

# Intestinal Tuberculosis versus Crohn's Disease: Evaluating the Role of Computed Tomography Enterography in Differentiating the Two

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## Abstract

Intestinal tuberculosis (ITB) and Crohn's disease (CD) are chronic inflammatory bowel disorders that are frequently misdiagnosed due to overlapping clinical, radiologic, endoscopic, and histologic resemblance. Recent trends indicate a change in the epidemiology of inflammatory bowel diseases, with previously low-incidence areas now reporting a continuous rise in incidence. The rising incidence of CD in countries such as India where TB continues to be endemic has made the differentiation of these two disorders a diagnostic challenge. Misdiagnosis leads to delays in initiating effective therapy with increased morbidity and mortality, hence the importance of making an accurate diagnosis at the earliest possible stage. This study aimed to evaluate the diagnostic value of computed tomography enterography findings in the differential diagnosis between ITB and CD.

## Keywords

- ▶ Crohn's disease
- ▶ computed tomography enterography
- ▶ intestinal tuberculosis

## Introduction

Crohn's disease (CD) and intestinal tuberculosis (ITB) are chronic granulomatous diseases that due to their overlapping clinical, endoscopic, and pathological findings are difficult to differentiate.<sup>1,2</sup>

The disease course of ITB is quite different from that of CD. ITB can be completely cured if diagnosed early and treated properly. However, CD is prone to recurrences, hence lies the importance of making accurate diagnosis at the earliest possible stage.<sup>3,4</sup>

Plain abdominal radiographs have little role in making a diagnosis of ITB or CD. Chest radiograph may show features of active or healed tuberculosis in up to 15% of patients.<sup>5</sup>

Barium meal follow-through (BMFT) may show thickening of mucosal folds, ulcerations, strictures, dilatation, and clumping of bowel loops in both these diseases and provides information on bowel motility.<sup>6,7</sup> However, this study takes a long time, is two dimensional, and provides no extraluminal information.

Barium enteroclysis has a higher sensitivity for detecting mucosal abnormalities and strictures.<sup>8,9</sup> It achieves good

distension of the small bowel loops to enable the detection of early abnormalities. Its disadvantages include discomfort to the patient due to the nasojejunal tube and active bowel distension, radiation and lack of information regarding the bowel wall, and extraintestinal manifestations.

Ultrasonography (USG) is a simple and widely available modality without the effects of ionizing radiation; however, it is not very useful in the differentiation of ITB from CD. The other limitations include operator dependence, bowel gas, obesity, and long scan times required for complete evaluation.

Computed tomography (CT) is often the initial investigation performed for the evaluation of suspected bowel pathology. The positive contrast only depicts bowel wall thickening, stricture, and dilatation, but not mucosal abnormality, and does not provide adequate distension of the bowel. CT enteroclysis is performed after inserting a nasojejunal tube and injecting neutral contrast agent to provide adequate distension of the small bowel.<sup>10</sup> The tube and active bowel distension often causes discomfort to the patient.

CT enterography (CTE) combines the improved spatial and temporal resolution of multiple detector row CT with

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large volumes of ingested neutral enteric contrast material to permit visualization of the small bowel wall and lumen. CTE can image the entire gastrointestinal tract and characterize extraintestinal manifestations, such as the lymph nodes, mesenteric changes, mural stratification, fibrofatty proliferation, fistulae, abscesses, adjacent organ involvement, and ascites that have an important role in differentiating CD and ITB.

Magnetic resonance enterography (MRE) recently has been gaining in popularity, especially for follow-up imaging of pediatric and young patients with established inflammatory conditions of the small bowel.<sup>11,12</sup> The lack of ionizing radiation is an advantage of MRE over CTE, especially when evaluating patients with known renal dysfunction. However, MRE is time consuming, expensive, and has variable reproducibility regarding image quality as compared with CTE.

## Technique

Patients are requested to abstain from all food and drink for 4 hours prior to scanning. Bowel is distended passively by ingesting neutral oral contrast agents, which include water, polyethylene glycol solution, or VoLumen (low-density barium in sorbitol), adding osmotic agents such as mannitol, sorbitol, or polyethylene glycol improves bowel distension.<sup>13,14</sup> We used mannitol (20%) that is prepared by diluting 400 mL of mannitol in 1,500 mL of water. This solution is ingested over 45 minutes, and the patient is scanned subsequently. The last 250 to 300 mL is ingested on table, just prior to scanning for gastric distension, and the patient is made to lie in right lateral decubitus for 3 to 5 minutes; 20 mg Buscopan is administered intravenously (IV) immediately prior to scanning to reduce bowel peristalsis.<sup>15</sup> Scanning was done in enteral phase acquired at 45 seconds, and bowel wall shows maximal enhancement in this phase<sup>16</sup> using 128-slice MDCT scanner (Philips Ingenuity, Suzhou, China) and 1.5 mL/kg of iohexol (Omnipaque 350 mg/mL 50 mL, GE Health Care, Shanghai, China). Summary of technique<sup>15</sup> is mentioned in ► **Table 1**.

Postprocessing techniques include reformatting of axial image data for coronal, sagittal, and maximum intensity projections.

Multiplanar reformatting of axial image data allows excellent demonstration and characterization of enteric and

extraenteric abnormalities.<sup>17</sup> Maximum intensity projection images are useful particularly for visualizing the mesenteric vasculature.

