

Case Study

Intestinal Tuberculosis in Surgical Pathology - Experience from a Tertiary Care Hospital ABC

Abstract:

Background: Intestinal tuberculosis (ITB) represents the most common type of abdominal TB .Definitive diagnosis of intestinal tuberculosis is made on the basis of morphological examination of surgical specimens in majority of cases as clinico-radiological features are non-specific in initial stages of the disease.

Aims: To analyze the surgical pathology data on intestinal tuberculosis of the hospital and to document findings of morphological examination.

Setting: A descriptive study of intestinal tuberculous lesions encountered in surgical specimens received during a period of three years in the histopathology section of a tertiary care hospital.

Material and Methods: 40 cases of intestinal tuberculosis out of 250 consecutive, surgically excised specimens of small and large bowel were included in this study. One year retrospective and two years prospective data is included in the study.

Results: Intestinal obstruction was the most frequent clinical presentation followed by perforation peritonitis in ITB cases in this series.9 patients had past history of pulmonary and/or intestinal tuberculosis. Out of 31patients without past history of TB, 25.80% were suspected of having TB preoperatively on the basis of clinical and imaging findings. Ileal and ileo-caecal region was most frequently involved .The three gross morphological forms of tuberculous enteritis seen were ulcerative in 82.5%, ulcero-hypertrophic in 15% and hypertrophic in 2.5 %cases. Characteristic caseating granulomas were seen in 60% cases.

Conclusion: Changes in clinical presentation of Intestinal TB are being observed. High index of suspicion is needed at every step of diagnosis of intestinal TB as many non-tuberculous lesions share same clinical and radiological findings.

Keywords: Intestinal tuberculosis, diagnostic delay, surgical pathology, morphological diagnosis

Introduction: Both pulmonary as well as extrapulmonary Tuberculosis is highly prevalent in India. Tuberculosis(TB) of gastrointestinal tract (GIT) represents the sixth most frequent form of extra-pulmonary tuberculosis and TB can involve any part of GIT[1,2].Intestinal tuberculosis (ITB) may occur with or without presence of pulmonary disease . With a high regional prevalence of the disease , cases of ITB are attributed to

reinfection [3]. Immunodeficiency due to various causes may contribute to cases occurring due to reactivation[4]. Pre-operative diagnosis of ITB is a challenge, as patients of intestinal TB present with non-specific clinical and radiological features that may mimic other diseases [5, 6]. Patients seek medical consultation for an advanced intestinal disease that necessitates surgical intervention for associated complications. Histological examination of biopsy or surgically excised tissue establishes the diagnosis of ITB [7]. Surgical pathology data of intestinal TB is analysed in the light of associated clinical and radiological findings to get insight into the changing pattern of the disease.

Material and Methods: 40 cases of intestinal TB in whom diagnosis was confirmed by histological examination were included in this analysis. These cases were selected from 250 consecutive specimens of small and large intestines (excluding appendix and autopsy material), from patients who were operated upon in the surgical operation theatres of the hospital during a period of three years. Cases in which diagnosis of abdominal TB was made on the basis of fine needle aspiration cytology of abdominal lymph nodes or examination of ascitic fluid were excluded from the analysis.

The specimens were in the form of resected segments of intestine, omental biopsy/ resection or biopsy from perforation edge and lymph node biopsy. The case proformas included details of clinical history, radiological investigations, past history of TB and treatment.

In gross examination 1) nature of the specimen 2) length of the intestine 3) presence and no of strictures and perforations and 4) presence of serosal tubercles were noted. The small and large bowel specimens were opened up longitudinally through the entire length along anti-mesenteric border. Mucosal and serosal surface of the specimen were examined for presence of ulcers, strictures, perforations, tubercles and wall thickening.

Representative sections were taken from pathological lesions, adjacent tissue along with proximal and distal resection margins of the specimen and accompanied lymph nodes when present. Routine paraffin processing of all the sections was followed by H&E staining. Fite-Faraco (FF) staining was carried out for sections that showed microscopic features of granulomatous inflammation. Cases that showed at least two criteria of 1) characteristic gross findings of ulcerative, hypertrophic types or fibrous strictures and 2) caseating or non-caseating granulomas on microscopy 3) with or without contributory FF staining were reported as intestinal TB. Cases not fulfilling all three criteria, were reported as suspicious of ITB.

Results:

Age and sex: Age range for ITB in this series was 14 to 70 years. Out of total 40 cases intestinal TB, maximum cases belonged to 4th followed by 3rd decade of life, as seen in Table 1.

