones and joints, miliary and meningeal involvement. Manifestations can be non-specific and mimic many conditions, including malignancies. Findings from endoscopy and radiological imaging are myriad, and depend on the stage of the disease and the time at which investigations are carried out. Hence, diagnosis can be difficult. Endoscopy is now the investigation of choice as it allows for visualisation and the sampling of tissue for histology and culture. This is complemented by radiological imaging. This pictorial essay reviews some of the endoscopic and radiological findings of non-human immunodeficiency virus associated proven GI TB infections that we have encountered in a tertiary referral centre.

**Keywords:** colonic tuberculosis, gastrointestinal tuberculosis, intestinal infection, oesophageal tuberculosis, tuberculosis

*Singapore Med J 2009;50(6):638-646*

**INTRODUCTION**

Tuberculosis (TB) infection is still common and remains an important cause of morbidity and mortality, particularly in underdeveloped and developing nations. Gastrointestinal (GI) TB is the sixth commonest extrapulmonary TB site to be affected, accounting for 3%-5% of all extrapulmonary TB involvement. Any part of the GI tract may be involved. Overall, the prevalence depends on the severity of pulmonary TB (PTB). 1% with minimally advanced, 4.5% with moderate advanced and 25% for those with severely-advanced PTB. In fatal cases of PTB, 55%-90% have GI involvement. Generally, 20%-25% of GI TB have evidence of PTB. Table I shows the frequency of GI tract involvement reported in the literature.

GI TB manifestations can be divided into three categories: the ulcerative form (60%), hypertrophic form (10%) and mass-like lesions (ulcerohypertrophic, 30%) that mimic malignancies. Manifestations depend on the host’s immune system. The ulcerative form occurs in those with a reduced immune response, whereas the hypertrophic form occurs in those with an enhanced immune system. The long axis of the ulcers is perpendicular to the long...
axis of the bowel. Healing often results in the formation of fibrotic strictures, especially if the ulcers are deep and circumferential. The hypertrophic form consists of a thickening of the bowel wall with scarring, fibrosis and a rigid mass-like appearance that mimics that of malignancies. The ulcerohypertrophic form is a subtype with a combination of the features of the ulcerative and hypertrophic forms.

The manifestations and symptom presentations (fever, weight loss, anorexia and night sweats) can be very non-specific and mimic many conditions, including malignancies. Endoscopy is the investigation of choice as it allows for direct visualisation and tissue sampling. However, it is limited by the accessibility of the small bowel. Radiological imaging, in particular computed tomography (CT) and contrast imaging, are complementary. Knowledge and awareness of the spectrum of manifestations and investigative findings are important. This pictorial essay reviews the endoscopical and radiological findings of proven GI TB infections encountered in a tertiary referral centre.

**OESOPHAGUS**

Oesophageal TB is extremely rare, accounting for only 0.15% of all TB deaths. Apart from the non-specific symptoms, common presentations include dysphagia, coughing with swallowing and haematemesis. The middle third of the oesophagus is usually involved. Direct extension from adjacent mediastinal structures is believed to be the main pathogenesis rather than through swallowed contaminated sputum or haematogeneous/lymphatic spread. The most common manifestation is a solitary ulcer with an excavating base and rolled-up nodular edges (Figs. 1a & b). Other manifestations include external compression, fistulous connections, pseudodiverticulosis and intramural dissection. Radiologically, these features are best seen on barium swallow examinations. Mucosal nodularity on barium examination can mimic oesophageal malignancies. Mediastinal involvement and sinus tract formation are best evaluated with CT. The most serious manifestation is the aorto-oesophageal fistula, which is almost universally fatal if not treated. The differential diagnosis includes carcinoma, Crohn’s disease, sarcoidosis and other infections (cytomegalovirus, human immunodeficiency virus, fungal and rarely, syphilis).
A middle-aged woman presented with chronic lower abdominal pain and weight loss. Ileoscopy photograph shows ileal nodules (white arrow) orientated perpendicular to the long axis of the bowel (bleeding from biopsy) seen just proximal to the ileocaecal valve. Histology showed caseating granuloma, giant cells and AFB (Ziehl-Neelsen stain). She also had calcifications of the liver. (b) Colonoscopic photograph shows an ulcerohypertrophic lesion in the ileum with friable mucosa secondary to tuberculosis in a middle-aged man who presented with chronic abdominal pain, weight loss and subacute bowel obstruction. The ileal lumen was obstructed. (c) Colonoscopic photograph shows a distorted caecum and ileocaecal valve due to a mass lesion in the ileum making ileocaecal valve intubation impossible in a young woman with a few months’ history of lower abdominal pain and abdominal mass. The overlying mucosa was normal. Blind biopsy of the ileum was positive for AFB. (d) Barium follow-through shows the “string sign” (white arrows) of the affected terminal ileum with dilatation of the proximal ileum (contrast study of the patient in Fig. 4c admitted for chronic abdominal pain and bowel obstruction).