## Intestinal Tuberculosis

The incidence of extrapulmonary TB is 15 to 20%, with 3% affecting the abdomen including the small bowel. Abdominal TB is the sixth most common extrapulmonary site of involvement. Only 15% of patients with abdominal TB have evidence of pulmonary disease, and chest radiography may be normal in 50 to 65% of these patients.<sup>5,18</sup>

ITB can be divided into three categories—ulcerative, hypertrophic, and ulcerohypertrophic—with the ulcerative type being the most common. Manifestations depend on the host's immune system. The *ulcerative form* occurs in patients with reduced immune response, where healing often results in the formation of fibrotic strictures, especially if the ulcers are deep and circumferential. The *hypertrophic form* consists of bowel wall thickening with scarring, fibrosis, and a rigid mass-like appearance that mimics that of malignancies. The *ulcero-hypertrophic form* is a subtype with a combination of the features of the ulcerative and hypertrophic forms.<sup>19</sup>

Imaging in the form of barium studies were the initial investigation for intestinal TB, but in the past decade, CT scan and, recently, CTE have almost replaced barium studies due to a better depiction of mural and extraintestinal involvement.

Abdominal tuberculosis may affect any part of bowel from the duodenum to rectum, but the most frequent site of ITB is ileocecal area (~90% in case of gastrointestinal TB). The sites of involvement in descending order of frequency are the ileocecal junction, followed by the ileum, caecum, ascending colon, jejunum, rest of the colon, rectum, duodenum, and stomach.<sup>20</sup>

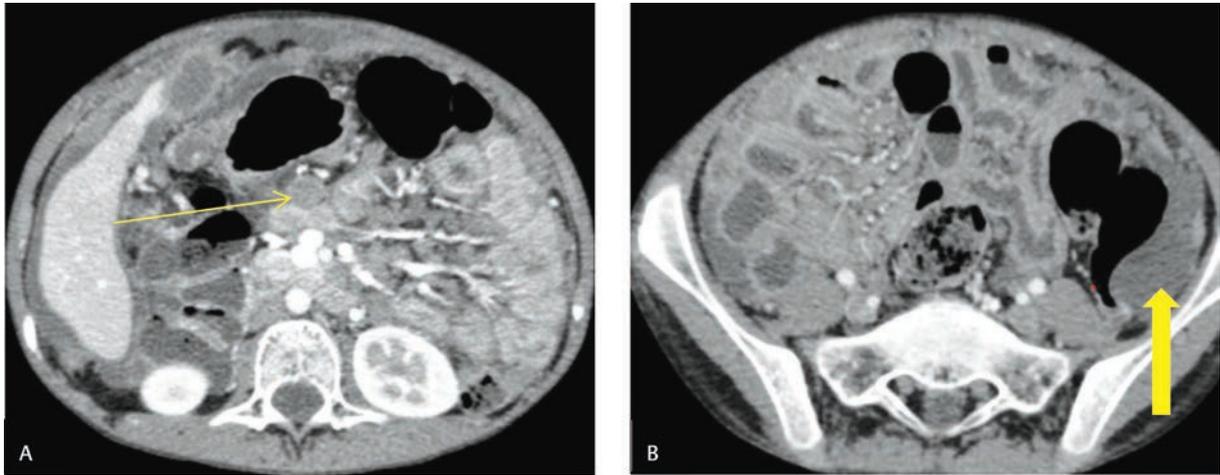
Peritoneal TB is the most common form of abdominal TB and involves alone or in combination with the peritoneal cavity, mesentery, and omentum. Three types of peritoneal TB are described<sup>21,22</sup>: *wet type* with ascites or pockets of loculated fluid (► **Figs. 1 and 2**); *dry type* with bulky mesenteric thickening and lymph adenopathy (► **Fig. 3**); and *third type* with mass formation due to omental thickening that may be mistaken for a tumor.<sup>21</sup>

Active ileocecal disease is characterized by circumferential wall thickening of terminal ileum, ileocecal junction, and cecum with narrowed lumen (► **Figs. 4–6**). Dilatation of the proximal bowel segment may be seen. Another predictor of active inflammation is enhancement of mucosa or the entire wall. Intestinal wall thickening is usually homogeneous without stratification. Wall stratification seen in CD results from contrast enhancement of mucosa and muscularis, with hypodense edema of submucosa causing a layered appearance.

Healing results in short-segment strictures that are seen as short segments of wall thickening without wall enhancement or stratification with proximal bowel dilatation.<sup>20</sup> Ileocecal valve may also become scarred with stricture and subsequent dilatation of the terminal ileum, which rarely may become patulous with loss of valve function. Usually,

**Table 1** Summary of the technique

1. Withhold all oral intake 4 h prior to examination
2. 1.5–2 L of oral neutral contrast (20% mannitol) given over 45 min, last 200–250 mL ingested on table prior to scanning for gastric distension
3. 20 mg Buscopan administered intravenously (IV) prior to scanning
4. 1.5 mL/kg of iohexol (max 150 mL) administered IV at 4 mL/s via 18-gauge cannula using automated power injector
5. Scanning is performed from diaphragm to symphysis pubis. Images acquired at 45 s post-IV contrast administration
6. 128-slice multiple detector computed tomography (MDCT) scanner Philips Ingenuia
7. Slice thickness 2 mm, reconstruction interval 0.75 mm



**Fig. 1** Axial (A) and (B) CTE images in a 19-year-old-male patient with wet tubercular peritonitis who presented with abdominal distension and fever for 1.5 months, showing mesenteric nodes (thin arrow), ascites (thick arrow), and peritoneal enhancement.

