CHRONIC DIARRHEA: AN UNUSUAL SYMPTOM OF GASTROINTESTINAL TUBERCULOSIS

Nathan David P. Concepcion and Gemma U. De Lima
St. Luke's Medical Center, Philippines

Abstract

Tuberculosis can affect practically any organ, as well as any segment of the gastrointestinal tract. The usual symptoms of gastrointestinal tuberculosis are colicky abdominal pain, weight loss and low grade fever. Chronic diarrhea is an uncommon symptom, but this may occur in the ulcerative type of intestinal TB. This article is intended to review the various imaging findings of gastrointestinal TB.

Key Facts

Clinical symptoms

- Constitutional symptoms occur in 33% of abdominal TB
- Chronic diarrhea seen in intestinal TB having mucosal ulceration

Pathogenesis

- Possible routes of spread:
  - ingestion of the TB bacilli;
  - hematogenous spread from a primary lung focus during childhood with subsequent reactivation;
  - through the lymphatics from infected nodes; and
  - direct spread from other adjacent infected structures

- Classified into ulcerative and ulcerohypertrophic

Introduction

Abdominal tuberculosis (TB) can occur at any age but is less common in children. It is more frequently seen in young adults and peaks at 20-40 years of age [1,2,3]. It constitutes about 12% of extra-pulmonary TB [4] and about 10% of all cases under the age of 10 years. [5]. There is little risk of transmission for extra-pulmonary TB, but a concomitant pulmonary disease may spread the disease [3].

The abdominal TB usually occurs in following four forms depending on the affected parts (in descending incidence): nodal, peritoneal, gastrointestinal and visceral or solid organ involvement [1,3,5,6,7,8,9,10].

The gastrointestinal tract from mouth to anus may be involved in abdominal TB. It can have a varied presentation and can mimic both common and rare diseases [4].

Clinical Presentation

Symptomatology of abdominal TB depends on the site of disease and the type of pathological involvement. Most patients usually present with colicky abdominal pain (80-95%) with or without vomiting, weight loss (40-90%), low grade fever (40-70%), anemia, night sweats, anorexia and malaise [6]. These constitutional symptoms are present in about one-third of patients [1].

Diarrhea is an uncommon symptom in TB, but can occur in about up to 29% [4,11]. At a case series by Zamora, et al. (2011) in the Philippines, only about 7% presented with diarrhea (a). This symptom, especially if chronic, may be observed in patients with intestinal tuberculosis demonstrating mucosal ulceration [1]. One study done by Ridaura-Sanz, et al. (2012) however conversely demonstrated that diarrhea was observed in 76% of patients. In this study, ulceration was observed in 82% of patients with intestinal TB [10].

Radiologic approach

- Radiographs may show signs of obstruction and/or perforation.
- Contrast studies are best to demonstrate the intestinal mucosa.
- Ultrasound is limited but is better than CT in the detection of ascites.
- CT provides evaluation of all abdominal organs but is the imaging modality of choice in the assessment of nodal, peritoneal and visceral types of abdominal TB

Gastrointestinal TB

- Most common involved area is the ileocecal region followed by the jejunum and colon due to increased rate of fluid and electrolyte absorption, abundance of lymphoid tissue, increased physiologic stasis and minimal digestive activity

Radiographic signs suggestive of ileocecal TB

"Fleischner" or "inverted umbrella" sign
- thickening of the valve or wide gaping of the valve with narrowing of the terminal ileum

"Chicken intestine"
- hypersegmentation of the contrast column

"Hourglass stenosis"
- luminal stenosis with smooth but stiff contours

Chronic diarrhea is also non-specific and may be seen in amebiasis, giardiasis, Yersinia infection, intestinal malabsorption and protein-losing enteropathy, small bowel stricture, malignancy, ulcerative colitis, Crohn's disease, peritoneal involvement, abdominal abscess or fistula [8,12,13,14].

Pathogenesis

TB can involve virtually any organ in the body. There are various ways tuberculosis can spread into the abdomen and gastrointestinal tract. One route is through ingestion of the tuberculous bacilli which eventually go into the tubular glands of the intestinal mucosa and lymphoid tissue in the submucosa. The second path is from hematogenous spread from a primary lung focus during childhood with subsequent reactivation. Another mechanism is through the lymphatics from infected nodes. Lastly, tuberculosis of the gastrointestinal tract can also come from direct spread from other adjacent infected structures [4,5,6,7,12,15,16].