STOMACH AND DUODENUM

The stomach and duodenum are rarely affected due to a combination of an acidic environment, a sparsity of lymphoid tissue and the rapid passage of swallowed mycobacterium. Clinical presentations include non-specific symptoms, abdominal pain or dyspepsia, GI bleeding and obstructive symptoms such as nausea and vomiting. Rare complications include obstructive jaundice. TB involvement is often unsuspected until the histology becomes available. Gastric TB is reported to be more common in males (2–3 times) and in those aged 20–40 years. Most patients have evidence of other organ involvement. Depending on the stage of the disease, manifestations range from localised to generalised gastric mucosa involvement. The antral-pyloric complex is commonly affected, resulting in gastric outlet obstruction. Other manifestations include pan-gastritis, non-healing ulcers (typically on the lesser curve), malignant-looking ulcers and sub-mucosal tumours (Figs. 2a & b) due to mesenteric lymphadenitis. Diffuse gastric involvement, also known as granulomatous gastritis, can mimic limitis plastica on a barium meal. The differential diagnosis includes peptic ulcer disease, malignancies, Crohn’s disease, sarcoidosis, fungal infection or idiopathic granulomatous gastritis.

The duodenum is the fourth most commonly-affected site, but over 90% of duodenal TB cases have other parts of the intestine involved. Manifestations include diffuse
Fig. 5 (a) Axial CT image shows a large lymph node, centrally hypoechoic, corresponding to caseation (white arrow), highly suggestive of TB infection in a patient with confirmed biliary TB. (b) Small bowel contrast study shows cobble-stoning (white arrow) and skip lesions characteristic of Crohn’s disease in a young man who initially presented with diarrhoea and bleeding per rectum. He later developed features of malabsorption, scrotal abscess and perianal fistula.

Fig. 6 (a) Colonoscopic photograph of a mildly inflamed ileocaecal valve with biopsy shows granuloma which is positive for AFB in a 70-year-old man who presented with weight loss, fever and neurological disorder later diagnosed as chronic inflammatory demyelinating polyneuropathy. He also had evidence of PTB. Treatment with anti-TB therapy led to resolution of the neurological symptoms. (b) Colonoscopic photograph shows another early ileocaecal valve involvement with ulceration and sloughing in a middle-aged woman with end-stage renal failure and who presented with abdominal pain. (c) Colonoscopic photograph shows an ulceration with necrotic sloughing progress as the condition progressed. (d) Colonoscopic photograph shows an ulcerohypertrophic caecum with multiple friable nodular lesions and grossly-thickened nodular ileocaecal valve with extension into the ascending colon (white arrow) in a middle-aged woman who presented with chronic abdominal pain and mass in the iliac fossa. The ileocaecal valve was thickened and incompetent.
isolated the rest of the spectrum and capsule endoscopy, endemic malabsorption postmortem. The majority (82.2%) had obstructive symptoms secondary to luminal narrowing, which consisted of ultrasonic mass lesions and regional adenopathy. Furthermore, these two conditions may coexist. The presence of centrally necrotic regional lymph nodes favours TB (Fig. 5a), whereas a cobble-stone appearance (Fig. 5b) and skip lesions favour Crohn's disease.

**JEJUNUM**

The jejunum is the third most commonly-affected site. Despite this, there are very few reports, probably as a result of difficulties in visualising this area, except in post-mortem studies. Apart from the non-specific symptoms, the most common symptom is chronic abdominal pain. Malabsorption is a well-recognised complication, probably as a result of bacterial overgrowth. Up to 70% of patients in endemic areas may have jejunal strictures. Ulcers are also common. With the advent of double balloon enteroscopy and capsule endoscopy, more cases will be diagnosed. The spectrum of lesions encountered is similar to those seen in the rest of the intestine.

**ILEUM**

The ileum is the most commonly-affected site, either in isolation or with the involvement of the adjacent bowel segments, especially the caecum. The main reasons for the predilection are due to a high density of lymphoid tissue, relatively longer faecal stasis, a neutral pH environment and absorptive transport mechanisms that allow swallowed mycobacterium to be absorbed. Common presentations include abdominal pain and an abdominal mass in the right iliac fossa. Depending on the stage of the disease, findings may range from a normal appearance to small polyps or nodules to extensive ulcerations, hypertrophic, ulcerohypertrophic and fibrotic lesions resulting in strictures, causing bowel obstructions and fistulae formations (Figs. 4a–d). Both endoscopy and radiological imaging can be used depending on the site affected. Rapid emptying of contrast, known as the “Stierlin’s sign”, is commonly seen in terminal ileum involvement due to persistent irritability of the mucosa. Bowel wall thickening, mass lesions and regional adenopathy are best seen on CT. Differentiating ileal TB from Crohn’s disease can be very difficult. Furthermore, these two conditions may coexist.