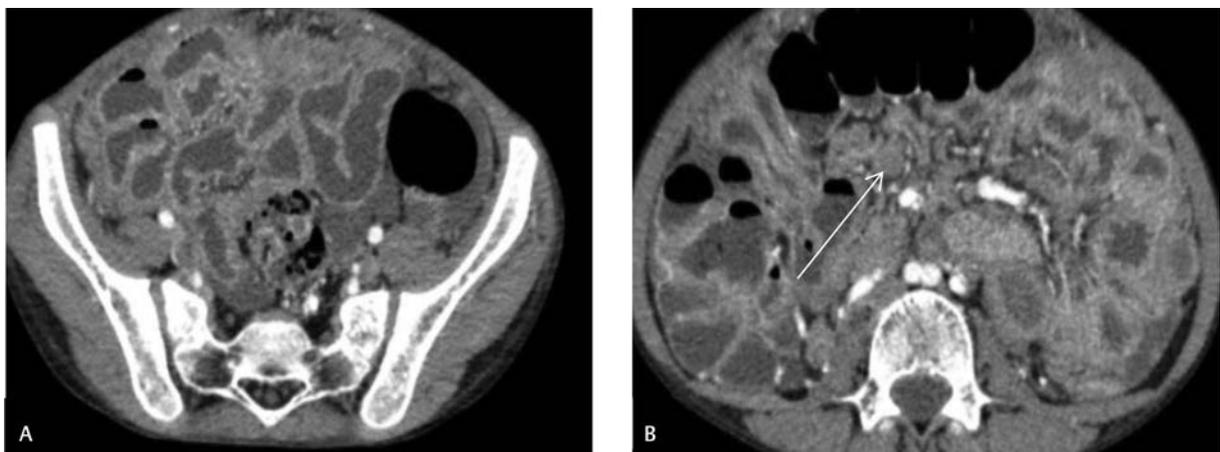


**Fig. 2** Axial CTE image in a 30-year-old man with TB peritonitis showing enhancing peritoneum (arrow) encasing small bowel loops giving a clustered centrally in a cocoon-like appearance.

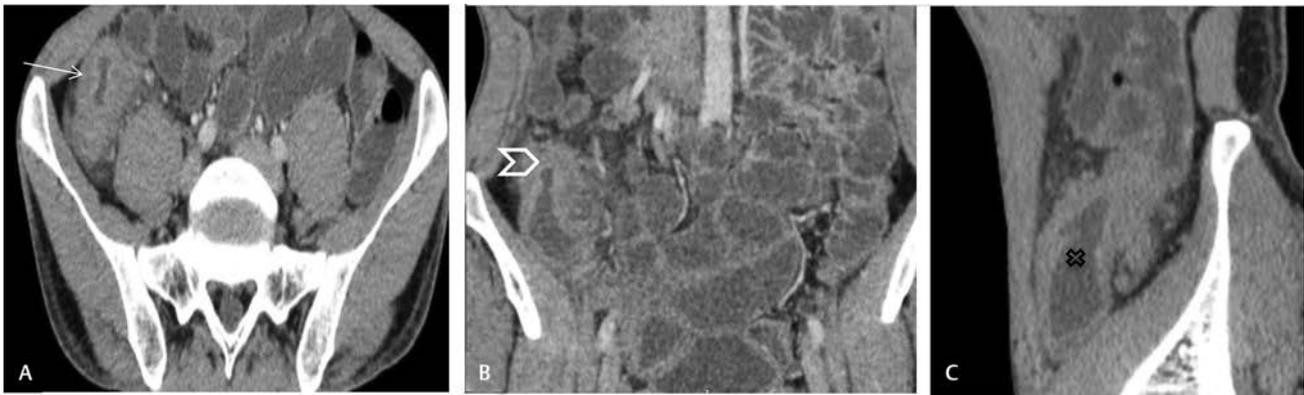
the segment of involvement is single in ITB, infrequently multiple segments of involvement may also be seen when differentiation from CD is difficult. Isolated segmental colonic involvement may be seen in 10% of abdominal tuberculosis, with sigmoid, ascending, and transverse colon being common sites.

Other complications include vascular complications, intussusception, and obstruction of the small bowel.<sup>20</sup>

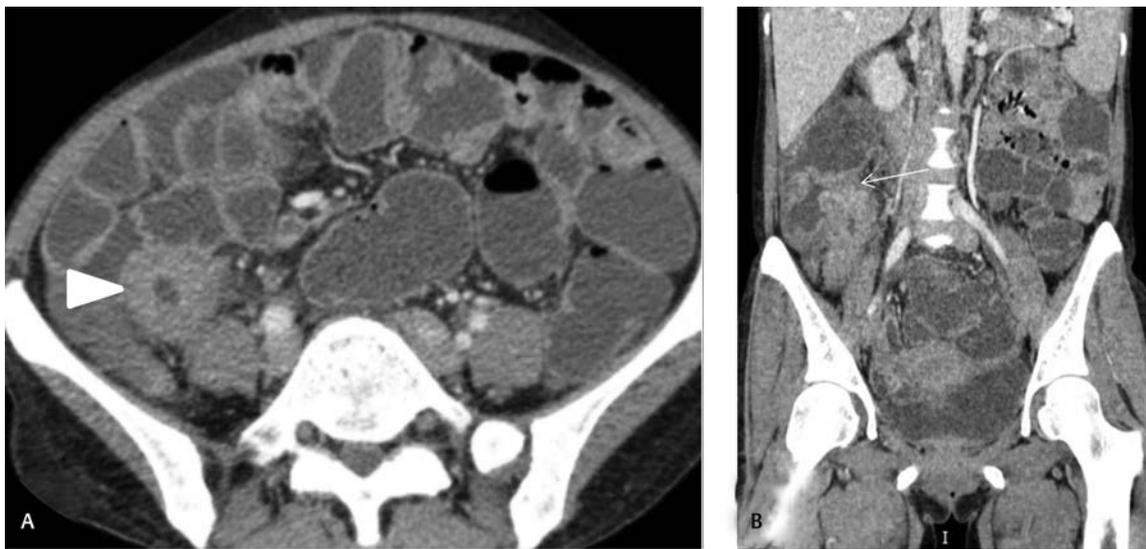
Extraintestinal changes include mesenteric nodal enlargement that may occur as discrete nodes or conglomerate nodal masses. Enlarged nodes are often necrotic, which helps in making an accurate diagnosis (► **Fig. 7**). On healing, the nodes may disappear or may show calcification. Perienteric and mesenteric fat stranding is uncommon. Omental or peritoneal thickening may be seen with omentum showing nodularity or smudgy pattern of enhancement. There may be associated abdominal cocoon (► **Fig. 2**), developing due to thin film of fibrosis encasing the bowel loops that appear clumped. This is seen on CTE or MRE as an area of clumped, often dilated, small