Organisms involved are *Mycobacterium tuberculosis* and *M. bovis* [4]. Primary intestinal tuberculosis is usually caused by *M. bovis* and results from ingestion of contaminated milk from infected cows [4,8,10,17].

Radiologic Approach to Diagnosis

Radiographic findings are nonspecific. Barium contrast studies remain superior for demonstrating the mucosal lesions of gastrointestinal TB [7].

Abdominal ultrasound is seldom helpful and limited in the detection of lymphadenopathy and peritoneal involvement due to the presence of bowel gas. However, it is better than computed tomography (CT) in the detection of ascites [2,5].

CT with its multi-planar capability, provides detailed evaluation of all features in a single study including solid, fluid-filled and hollow organs, particularly of the intra- and retroperitoneal compartments [5,6]. CT is the imaging modality of choice in the detection and assessment of the nodal, peritoneal and visceral types of abdominal TB [7].

Magnetic Resonance Imaging (MRI) may also show similar findings as with CT but motion (from bowel peristalsis) and breathing artifacts limit the use of MRI. One advantage over CT is that there is no ionizing radiation.

Other radiographic signs suggestive of ileocecal TB

"Goose neck deformity"
- loss of normal ileocecal angle and dilated terminal ileum, appearing suspended from a retracted, fibrosed cecum

"Stierlin sign"
- lack of barium retention in the ileum, cecum and ascending colon, with a normal configured column of barium on either side; narrowing of the terminal ileum with rapid emptying into a shortened, rigid or obliterated cecum

"String sign"
- persistent narrowing / stenosis of the terminal ileum, sometimes annular ("napkin ring") or with dilatation of the more proximal ileal segment ("purse string")

Laboratory Diagnosis

- high index of suspicion should be present
- biopsy with histologic evidence remains the gold standard in the diagnosis of abdominal TB
- hallmark of TB is caseation necrosis

Gastrointestinal Tuberculosis

Gastrointestinal TB was originally classified in adults into hyperplastic, ulcerohyperplastic and ulcerative types by Hoon et al. (1950), and alternatively into ulcerative and ulcerohypertrophic types by Tandon and Prakash (1972). The ulcers are usually seen in the small intestines. TB in the colon and ileocecal region is usually ulcerohypertrophic and may mimic Crohn's disease (CD) [4,7]. The ulcerative type of intestinal TB can present with chronic diarrhea while the hypertrophic type may simulate neoplasms [1]. There is no clear distinction between these types, and co-existence may occur [7].

The most common area of involvement in the gastrointestinal tract is the ileocecal region followed by jejunum and colon [7]. This is said to be due to increased rate of fluid and electrolyte absorption, abundance of lymphoid tissue, increased physiologic stasis and minimal digestive activity [4,7,13,16,18].

Ileocecal TB

The ileocecal region, particularly the terminal ileum, is the most common site of gastrointestinal TB involvement, with reported incidence ranging from 64% [7] to 90% [1,6,11,12,13,15,17]. The terminal ileum, ileocecal junction and the cecum are concurrently involved in the majority of cases.

The most common complication is obstruction due to luminal narrowing caused by the hyperplastic mural thickening at the cecum, ileal strictures and/or by adhesions [4,7]. Malabsorption is also a common complication and may present with chronic diarrhea [4].

Plain abdominal radiographs show nonspecific findings such as enteroliths, signs of obstruction (e.g. dilated bowel loops with multiple air fluid levels), or pneumoperitoneum to indicate perforation [7].

Administration of oral contrast may be of help to diagnose ileocecal TB. Early in the disease, there may be spasm and hypermotility followed by thickening of the ileocecal valve [7,9,19]. Aphthous ulcers may also be observed at the onset [9,11,13,20]. In later stages, the terminal ileum shows annular stenosis. The cecum classically becomes amputated or conical and retracted [9,13,19,20].