M: F ratio was 1: 0.6

Table 1: Age distribution in 40 cases of intestinal TB

Age (Years)	No of cases	Percentage
1-10	00	00
11-20	05	12.5
21-30	11	27.5
31-40	16	40.0
41-50	07	17.5
51-60	00	00
61-70	01	2.5
Total	40	100 %

75

76 **Symptoms:**As depicted in Table 2, non-specific abdominal pain was the most common
77 presenting symptom followed by vomiting and nausea. A single patient was having more than
78 one symptoms.

79 **Table 2:** Presenting symptoms in 40 cases of intestinal TB

Symptom	Number of cases	Percentage
Abdominal Pain	30	75.0
Nausea	20	50.0
Vomiting	28	70.0
Distension	13	32.5
Constipation	05	12.5
Diarrhoea	03	7.5
Weight loss	11	27.5
Fever	08	20.0
Night sweats	02	5.0
Anorexia	07	17.5

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81 **Clinical presentation:** Out of 40, 26 patients (65 %) had presented with clinical signs of
 82 intestinal obstruction, subacute in 22 (55 %) and acute in 4(10 %).

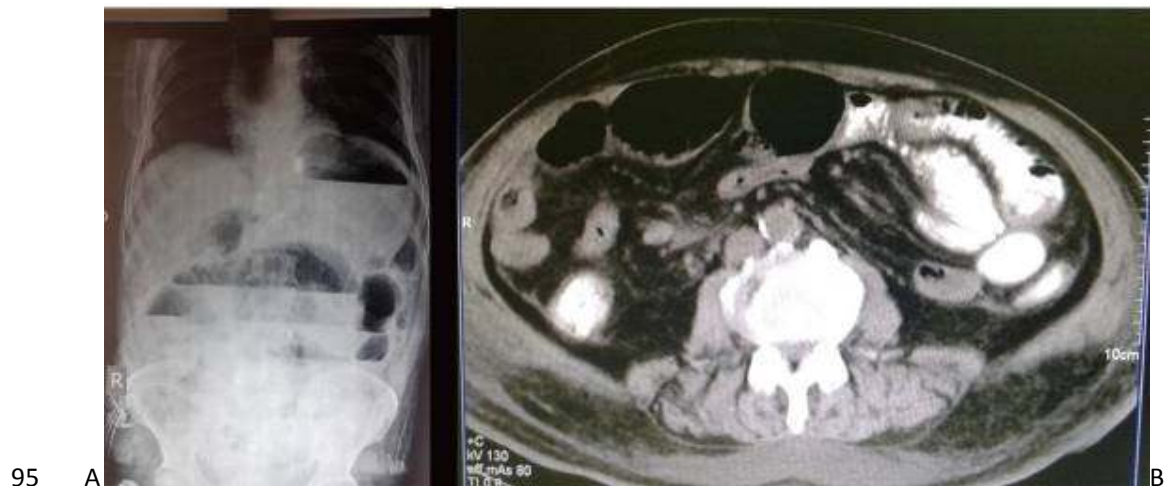
83 12 patients (30%) were pre-operatively diagnosed of having perforation peritonitis that
 84 included 2 cases of pyoperitoneum .

85 2 (5%) patients had lump in right lower quadrant of abdomen on the basis of clinical findings.

86 Nine patients had past history of TB. Out of these 6 patients had completed treatment for
 87 pulmonary and 2 for intestinal TB during previous year. A 19 year old female was a known
 88 case of both pulmonary and intestinal TB, had received anti-TB treatment for six months,
 89 presented with perforation peritonitis and underwent omental biopsy. Out of 31 patients,
 90 without past history of TB, only 8(25.80%) were suspected of having ITB on the basis of
 91 clinical findings.

92 **Radiological investigations** in 40 patients in the form of X-ray and USG or CT abdomen had
 93 revealed evidence of **intestinal obstruction (Figure 1A & B).**

94 **Figure 1 A & B**



96 **Figure 1A:** X-ray abdomen showing features of obstruction-Dilated bowel loops with multiple air
 97 fluid levels.

98 **Figure 1B:**CT abdomen-Multiple dilated contrast filled small bowel loops with collapsed ascending
 99 colon suggestive of small bowel obstruction

100 Intestinal Obstruction was diagnosed in maximum 24 (60%) cases, followed by ileal
 101 perforation in 12 (30%) cases. Jejunal strictures were identified in 2 cases, caecal wall
 102 thickening and gangrenous intestines were seen in one case each. ITB was suspected only in
 103 8(25.80 %) out of 31patients without past during previous year history, on the basis of
 104 available radiological investigations.