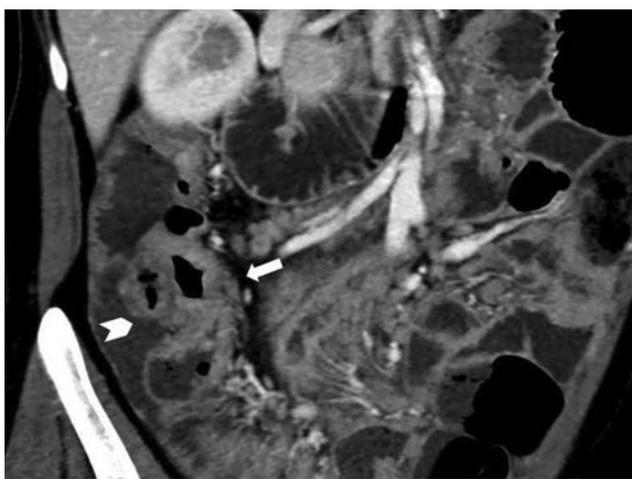
**Fig. 3** Axial (A) and (B) CTE images in a 44-year-old man with abdominal discomfort and low-grade fever showing mesenteric nodes (thin arrow) and peritoneal enhancement—DRY tubercular peritonitis.



**Fig. 4** Axial (A), coronal (B), and sagittal (C) CTE images in a 30-year-old patient with ITB showing gross thickening of cecum (arrow) ileocecal junction (arrowhead) with dilatation of terminal ileum (X).



**Fig. 5** Axial (A) and coronal (B) CTE images in a 26-year-old woman with low-grade fever and weight loss showing thickening and contraction of cecum (arrowhead) with pericecal fat stranding and gross thickening of ileocecal valve (arrow) consistent with ITB.



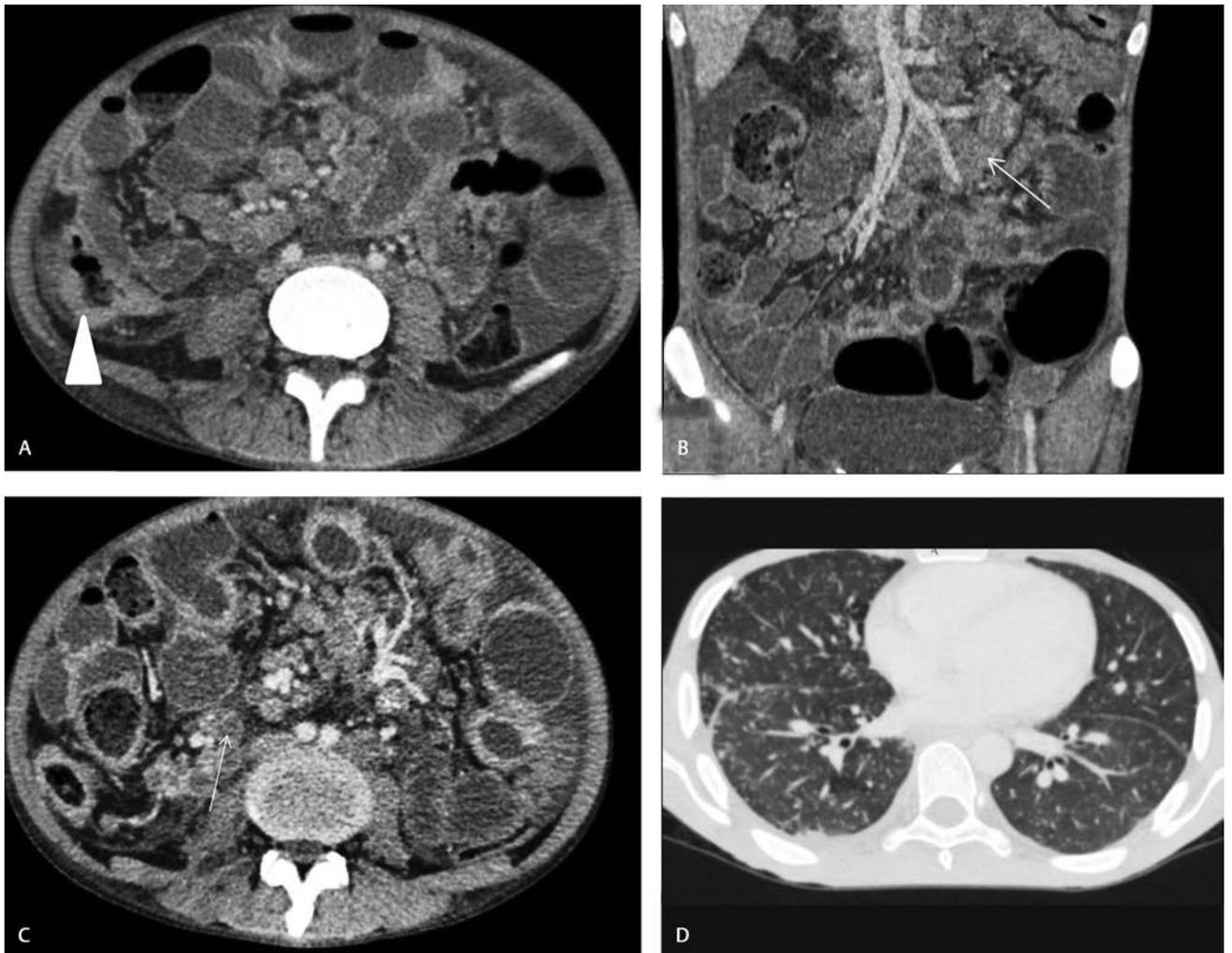
**Fig. 6** Ileocecal Koch's: Oblique coronal reconstruction through the abdomen in the venous phase of a 25-year-old woman with fever and weight loss shows a contracted cecum (arrowhead) and significantly thickened, heterogeneously enhancing terminal ileum and ileocecal junction without wall stratification (arrow) suggestive of TB. Necrotic nodes are seen just above the arrowhead. Ascitis with tiny peritoneal nodules are seen just lateral to the arrowhead.