Several radiographic signs have been described for ileocecal TB:

1. **"Chicken intestine"** - hypersegmentation of the contrast column

2. **"Hourglass stenosis"** - luminal stenosis with smooth but stiff contours

3. **"Fleischner" or "inverted umbrella" sign** - thickening of the valve or wide gaping of the valve with narrowing of the terminal ileum [7,9,13,18,20]

4. **"Goose neck deformity"** - loss of normal ileocecal angle and dilated terminal ileum, appearing suspended from a retracted, fibrosed cecum.

5. **"Stierlin sign"** - lack of barium retention in the ileum, cecum and ascending colon, with a normal configured column of barium on either side; narrowing of the terminal ileum with rapid emptying into a shortened, rigid or obliterated cecum [7,13]

6. **"String sign"** - persistent narrowing indicating stenosis of the terminal ileum, sometimes annular ("napkin ring") or with dilatation of the more proximal ileal segment ("purse string"). (*Figure 1*)

Both Stierlin and String signs can also be seen in CD and hence are not specific for TB.
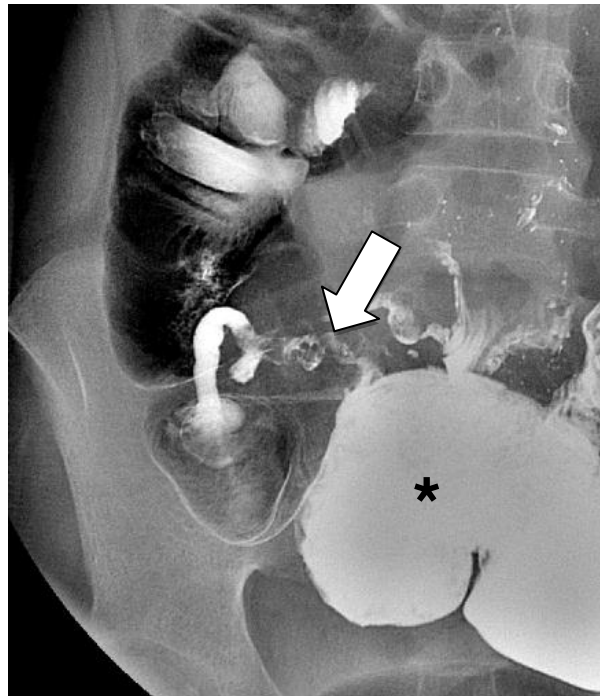
Figure 1. A 15-year old female who underwent a small intestinal series showing "string"-like narrowing (*arrow*) of the terminal ileum with a dilated more proximal ileal segment (*asterisk*).

Computed tomography may show concentric wall thickening in the cecum and terminal ileum (*Figure 2*) with mesenteric lymphadenopathy that show central areas of low attenuation indicative of caseous necrosis. It may also be eccentric and usually affect the medial wall of the cecum. There could be exophytic extension with engulfment of the terminal ileum. These are more consistent with TB rather than CD, lymphoma or carcinoma [7,9,10,18,19,20].
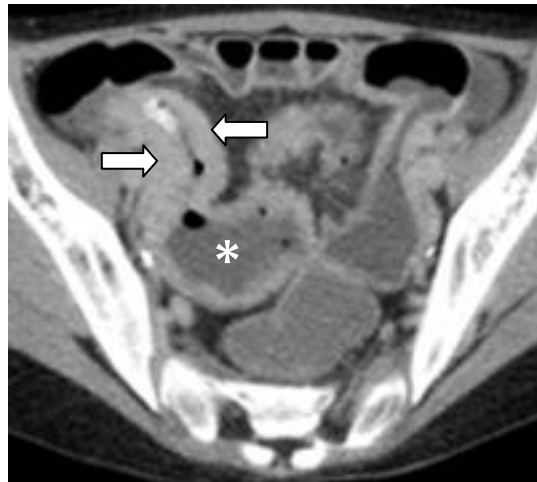
Figure 2. Computed tomography showing the typical mural thickening in the terminal ileum (*arrows*) with dilatation of the more proximal ileal segment (*asterisk*).