105 Table 3 shows the **operative procedures** that, 40 patients included in this study underwent.
 106 Resection of the involved segment of intestine was the most frequently performed procedure.

Table 3: Types of Operation

Surgical Procedure	No of cases	Percentage
Biopsy	04	10.0
Adhesiolysis	04	10.0
Stricturoplasty	06	15.0
resection of affected ileal segment & ileo-ileal anastomosis	19	47.5
resection of affected ileal segment, exteriorisation of ends & stoma reversal with ileo-ileal anastomosis	04	10.0
Limited right hemicolectomy, exteriorisation of ends & stoma reversal with ileo-colic anastomosis	03	7.5
Total	40	100

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109 **Site of involvement:** Ileum and ileo-cecal area together formed the commonest site of
 110 involvement in our series and 7 surgical specimens revealed presence of tubercular lesions in
 111 small as well as large intestines.

112 **Table 4:** Site-wise distribution of cases of intestinal TB

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Site	No of cases	Percentage	Cases with Lymph node involvement
Small intestine	31	77.5	
Jejunum	3	7.5	
Ileum	22	55.0	4
Ileo-cecal area	6	15	4
Large intestine	2	5.0	
Ascending colon	1	2.5	
Transverse colon	1	2.5	
Both small & large intestine	7	17.5	2

total	40	100	10
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Morphological examination : On gross examination, the most frequently identified morphological form was ulcerative and included classical **transverse ulcers, serosal tubercles and perforations (Figure 2A&B)**, strictures or fistula formation .

Figure 2A& B: A



Figure 2A: Gross specimen of resected small intestinal segment showing circumferential transverse ulcer. Inset- Classical transverse ulcer

Figure 2B: Gross specimen of resected ileum showing multiple tubercles on the serosal surface with an area of central perforation (large arrow)

In this study, multiple macroscopic lesions of single form or different forms (combined lesions) were present in 30 (75 %) cases while remaining 10 cases (25%) showed presence of a single gross lesion.

Strictures occurred most frequently in ileum, followed by in jejunum and colon. Strictures were identified in 23 surgical specimens (57.50 %) –Single in 5, multiple in 6, associated with perforation in 7 and with ulcer in 5 cases.

Perforations were identified in ileum and jejunum in 17 cases (42.50 %). Single in 3, multiple in 6, associated with stricture in 7 and with gangrene in 1 case.

Characteristic transverse ulcers were seen in ileum in 10 (25%) cases and were single in 2, multiple in 3 and associated with strictures in 5 cases.

A single resected ileal segment from a 14 yr boy was seen to be studded with multiple tubercles on serosal surface .Two specimens were in the form of lumps of thickened omentum and coiled intestines.

Microscopic features observed in three forms of gross lesions in 40 cases of intestinal TB are depicted in table 5.

Table No 5: Types of macroscopic lesions and microscopic features

Type of lesion	No of cases	Presence of Caseating granulomas	Presence of non-caseating granulomas	Non-specific chronic inflammation
Ulcerative	33	22 (66.66%)	10 (30.30%)	01 (3.03%)
Ulcer-hypertrophic	06	02 (33.33)	02 (33.33%)	02 (33.33%)
Hypertrophic	01	-	01	-
TOTAL	40	24	13	03

Microscopic examination of sections from intestines had revealed classical caseating granulomas (Fig3A) in 24 (60%) , granulomas without caseation in 13(32.50 %). 3 cases (7.5%) showed non-specific chronic inflammation without granuloma in multiple sections.7 mesenteric lymph nodes also showed presence of caseating granulomas.

FF stain was positive (Fig 3B,inset) in sections from, intestine in12cases (30%) and lymph nodes in 7 cases that were showing caseating granulomas(Fig3B). All 19 cases that were positive with Fite-Faraco staining also showed granulomas.