bowel loops with thin hypodense or hypointense capsule around it. In long-standing cases, there may be proliferation of surrounding fat, although infrequently. Associated involvement of other organs such as the liver, spleen, or peritoneum also helps in making a diagnosis (►Fig. 8).<sup>23</sup>

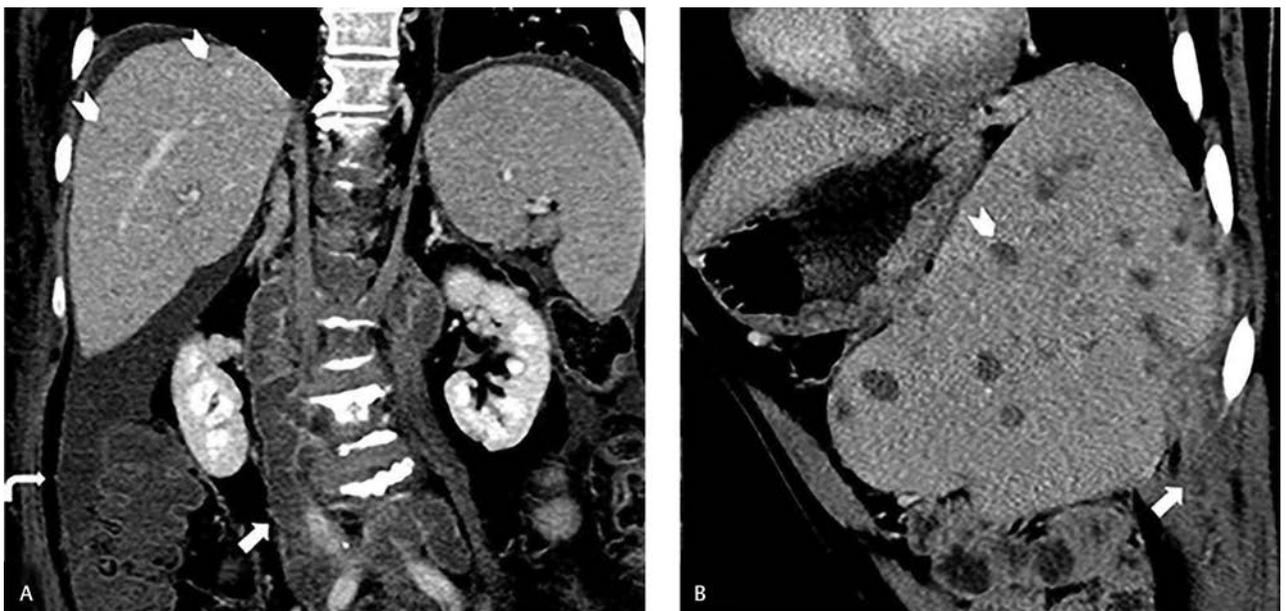
### Crohn's Disease

CD is characterized by chronic, transmural, often granulomatous, and intestinal inflammation. The small bowel is involved in almost 80% of the cases, with the ileocecal region affected in 50%.<sup>24</sup> Enteric involvement of CD tends to be transmural, segmental, and usually discontinuous also known as *skip lesions*<sup>16</sup> (►Fig. 9). Small bowel disease is multifocal with areas of different activity, some areas with acute inflammation, and others with fibrostenosing disease (►Fig. 10).

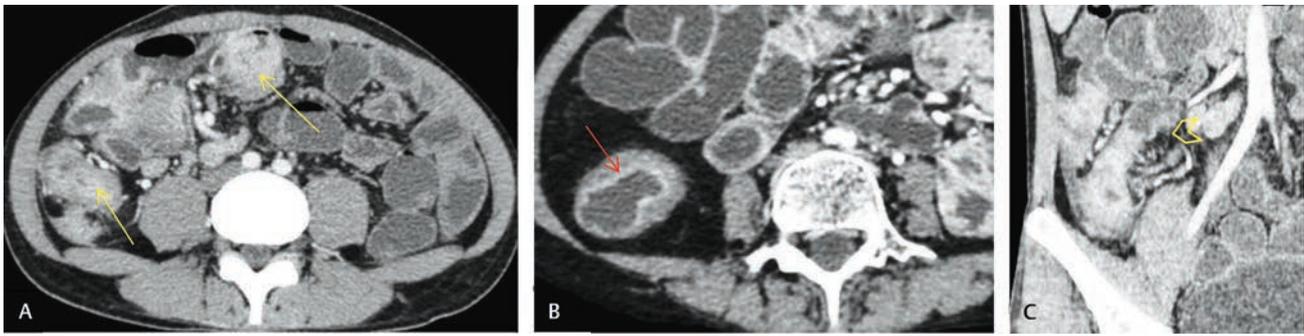
CD has been classified into four stages that help in planning therapy<sup>25</sup>: (1) active inflammatory, (2) fibrostenotic, (3) penetrating, and (4) reparative or regenerative subtypes. Active inflammation shows various features on imaging, as ulceration and mucosal enhancement. Fibrostenotic disease suggests a