Multiple segment concentric narrowing involving the jejunum and ileum (*Figure 3A-C*) can also be seen. According to Debi et al. (2014), enteroclysis followed by barium enema may still be the best protocol for evaluation of intestinal TB [7].
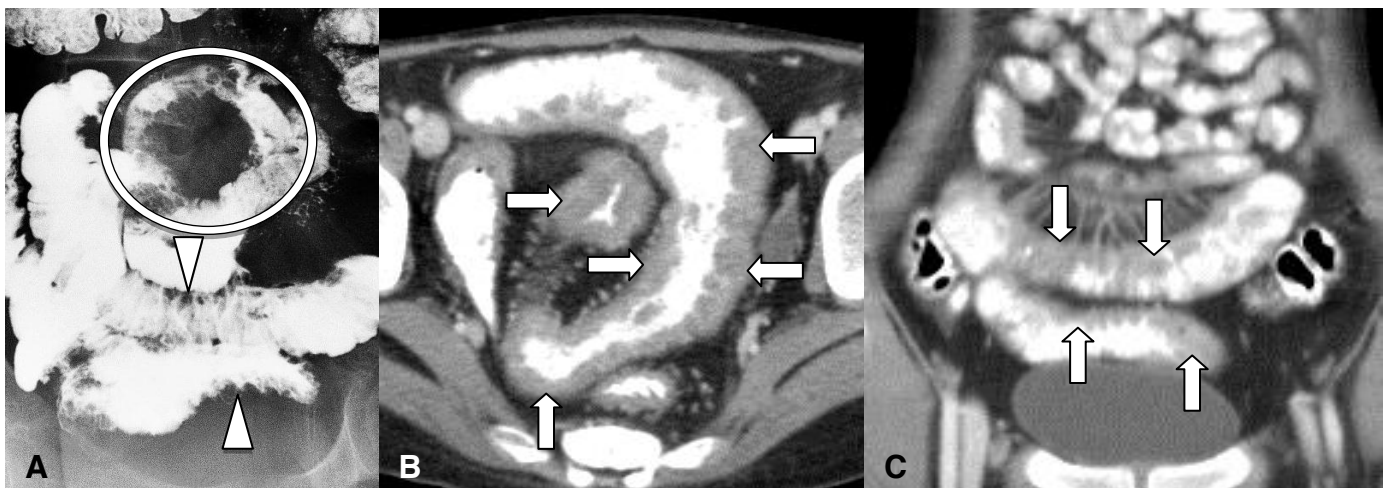
Figure 3A-C. Small intestinal series shows irregular mucosal outline (*arrowheads*), separation of loops (*encircled*) and CT scan demonstrating mural thickening (*arrows*) in various segments of the intestinal tract of a 13-year old. (A-C) ileum, (D-E) rectosigmoid colon and (F-H) descending duodenum

Jejunal TB

The jejunum, if affected, is more commonly seen in patients with ileocecal TB. Isolated jejunal involvement however is rare, and if present, may mimic CD [7]. Kolawole in 1975 recorded 22 (16%) patients with jejunal TB among 136 gastrointestinal TB cases [16].

Small bowel series may reveal a disordered small bowel pattern characterized as segmental dilatation [16] or separation [20] of the jejunal loops, with dilution and delay in transit of the contrast medium through the small intestines [16]. Strictures, single or multiple, with short or long segment involvement have also been documented [7], more towards the proximal jejunum [16].

Colorectal TB

Isolated involvement of the colon is about 11% and may increase in the immunocompromised patients including patients with AIDS. Isolated or segmental colon involvement apart from cecum varies between different studies. According to Shah, et al. (1992), the most common site was transverse colon, followed by rectum, (*Figure 3D-E*) and ascending colon. Vij in 1992 [11] showed that the hepatic flexure was the most common site of colorectal TB. A more recent study by Mukewar (2012) however, mentioned that the ascending colon was most common, followed by transverse colon, and then descending colon. Multifocal involvement is seen in 28-44% of cases with colorectal TB [7].