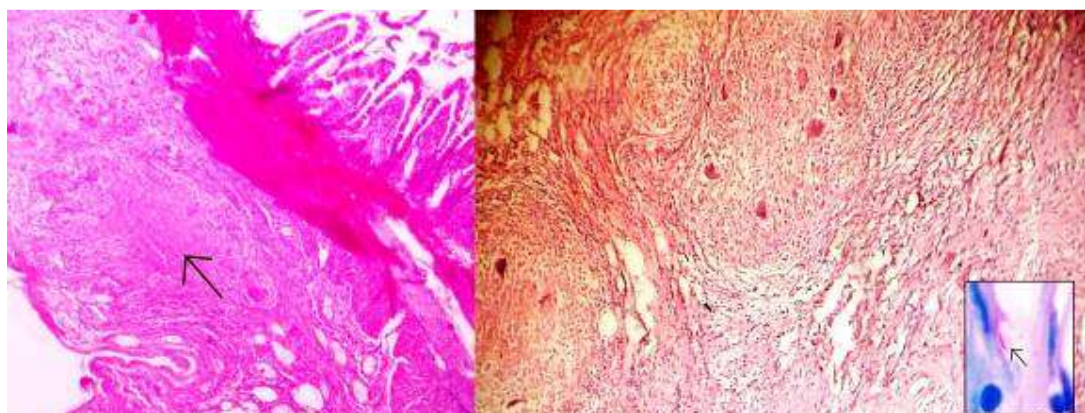


Figure 3A : Photomicrograph – section from ileum showing caseating granuloma in submucosa, arrow (HE,100X)

Figure 3B : Photomicrograph – section from mesenteric lymph node showing well-formed multiple caseating granulomas with giant cells(HE,100X).Inset-Fite-Faraco stain showing an acid-fast bacillus (1000X).

Out of 40 patients,15 (37.50 %) patients had shown Reactivity to HIV I & II antigens. Out of these 15 patients, 3 were known cases of ITB, 2 of PTB and a single patient with past history of both PTB & ITB.

Patients with histopathological diagnosis of intestinal TB as well as those reported as suspicious of TB, were referred to the Department of TB and Chest diseases of the Hospital where they were started with Combined Anti Tubercular (CAT) therapy. None of the patients of this series reported to the hospital for surgical intervention within six months of initiation of CAT therapy.

Discussion: Pulmonary as well as extra-pulmonary tuberculosis (TB) has made a global comeback [4,8]. India is the highest TB burden country in the world with a current prevalence of 2.8 million cases [9].Intestinal TB or tuberculous enteritis represents frequent form of abdominal TB, that is a common type of extra-pulmonary tuberculosis.

ITB is predominantly a disease of young adults with slight male preponderance. Age and sex occurrence of the present study correlated with that of other studies [10,11].

Cases of ITB without evidence of active pulmonary involvement on X-ray chest exceeded those with evidence of pulmonary involvement -33(82.2%) Vs 7(17.5%) respectively, in this study.Similar disease pattern is observed in other studies[5,12]. Most cases of abdominal TB(that includes ITB) in India are caused by Mycobacterium tuberculosis .Tubercle bacilli reach the gastrointestinal system via (1)hematogenous spread from the primary lung focus with later reactivation or miliaryTB,(2)ingestion of bacilli in sputum from an active pulmonary focus,(3) direct spread from adjacent organ like fallopian tubes or (4) Through lymph channels from infected nodes[2,8]. Intestinal involvement in TB is not attributed to M bovis because of practice of boiling of milk before drinking and large scale pasteurization of milk in recent years . In absence of active lung disease, ITB that is a frequent form of abdominal TB, probably occurs due to reactivation of latent infection due to suppression of host defences due to various reasons [4,13]. Reinfection plays an important role in regions of high contagion[3]. However, as culture studies were not done, causative organism could not be confirmed in our cases.

ITB can mimic other non-neoplastic and neoplastic abdominal conditions. Pre-operative diagnosis of ITB remains a challenge even in highly endemic areas because of non-specific clinical presentation and investigative findings [6, 14]. TB is regarded as a disease with insidious onset, indolent course and late presentation with complications[15,16].The variable symptoms of abdominal pain, discomfort or GI upset present for some time are often neglected by the patient and also the clinician.Patients reach medical centres only on aggravation of existing symptoms or development of symptoms like vomiting and abdominal distension indicative of complications. Associated constitutional symptoms may not be always noticed, but when present, are clues to diagnosis of ITB.

Subacute intestinal obstruction was the most common complication and mode of presentation in our study and also observed by other workers [17,18,19]. Occurrence of increased number of perforation peritonitis about 30% cases in the present and other studies[10] is indicative of changing presentation pattern of ITB. While Kapoor [4] has observed that 5-9% of small intestinal perforations occur due to TB in India, tubercular perforation is quoted as one of the major causes of GI perforations in a recent study [20]. Malik [21] had made an observation that abdominal TB is emerging as common mode of presentation of acute bowel obstruction.