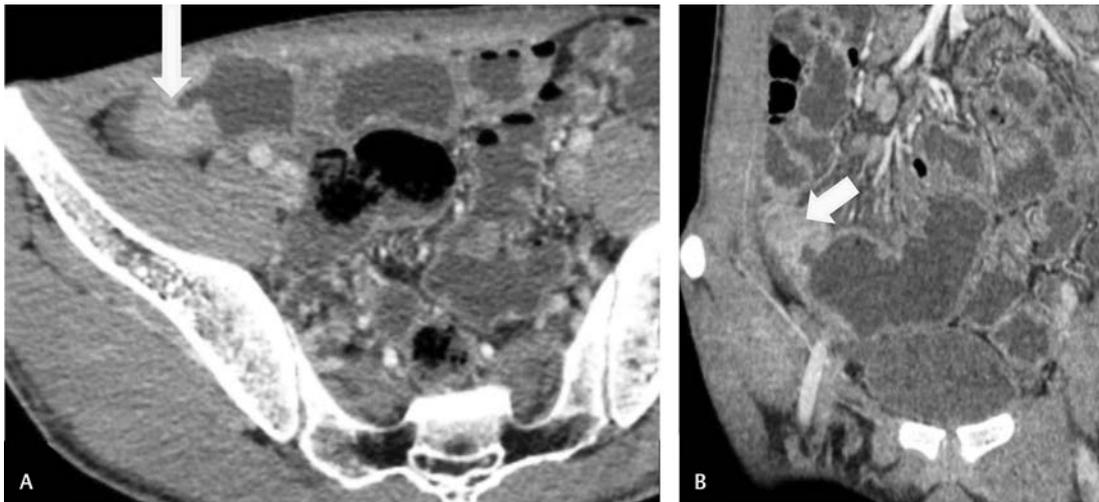
**Fig. 7** Axial (A), coronal (B), and axial (C) CTE images in a 38-year-old man with ileocecal TB showing thickening of cecum and ileocecal junction (arrowhead) with enlarged necrotic nodes (arrows) and axial (D) CT chest image shows multiple centrilobular nodules in bilateral lung fields giving a tree in bud appearance



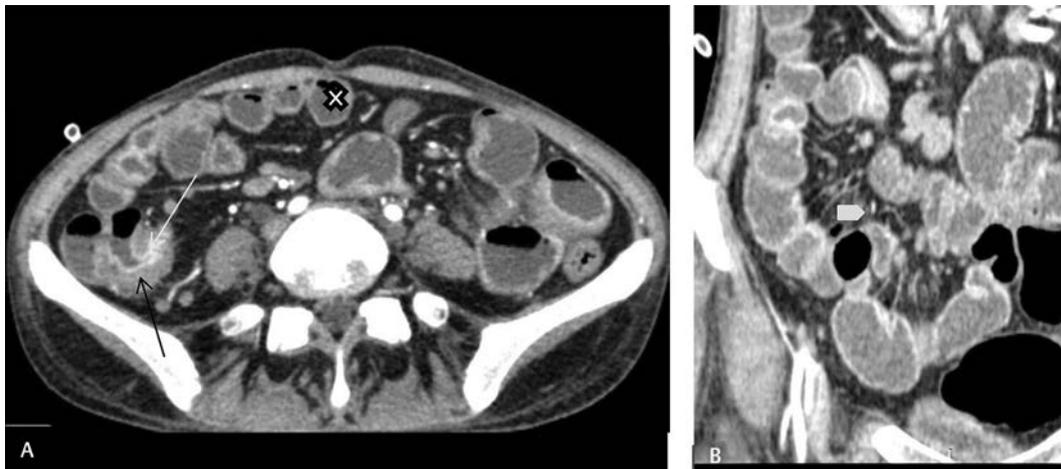
**Fig. 8** Hepatic perit spleen Koch's: Oblique coronal reconstruction through the abdomen in the venous phase of a 68-year-old diabetic man with pulmonary TB. (A) Several tiny hepatic nodules (arrowheads), peritoneal thickening (curved arrow), and coalescent necrotic retroperitoneal nodes (straight arrow). (B) Multiple small splenic hypodense nodules (arrowhead). Some of these nodules have coalesced to form a sinus leading to the perisplenic region and lateral abdominal wall (arrow).



**Fig. 9** Active Crohn's disease in a 45-year-old woman. Axial (A), axial (B), and coronal (C) CTE section Multifocal involvement mucosal hyperenhancement (red arrow) and mural stratification (yellow arrow) of the terminal ileum. Coronal CTE image shows mesenteric hypervascularity (arrowheads) adjacent to the involved bowel segment, indicating active Crohn's disease.



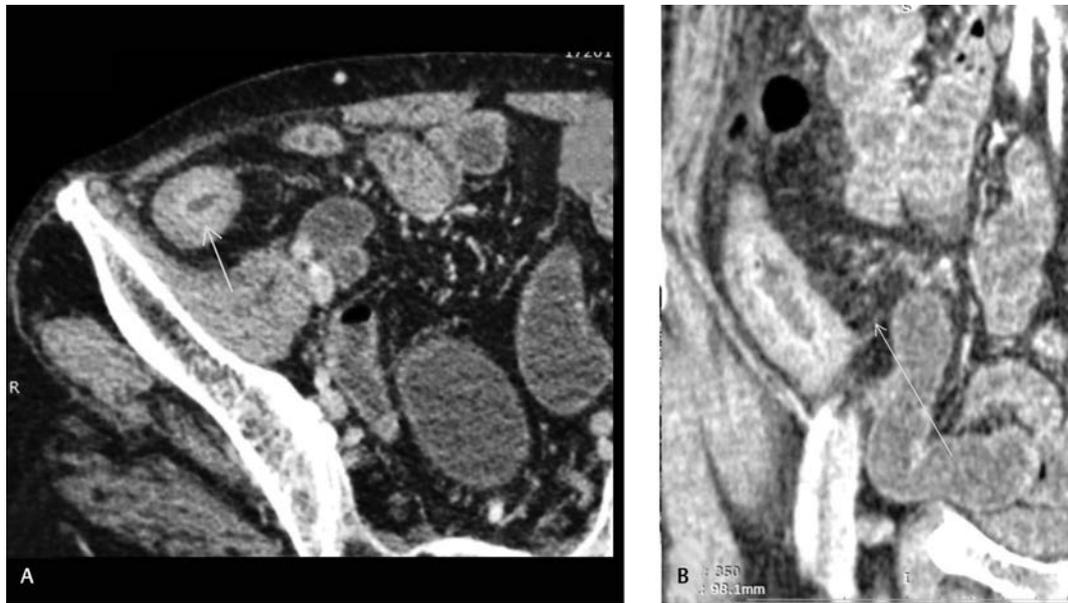
**Fig. 10** Fibrostenosing Crohn's disease in a 32-year-old man. Axial and coronal CTE image shows a segmental stricture involving proximal ileal loop. Homogenous mural thickening is seen at the strictured segment without mural hyperenhancement, suggesting fibrostenotic disease (arrow).