The imaging findings in the early stage of colorectal TB are nonspecific and include spasm and hypermotility of the intestine. Strictures are the most common radiologic features, followed by colitis and polypoid lesions. Complications in the form of perforations and fistulae, as with other forms of GI TB, can also be seen in up to 18.9% of cases [7].
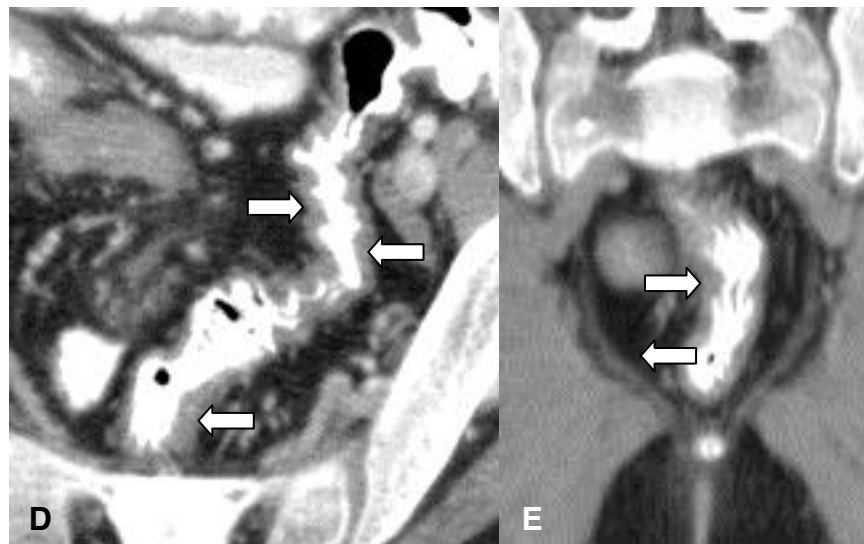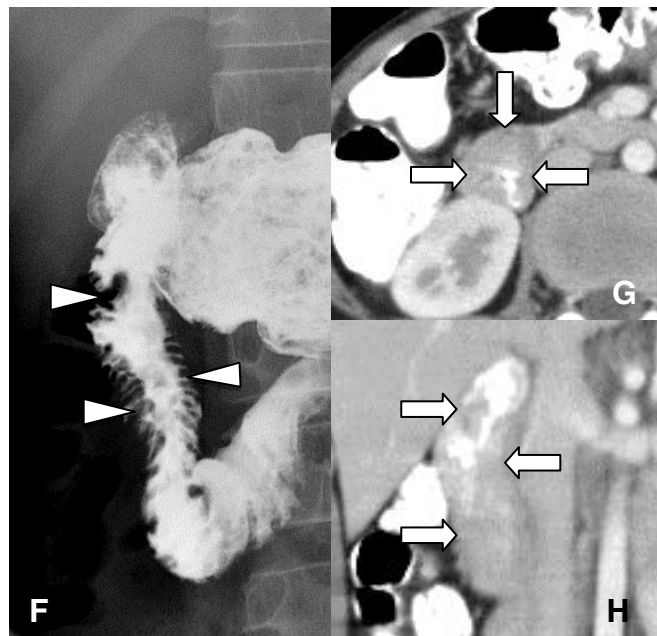

Figure 3D-E. Small intestinal series shows irregular mucosal outline (*arrowheads*), separation of loops (*encircled*) and CT scan demonstrating mural thickening (*arrows*) in various segments of the intestinal tract of a 13-year old. (A-C) ileum, (D-E) rectosigmoid colon and (F-H) descending duodenum

TB of the esophagus, stomach and duodenum are rare, which may be attributed to scanty lymphoid tissue in the stomach [4,16,20], thick gastric mucosa, rapid passage through the stomach [4,16], and bactericidal property of the acid [7].

Duodenal TB

Duodenal TB is only about 1% of abdominal TB and 2-2.5% of all gastrointestinal TB cases [4,7]. It often occurs in isolation, without pulmonary lesions in more than 80% of cases [4].   The third duodenal portion (transverse segment) is the most common site [7].

Contrast studies demonstrate presence of nonspecific narrowing (''string sign''). Cross sectional imaging also demonstrates luminal narrowing due to extrinsic compression from adjacent infected lymph nodes and/or intrinsic mural thickening (*Figure 3F-H*), the former being more common. In later stages, strictures and fistulas have been noted [7].

Figure 3F-H.   Small intestinal series shows irregular mucosal outline (*arrowheads*), separation of loops (*encircled*) and CT scan demonstrating mural thickening (*arrows*) in various segments of the intestinal tract of a 13-year old. (A-C) ileum, (D-E) rectosigmoid colon and (F-H) descending duodenum

Gastric TB

The gastric involvement is usually associated with pulmonary tuberculosis (PTB) or in the immunodeficient state. Primary involvement of the stomach is rare (0.4-2%) [4,7]. The antrum and distal body are usually affected [7,19].