Initial imaging findings in ITB are non-specific and Plain x-ray abdomen, Barium studies,ultrasound or CT show characteristic findings in advanced cases when the lesions become well developed[2].

Endoscopic appearances of tuberculous lesions are characteristic and can contribute to diagnosis of ITB, only if the involved intestinal segment is accessible to endoscopy and submucosa is included in the biopsies. Increased number of patients showing colonic involvement either as isolated colonic TB or combined with small intestinal involvement are identified as more patients are being subjected to colonoscopies[22].Barium meal follow through , CT enteroclysis or diagnostic endoscopies were not performed in our patients.

Although TB can involve any part of GIT, the most frequent site of involvement is ileum and ileocaecal region of small intestines followed by colon and jejunum in present as well as other studies [10,16,23]. In ITB ,the predilection of the tubercular bacillus for ileo-caecum is attributed to relative physiological stasis of the area that results into increased rate of fluid and electrolyte absorption, causing more complete digestion that permit free contact of the organisms with the mucosal lining absorption and an abundance of lymphoid tissue at the site [24].

The ulcerative gross morphologic type commonly affects the ileum and jejunum and is characterised by a single or multiple superficial, transverse ulcers the healing of which may lead to stricture formation. As the disease progresses, tissue breakdown due to ischemia caused by vascular thrombosis, play a role in the pathogenesis of perforation in ITB , in addition to reduced fibrosis attributable to altered host response due to some kind of immunodeficiency and early intervention. Caseating granulomas that extend upto serosa cause gut wall thinning and together with tubercular vasculitis may cause bleeding. Enterocutaneous fistula develop after bowel surgery,in patients with active disease or because of caseous tuberculous abscess formation on the serosal surface of intestine. The occurrence of stricture formation, perforation, bleeding or fistula formation results into frequent clinical presentation as intestinal obstruction or perforation peritonitis. The hypertrophic or ulcero-hypertrophic types commonly affect the ileo-cecal region and result into obstruction by luminal narrowing or right iliac fossa lump formation [13].

Microscopically multiple, variable sized granulomas composed of central caseous necrosis and epitheloid cells (specialised macrophages), Langhan's giant cells and lymphocytes surrounded by fibrosis are seen in the wall of intestine. These caseating granulomas seen in

submucosa & serosa are histologic characteristic of ITB but sometimes seen only in the regional lymph nodes [23].

In the present study 32.5% surgical specimens showed granulomas without caseation .7.5% revealed only chronic inflammation on microscopic examination and granulomas were not identified even on multiple sections. A few tubercular lesions may show granulomas without caseation [5] or only non-specific chronic inflammation [1]. Although important, a clear distinction of ITB from Crohn's disease may not be possible in some cases that do not show classical caseating granulomas [14]. Immuno-suppressants given in these patients can result in systemic spread of TB with fatal consequences[22]. Clinical response to AKT can confirm or rule out diagnosis of ITB in these patients.

On the basis of clinico-radiological and gross features, three cases of this series that showed only chronic inflammation were reported as suspicious of TB and referred to TB centre. Good response to AKT established diagnosis of ITB in these 3 patients.

FF stain is confirmatory when positive, but tissue positivity remains low in intestines, 30 % in our study and 37.5% in study by Dasgupta [13].

Anti-TB therapy remains mainstay of treatment in ITB, before and after surgery [2, 5,6].

In summary **Key findings** of our study are-

1. Cases of ITB that occurred in patients without pulmonary involvement exceeded those with pulmonary involvement, irrespective of presence of known immunodeficiency state in these patients.

2. Increased number of ITB cases presented clinically as cases of perforation peritonitis than quoted in previous series.

3. Multiple and combined morphological lesions were observed in the surgical specimens of many patients indicating advanced disease with development of complications at presentation.

In absence of prompt diagnosis, intestinal TB continues to be a cause for increased morbidity, mortality and escalated health care cost associated with the treatment of advanced disease in these patients.

Conclusion: Change in disease presentation, non-specific clinical picture and radiology findings in early stages of disease often result in delay in diagnosis of intestinal tuberculosis, thereby increasing occurrence of complications that necessitate surgical intervention. High index of suspicion is needed at every step for prompt diagnosis of ITB.

ETHICAL APPROVAL

Institutional Ethics Committee, Indira Gandhi Government Medical College, Nagpur had given approval.

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