### Table 1. Sites and frequency of tuberculosis involvement of the gastrointestinal tract.

<table>
<thead>
<tr>
<th>Site</th>
<th>Frequency among GI TB (%)</th>
<th>Overall TB (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophagus</td>
<td>1-3 (4.7)</td>
<td>0.15 (0.04)</td>
</tr>
<tr>
<td>Stomach</td>
<td>NA (4.7)</td>
<td>0.1-2.3 (0.04)</td>
</tr>
<tr>
<td>Small bowel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duodenum</td>
<td>2-3 (4.7)</td>
<td>0.2-0.6 (0.04)</td>
</tr>
<tr>
<td>Jejunum</td>
<td>NA (0)</td>
<td>NA (0)</td>
</tr>
<tr>
<td>Ileum</td>
<td>38 (9.5)</td>
<td>NA (0.09)</td>
</tr>
<tr>
<td>Colon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ileoceleal</td>
<td>85-90 (38)</td>
<td>NA (0.36)</td>
</tr>
<tr>
<td>Appendix</td>
<td>NA (19)</td>
<td>≤ 4 (0.18)</td>
</tr>
<tr>
<td>Ascending colon¹</td>
<td>35 (22.8)</td>
<td>NA (0.23)</td>
</tr>
<tr>
<td>Transverse colon¹</td>
<td>16 (0)</td>
<td>NA (0)</td>
</tr>
<tr>
<td>Descending colon</td>
<td>8 (0)</td>
<td>NA (0)</td>
</tr>
<tr>
<td>Recto-sigmoid colon</td>
<td>13 (0)</td>
<td>NA (0)</td>
</tr>
<tr>
<td>Anal</td>
<td>NA (4.7)</td>
<td>NA (0.04)</td>
</tr>
</tbody>
</table>

* prevalence rates listed are based on literature searches of relevant articles. The data in parenthesis refers to the frequency in our local setting (based on data from 1997 to 2004, from National TB Coordinating Centre, NTCC).

¹ includes hepatic flexure
² includes splenic flexure

GI TB: Gastrointestinal tuberculosis; NA: Not available.

Note: Data on the prevalence of GI involvements including our local data is probably an underestimate of the actual involvements; early stages might not be diagnosed as further investigations are often not carried out once the diagnosis has been made.
Large Bowel

The colon is the second most commonly-affected site, especially the caecum and the ascending colon, decreasing in frequency with increasing distance from the caecum. Common presentations include abdominal pain, a chronic abdominal mass and altered bowel habits. Serious complications include intestinal obstruction (15%-60%), fistulae (25%), perforation (15%, with a mortality of 30%-40%) and less frequently, massive haemorrhage.

Appendix

Appendicular TB is rare, accounting for up to 2.9% of all appendectomies done in the endemic area. Presentations resemble acute appendicitis. Most are diagnosed when the histology unexpectedly show granulomas with or without caseation and AFB.

Caecum and Ascending Colon

The caecum is commonly involved, along with the terminal ileum. In the early stages, the endoscopical appearances may be normal, resemble mild non-specific colitis or consist of small polyps (Figs. 6a & b). With progression, the caecal and ileal walls become thickened, with enlargement of the draining lymph nodes. The caecum is typically involved as the ulcerohypertrophic type, resulting in mass-like lesions mimicking malignancies or Crohn’s disease (Figs. 6c & d). CT imaging may show a thickened ileum with caecal and ascending colon involvement as the disease progresses (Figs. 7a & b). A chronically-scarred caecum often assumes a deformed cone configuration, which is well appreciated on barium studies. The ileo-caecal valve usually becomes enlarged and patulous. A swollen gaping ileo-caecal valve, a cone-shaped caecum and a narrowed adjacent terminal ileum give rise to the “inverted umbrella” defect seen on barium studies, better known as the “Fleischner sign”. However, these signs may not be often present.

The ascending colon may be involved in isolation but usually occurs in association with caecal involvement. The findings are similar to those of caecal involvement. Strictures often mimic a malignancy (Fig. 8), although a short segment involvement usually gives rise to an hour-glass shaped stricture rather than an apple-core one (as with malignancy) on barium studies. Involvement can also mimic ulcerative colitis. Severe nodular or constrictive involvement can lead to bowel obstruction. Crohn’s disease...
and colon cancer can be difficult to differentiate from TB involvement endoscopically (Figs. 9a & b), and often requires histology or culture confirmation.