On imaging, these lesions most commonly appear as benign ulcers or erosions lesion along the lesser curvature and pylorus. In the later stages, distortion and pyloric stenosis may ensue [7].

Esophageal TB

Involvement of the esophagus accounts for only 0.2-1% of gastrointestinal TB, but it is more commonly seen in AIDS patients [4,7]. It is usually secondary to an extrinsic compression due to contiguous tubercular mediastinal nodal involvement [7,19].

On barium studies, extrinsic TB is seen as narrowing or displacement of esophagus especially at the middle third or at the level of the carina. In late stages, ulcers, strictures and fistulae are formed. Traction diverticulae can likewise occur in fibrotic mediastinal disease [7,16].

Table 1. Summary of Gastrointestinal Findings

Segment/s involved	Incidence	Common location	Early stage	Late stage
Ileocecal	64-90%	terminal ileum, ileocecal valve and cecum	spasm and hypermotility, thickening of the valve, aphthous ulcers	luminal narrowing due to mural thickening, strictures and adhesions; amputation of cecum
jejunal	16%	Proximal jejunum	disordered small bowel pattern: segmental dilatation or separation of loops, dilution and delay in transit of the contrast medium through the intestines; strictures	
colorectal	11%	transverse colon (*Shah 1992*); hepatic flexure (*Vij 1992*); ascending colon (Mukewar 2012)	spasm and hypermotility	strictures, colitis and polypoid lesions; perforation and fistula
duodenal	2-2.5%,	third (transverse) portion	extrinsic narrowing due to adjacent nodes **>** intrinsic wall thickening	stricture and fistula
gastric	0.4-2%,	lesser curvature and pylorus	intrinsic benign ulcers or erosions	distortion and pyloric stenosis; sinus or fistula
esophageal	0.2-1%	middle segment, level of carina	extrinsic narrowing or displacement due to adjacent nodes	ulcers, strictures and fistulae

Other Differential Considerations

Intestinal TB has diverse clinical presentations which are mostly vague and non-specific, thus making the diagnosis difficult. It may clinically and radiographically mimic various medical and surgical conditions. Therefore, it should be highly considered in patients with prolonged and unexplained abdominal symptoms like diarrhea particularly in endemic locations.

Diarrhea due to mucosal ulceration may be seen in gastrointestinal TB [1,21], particularly in patients with ileocecal with or without jejunal TB. However, this symptom is more common in inflammatory bowel diseases such as Crohn's disease [21]. Both are chronic granulomatous diseases and in areas where TB and CD incidences overlap, differentiation may be challenging. Aphthous ulcers in TB are larger and more linear / stellate when compared to those in CD [9,11,13,20].

Differential diagnoses may depend on which segment is involved. In TB of the esophagus, tumors have to be ruled out. Gastric involvement can mimic peptic ulcer disease, but presence of a sinus or fistula suggests tuberculosis [7,19]. Carcinoma, lymphoma and syphilis may also appear similarly [7,20]. When the duodenum is affected, superior mesenteric artery syndrome may have comparable findings [7]. Pancreatic or peripancreatic masses may also be possible [16].

Other types of colitis such as pseudomembranous and ischemic colitis, and malignancy are likewise included in the differential diagnosis of TB colitis [7,13]. However, presence of eccentric medial cecal involvement with exophytic extension and engulfment of the terminal ileum are more consistent with TB rather than CD, lymphoma or carcinoma [7,9,10,18,19,20]. Cecal amputation in ileocecal TB may also be seen in amebiasis. However, amebiasis rarely involves the small bowel [9,13,19,20].

Laboratory Diagnosis

Clinical, laboratory and radiological features are nonspecific. A high index of suspicion should be present. Biopsy with histologic evidence remains the gold standard in the diagnosis of abdominal TB [6]. The hallmark of TB is caseation necrosis [7,10]. A combination of histology and culture of the biopsy material can be expected to help establish the diagnosis.