**Fig. 11** Active Crohn's disease in a 20-year-old man. Axial CTE section shows mucosal hyperenhancement (black arrow) and mural stratification (white arrow) of the terminal ileum, an appearance that contrasts markedly with that of nondiseased ileal segments (X). Axial (A) and coronal (B) CTE image shows mesenteric hypervascularity (comb sign) (arrowhead) adjacent to the involved bowel segment, indicating active Crohn's disease.

healing phase due to collagen deposition and stricture formation. Penetrating disease occurs due to the extension of deep ulcers, resulting in extraintestinal inflammation, abscesses, sinuses, and fistulas. Often, multiple stages coexist in the

same patient or bowel segment.<sup>25</sup> Similar to ITB, the ileocecal region is the most common site of involvement. Involvement of multiple segments with normal intervening bowel segment is typically seen, but this alone may not be specific.



**Fig. 12** Axial CTE section shows mucosal hyperenhancement and mural stratification of the terminal ileum. Axial (A) and coronal (B) CTE image shows mesenteric hypervascularity (arrow), comb sign, adjacent to the involved bowel segment indicating active Crohn's disease.



**Fig. 13** Crohn's stricture: Oblique coronal reconstruction through the abdomen in the venous phase of a 56-year-old man, with symptoms of recurrent subacute intestinal obstruction showing a stricture (arrow) with wall stratification and intense enhancement of the mucosa suggestive of active inflammation.

CD has a variety of appearances at CTE depending on disease activity and associated complications such as fistula or abscess. On CTE, enteric findings such as mural hyperenhancement, bowel wall thickening, mural stratification and extraenteric findings such as engorged vasa recta ("comb sign"),<sup>26</sup> and increased attenuation of the mesenteric

fat are features of active inflammatory small bowel CD<sup>26,27</sup> (►Figs. 11–13). Among these findings, combination of mural hyperenhancement and bowel wall thickening is the most sensitive CTE findings suggesting the active inflammatory CD.

Mural enhancement is the most sensitive indicator of active CD<sup>28</sup>; therefore, bowel loops with similar distension should be compared as both the jejunum and normal collapsed loops may demonstrate regions of higher attenuation simulating enhancement.

A mural attenuation threshold of 109 HU and an abnormal to normal loop enhancement ratio of >1.3 have been used to objectively correlate mural hyperenhancement and bowel wall thickness with disease activity on CTE and highly correlated with histologic findings of active disease. Visual assessment, however, presents higher specificity than quantitative measurements.<sup>29</sup>

The term *mural stratification* denotes the visualization of bowel wall layers at CT after administration of IV contrast<sup>28,30,31</sup> (►Fig. 12). Bilaminar mural stratification refers to mucosal hyperenhancement and decreased intramural attenuation, and trilaminar mural stratification refers to alternating areas of high and low attenuation due to mucosal and serosal hyperenhancement and low intramural attenuation. The low intramural attenuation can represent edema, inflammatory infiltrate, or fat. Mural stratification due to intramural edema is more indicative of active disease compared with a homogeneously enhanced wall,<sup>32</sup> whereas the presence of intramural fat indicates chronic process.<sup>27</sup>

In active CD, increased attenuation of the mesenteric fat is often seen due to edema or prominence of vasa recta. Prominence of the vasa recta is known as the "comb sign."<sup>26,33</sup> This sign, along with increased mesenteric fat attenuation, is the most specific CT feature of active CD.<sup>34</sup> Findings suggestive of chronicity in CD include submucosal fat deposition, pseudo-sacculation, surrounding fibrofatty proliferation, and fibrotic

strictures. Inflammatory involvement of the mesenteric border of the affected bowel segment with associated asymmetric fibrosis and pseudosacculation of the antimesenteric border is a hallmark.<sup>16</sup>

The transmural inflammation with increased intraluminal pressure proximal to the site of strictures may lead to extension of the inflammatory process across the serosal surface into the adjacent mesentery or structures, resulting in extraenteric complications as fistula, sinus tract, and abscess. CTE has an important role in the evaluation of extraenteric complications of CD<sup>25,35</sup> (► **Figs. 14** and **15**).

CTE has high sensitivity for the detection of bowel strictures occurring as a complication of CD. Reversible strictures are characterized by mucosal hyperenhancement, mural stratification, fat stranding, and engorgement of the vasa recta; however, transmural fibrosis may result in a lack of enhancement and loss of stratification.<sup>16</sup> It is important to differentiate between active and fibrotic strictures (► **Fig. 8**) because the former warrants medical management whereas the latter may require surgical intervention.<sup>35</sup>