Transverse, descending, sigmoid colon and rectum
The involvement of these parts of the colon is more common than the stomach, duodenum and oesophagus. However, isolated involvement, also known as segmental colonic TB, is rare. The ileocelecum or the ascending colon tends to be involved simultaneously. Findings are similar to those encountered in the proximal colon. Endoscopical and radiological findings include those of non-specific colitis, aphthoid ulcers, colitis resembling inflammatory bowel disease, diminutive to large nodular polyps or mass lesions resembling colorectal malignancies. In addition to the non-specific symptoms, manifestations of segmental colonic TB include chronic abdominal pain, altered bowel habit and bleeding per rectum. Bleeding tends to be minor, although massive haematochezia have been reported.

Extra-enteric involvement
As the simultaneous involvement of other organs is common, it is important to search for the presence of TB infection in other organs, especially the chest and liver. Hepatic calcifications may be seen, ranging from a few specks to heavy calcifications (Fig. 10a). Tuberculous lymph nodes are typically centrally hypodense on CT (Fig. 5a), corresponding to caseation. Peritoneal and omental involvement give rise to large irregular masses (sometimes with central necrosis) and high density ascites (Fig. 10b). The mesentery and the peritoneum may be involved (Fig. 10c). Solid organ involvement, commonly the liver and the kidney, often manifest as calcified hypodense masses. These are best evaluated with CT. Suggestive symptoms, laboratory investigation findings of elevated erythrocyte sedimentation rates, anaemia and hypoalbuminaemia, should heighten suspicion for GI TB.

CONCLUSION
This pictorial essay underscores the varied manifestations of patients with underlying GI TB and the importance of knowledge of the different manifestations and investigative findings (endoscopical and imaging) in the management of these patients. In our patients, the findings from endoscopy and radiological imaging represent those cases that have advanced disease. As treatment for TB infections is standardised and effective, making the correct diagnosis early is very important. Clinical awareness and suspicion are very important. These should be supplemented by other investigations such as histology, culture, use of a skin test for TB exposure, and the use of more advanced tests such as the polymerase chain reaction and fluid adenosine deaminase. Knowledge of the local or regional prevalence and the spectrum of TB manifestations are also very crucial.

REFERENCES
Question 1. Concerning gastrointestinal tuberculosis:
(a) The gastrointestinal tract is the most common extrapulmonary site to be affected, accounting for 3%–5% of all extrapulmonary tuberculosis.  
(b) Manifestations can be non-specific and may mimic malignancies.  
(c) Findings are dependent on the stage and severity of the infection at the time of investigation.  
(d) Prevalence is correlated with the severity of pulmonary involvement.

Question 2. Regarding gastrointestinal tuberculosis involvement of the oesophagus and stomach:
(a) Oesophageal involvement is extremely rare.  
(b) The most common manifestation is aorto-oesophageal fistula.  
(c) Gastric manifestations mimic many conditions and a diagnosis is often made after histological examination.  
(d) Rapid transit, sparse lymphoid tissue and an acidic environment are important factors.

Question 3. Regarding the involvement of the small bowel by tuberculosis:
(a) The duodenum is the fourth most commonly-affected site and simultaneous involvement of the antrum is common.  
(b) The jejunum is rarely affected.  
(c) Ulcers and strictures are common manifestations in the jejunum.  
(d) Malabsorption is directly due to tuberculous involvement.

Question 4. Concerning tuberculous ileal involvement:
(a) The ileum is the most commonly-affected site either in isolation or in association with caecal involvement.  
(b) Abdominal pain and a right iliac fossa mass are unusual.  
(c) The “Stierlin’s sign” indicates rapid emptying secondary to persistent irritability of the ileum.  
(d) Crohn’s disease can be easily differentiated from tuberculous involvement of the ileum.

Question 5. Regarding large bowel tuberculosis:
(a) Segmental colonic involvement is very common.  
(b) Complications include bowel obstructions, fistula formation and perforation.  
(c) Appendix involvements are often incidental findings.  
(d) Differential diagnosis of colonic tuberculosis includes colorectal cancer.

Doctor’s particulars:
Name in full: ________________________________  
MCR number: ________________________________  Specialty: ________________________________  
Email address: ________________________________

Submission instructions:
(1) Log on at the SMI website: http://www.sma.org.sg/cme/smj and select the appropriate set of questions.  
(2) Select your answers and provide your name, email address and MCR number. Click on “Submit answers” to submit.

Results:
(1) Answers will be published in the SMJ August 2009 issue.  
(2) The MCR numbers of successful candidates will be posted online at www.sma.org.sg/cme/smj by 15 August 2009.  
(3) All online submissions will receive an automatic email acknowledgement.  
(4) Passing mark is 60%. No mark will be deducted for incorrect answers.  
(5) The SMI editorial office will submit the list of successful candidates to the Singapore Medical Council.