Biopsy however may not be feasible in some cases. In such cases, the diagnosis of abdominal TB may be inferred based on a combination of the following: [4,5]

1. Culture or identification of *M. tuberculosis* in the sputum of a patient with abdominal symptoms and signs suggestive of TB.
2. A positive Mantoux or Tine skin test, although present in only 50-78% of abdominal TB cases
3. Documented TB infection elsewhere in the body
4. Positive TB culture of the ascitic fluid
5. Increased alpha-interferon and/or adenosine deaminase levels in the ascitic fluid
6. Response to appropriate anti-TB therapy

Conclusion

Intestinal TB has diverse clinical presentations which are mostly vague and non-specific, thus making the diagnosis difficult. It may clinically and radiographically mimic various medical and surgical conditions. It should be considered in patients with prolonged and unexplained abdominal symptoms like diarrhea.

In the absence of histopathologic evidence, pattern recognition of the radiologic findings can help in the diagnosis of TB. A high clinical index of suspicion is also necessary to obtain an accurate diagnosis.

References

1. Sood R. Diagnosis of abdominal tuberculosis: role of imaging. *J Indian Acad of Clin Med* 2001; 2(3): 169-177.
2. Andronikou S and Wieselthaler N. Modern imaging of tuberculosis in children: thoracic, central venous system and abdominal tuberculosis. *Pediatr Radiol* 2004; 34: 861-875.
3. Perez-Solis D, et al. Disseminated Tuberculosis. *Radiology* 2006; 238: 366-370.
4. Sarkar DN, et al. Abdominal tuberculosis - A Review. *Bangladesh J Med* 2011; 22: 51-59.
5. Andronikou S, Welman CJ and Kader E. The CT features of abdominal tuberculosis in children. *Pediatr Radiol* 2002; 32: 75–81.
6. Zamora JMB, Laya BF and Bautista MW. Computed tomography scan manifestations of abdominal tuberculosis in children. *St. Luke's J Med* 2011; 7(1): 43-50.
7. Debi U, et al. Abdominal tuberculosis of the gastrointestinal tract: Revisited. *World J Gastroenterol* 2014; 20(40): 14831-14840.
8. Tinsa F, et al. Abdominal Tuberculosis in Children. *JPGN* 2010; 50 (6): 634-638.
9. Engin G, et al. Imaging of Extrapulmonary Tuberculosis. *Radiographics* 2000; 20: 471-488.
10. Zissin R, et al. Computerized Tomography Findings of Abdominal Tuberculosis: Report of 19 Cases. *IMAJ* 2001; 3: 414-418.
11. Vij JC, et al. A Clinicopathological Study of Abdominal Tuberculosis. *Ind J Tub* 1992; 39: 213-220.
12. Epstein BM and Mann JH. CT of the Abdominal Tuberculosis. *AJR* 1982; 139: 861-866.
13. Harisinghani MG, et al. Tuberculosis from Head to Toe. *Radiographics* 2000; 20: 449-470.
14. Abad CL, et al. A Gut Instinct. *N Engl J Med* 2014; 371: 560-564.
15. Yang Z-G, et al. Tuberculosis Versus Lymphomas in the Abdominal Lymph Nodes: Evaluation with Contrast- Enhanced CT. *AJR* 1999; 172: 619-623.
16. Kolawole TM and Lewis EA. A radiologic study of tuberculosis of the abdomen (gastrointestinal tract). *Am J Roentgenol Radium Ther Nucl Med* 1975; 123(2): 348-58.
17. Ridaura-Sanz C, et al. Clinical Study Intestinal/ Peritoneal Tuberculosis in Children: An analysis of autopsy cases. *Tuberculosis Research and Treatment* 2012; 1-6.
18. Balthazar EJ, Gordon R and Hulnick D. Ileocecal Tuberculosis: CT and Radiologic Evaluation. *AJR* 1990; 154: 499-503.
19. Burrill J, et al. Tuberculosis: A Radiologic Review. *RadioGraphics* 2007; 27:1255–1273.
20. Jadvar H, et al. Still the Great Mimicker: Abdominal Tuberculosis. *AJR* 1997; 168: 1455-1460.
21. Pulimood AB, et al. Differentiation of Crohn's disease from intestinal tuberculosis in India in 2010. *World J Gastroenterol* 2011; 17(4): 433-443.

Corresponding author:
Nathan David P. Concepcion
St. Luke's Medical Center, Philippines
npconcepcion@stluke.com.ph