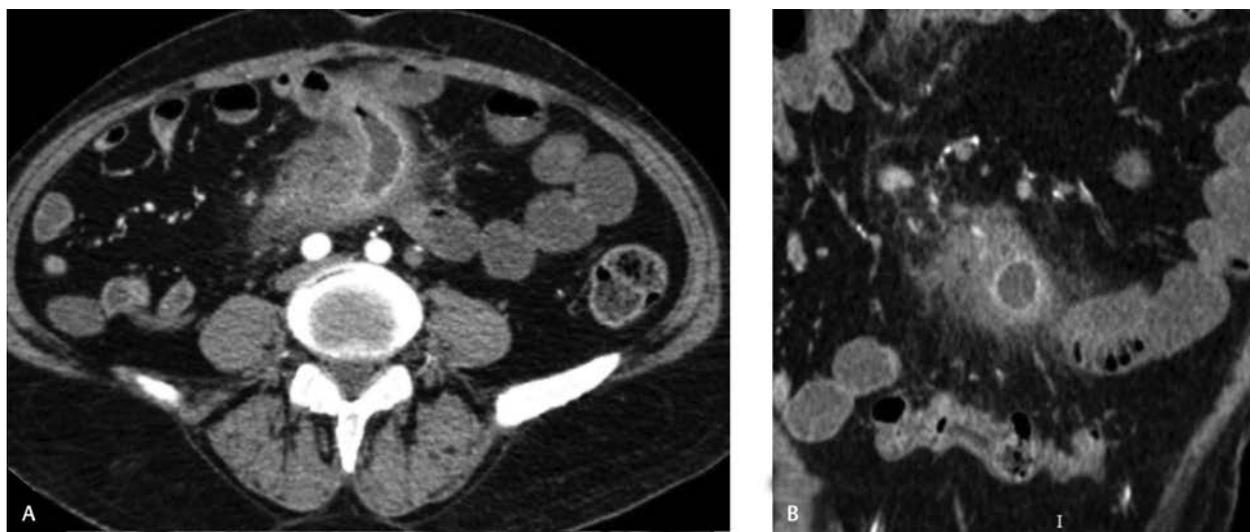
Extraenteric findings such as cholelithiasis, urolithiasis, and sacroiliitis are also picked up on CT.<sup>36</sup>

Radiologic features are helpful in differentiating ITB from CD.<sup>1,37</sup> These differences are presented in ► **Table 2**.

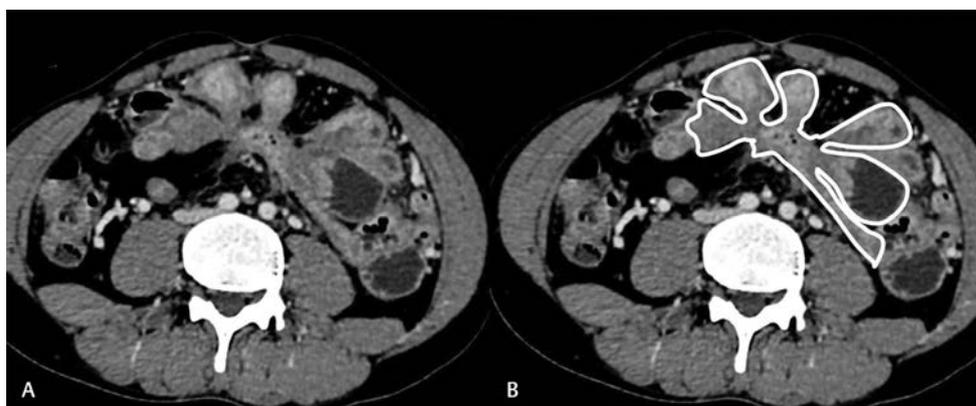
Radiologic investigations provide useful clues to aid diagnosis, but their major role is in assessing the extent of the disease.<sup>38</sup>

Endoscopy plays an important role in diagnosis.<sup>39,40</sup> Apart from visual inspection, mucosal biopsy can be obtained for histopathology, culture, and molecular tests. CD patients usually have longitudinal ulcers, cobblestone appearance of mucosa, and anorectal involvement.<sup>41</sup> Transverse ulcers, patulous ileocecal valve, and involvement of fewer of colonic segments are commoner in ITB.

ITB and CD are both chronic granulomatous diseases with subtle histologic differences between them. Histologic features suggesting ITB include confluent granulomas, multiple granulomas, large granuloma size, bands of epithelioid histiocytes lining ulcers, submucosal granulomas, and disproportionate submucosal inflammation, that is, submucosal inflammation that significantly exceeds mucosal inflammation. Although caseation and necrosis in granulomas or positive stain for acid-fast Bacillus (AFB) is virtually diagnostic for ITB, the problem is the poor yield of endoscopic sampling,



**Fig. 14** Crohn's disease in a 34-year-old woman. (A) Axial and (B) coronal CTE image shows enteroenteric fistula involving ileal loops (arrow) with adjacent fat stranding.



**Fig. 15** Fistulizing Crohn's: axial sections through the abdomen in the venous phase of a 43-year-old man show a radiating pattern of fistulae connecting adjacent small bowel loops in panel A. The outline of the fistulae has been drawn in panel B.

**Table 2** Differentiating features of ITB and CD

Features	ITB	CD
Site of involvement	ICJ with terminal ileum	Terminal ileum
Length of involvement	Short segment	Long segment
Wall thickness	<6 mm	>6 mm
Skip lesions	Uncommon	Common
Mural hyperenhancement	Rare	In active CD
Mural stratification	Uncommon	Common
Interbowel fistula	Rare	Common
Mesenteric abscess	Rare	Common
Increased mesenteric vascularity	Uncommon	Common (comb sign)
Ascites	Frequent	Uncommon
Peritoneal thickening	Often associated	Uncommon
Omental caking, nodularity	Frequent	Rare
Mesenteric nodes	Large (>1 cm), necrotic	Small, homogenous

Abbreviations: CD, Crohn's disease; ICJ, ileocolic junction; ITB, intestinal tuberculosis.

which is diagnostic in <30% of cases. Features seen more frequently in CD include microgranulomas, nonconfluent granulomas, single granulomas as the only foci of granulomatous inflammation, and architectural distortion distant from granulomatous inflammation.<sup>1</sup>

## Conclusion

CTE is a valuable tool for differentiating ITB from CD. It helps in making a diagnosis, defining the extent of disease, and assessing the presence of active inflammation and complications. Although overlapping findings occur with ITB, a combination of findings helps us differentiate between the two.

### Conflict of Interest

None declared.

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