

Clinicopathological Study of Tuberculous Lesions of Small and Large Intestine (Including Appendix)

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Abstract

Background: Tuberculosis in India continues to be a major health problem with approximately one eighth of total cases being extra pulmonary. The gastrointestinal tract is involved in 66-75% of cases of abdominal tuberculosis. The pathologist plays a central role in diagnosis of intestinal tuberculosis (ITB). Many intestinal lesions especially non-neoplastic share the same clinical background, where characteristic pathological features not only suggest specific diagnosis but also the extent and severity of the disease. *Aim:* To study the profile of tuberculous lesions of small and large intestine including appendix in relation to age and sex distribution, the clinical presentation and regional distribution of the lesions. *Method:* A prospective study of 30 diagnosed cases of ITB encountered in surgically excised specimens of small and large bowel including appendix carried over a period of five years. The diagnosis was based on the presence of caseating or non-caseating epithelioid cell granulomas, acid-fast bacilli (AFB) on histology. *Results:* Intestinal obstruction was the most frequent clinical presentation in ITB cases in this series. The mean age was 34.2 years with M: F ratio of 2:1. Ileum and ileocaecal region were most frequently involved. The three gross morphological forms of tuberculous enteritis seen were ulcerative in 70%, ulcero-hypertrophic in 20% and hypertrophic in 10% cases. Characteristic caseating granulomas were seen in 60% cases. *Conclusion:* Along with clinical, radiological and endoscopic evaluation, the present study showed that histopathological analysis also plays an important role in the diagnostic and therapeutic approach to intestinal tuberculosis.

Keywords: Intestinal Tuberculosis (ITB); Acid- Fast Bacilli (AFB).

Introduction

Tuberculosis had been recognised as a disease from the ancient time, and Hippocrates in the 4th century BC bestowed the name Phthisis, meaning wasting. The association of intestinal ulceration, perforation and peritonitis was vividly described in 1643 in the autopsy report of Louis XIII. This is considered one of the earliest reports of secondary intestinal tuberculosis. At the beginning of the 20th century it had become customary to describe three forms of abdominal tuberculosis (Anderson 1953; Boyd 1943) – 1) Ulcerative tuberculosis or tuberculous enteritis 2) tuberculous peritonitis 3) hyperplastic tuberculosis [1,2].

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Armstrong (1952) describes the modes of infection and pathological changes in different types of lesions in abdominal tuberculosis as- Modes of infection – (a) Primary by ingestion (b) Secondary by ingestion, haematogenous spread, lymphatic spread [1,2].

In both primary and secondary intestinal infections the site is more commonly in the lower part of ileum especially in the ileocaecal region. The tubercular lesions start in the peyer's patches and solitary lymph follicles which show swelling, caseation, softening and ulceration. The ulcers spread transversely round the gut. The walls and edges are thickened and raised. The floor is caseous and often shows miliary tubercles which may also be found on the peritoneal surface of the bowel. The mesenteric and para-aortic lymph nodes are usually enlarged [1,2].

Tuberculous lesions in the small intestine not only mimic Crohn's disease, but lymphoma and ischemic strictures, and there can be multiple skip lesions. On histological examination, the mucosal ulcers do not

usually penetrate the muscularis mucosae, but deep to this there are masses of granulomas which may coalesce and often show central necrosis with caseation. The granulomas are scattered in all layers of the intestine and may involve the serosa. They may be caseating or non-caseating. In non-caseating tuberculosis, the granulomas are more numerous, larger and well defined, and may coalesce. The final stage in the granulomatous inflammatory reactions in the small intestine is fibrosis, uncommon in Crohn's, which leads to multiple stricture formation and eventually intestinal obstruction [1,2].

Tuberculosis (TB) can involve any part of the gastrointestinal tract from mouth to anus, the peritoneum and the pancreatobiliary system. It can have a varied presentation, frequently mimicking other common and rare diseases [3]. The clinician must look for tuberculosis, and confirm or exclude this treatable malady in any patient who presents with gastrointestinal disease. Both the incidence and the severity of abdominal tuberculosis are expected to increase with increasing incidence of HIV infection in India.

Intestinal tuberculosis (ITB) may occur with or without presence of pulmonary disease. 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 [4]. 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 [5].

Materials and Methods

This was a prospective study of tuberculous lesions of small and large bowel including appendix over a period of five years (Jan 2011 to Dec 2015). These cases were selected from 205 consecutive specimens of small and large intestines including appendix, from patients who were operated in our hospital during a period of five years.

Clinical data and endoscopic findings were noted from patient's records. Clinical data was collected according to age and sex of the patient, mode of presentation and complications if any. All surgically resected specimens were received in 10% buffered formalin. The lymph nodes if any, were dissected from specimen and examined. In large and small bowel specimen, bowel was opened longitudinally through entire length, along antimesenteric border. The specimen was pinned on a corkboard and fixed overnight in the formalin.

In gross examination 1) nature of the specimen 2) length of the intestine 3) presence and number of strictures and perforations and 4) presence of serosal tubercles were noted. Mucosal and serosal surface of the specimen were examined for presence of ulcers, strictures, perforations, tubercles and wall thickening.

Sections were given from pathological lesions and adjacent tissue along with proximal and distal resection margins. In appendix, transverse section from pathological lesions and adjacent tissue were given. Sections were processed routinely and were embedded in paraffin. 4-5 micron thick sections were cut and stained routinely with H & E and Ziehl-Neelsen stain.

Cases that showed at least two criteria of 1) characteristic gross findings of ulcerative, hypertrophic types or fibrous strictures and 2) caseating or noncaseating granulomas on microscopy 3) with or without contributory ZN staining were reported as intestinal TB.

Observations & Results

The present study was carried out to analyse clinicopathological correlations of tuberculous small and large bowel lesions including appendix from 1/01/2011 to 30/12/2015 encountered in our hospital. Detailed clinical and investigational data were collected and macroscopic and microscopic features were studied. Based on these studies the following observations were made.

Age and Sex Distribution

Age range for ITB in this series was 12 to 70 years. Out of total 30 cases of intestinal TB, maximum cases were seen in the age group of 21-30 years (33.3%), as seen in Table 1. M: F ratio was 2: 1.

Clinical Presentation

As depicted in Table 2, abdominal pain was the most common presenting symptom followed by fever, nausea and vomiting.

Of the 30 cases, 20 (66.66%) presented with subacute to acute intestinal obstruction and 6 (20%) presented with intestinal perforation and 4 (13.33%) presented with lump in abdomen. Evidence of tuberculosis in organs other than the intestine was found in 5 (16.66%) cases. Of these, 4 (13.33%) cases showed evidence of pulmonary TB on imaging studies and 1 case had previous history of intestinal TB.

Gross Morphology

On gross examination, the most common site of involvement was the ileum in 16 (53.33%) cases followed by concurrent involvement of the ileum and caecum was seen in 6 (20%) cases. Other sites of involvement were caecum in 2 cases (6.66%) cases, descending colon and rectum in 2 (6.66%) cases, anal canal in only 1 (3.33%) and appendix was involved in 2 (6.66%) cases (Table 3).

The most common gross morphological features identified were ulcers in 21 (70%) (Figure 1) and strictures in 9 (30%) cases (Figure 2). Out of 30 cases,

6 resected specimens (20%) were associated with enlarged mesenteric lymph nodes. And the specimen of appendix was having a thickened wall.

Microscopic Examination

Microscopic examination of sections from intestine had revealed classical caseating granulomas in 19 (63.33%)(Figure 3 & 4) and granulomas without caseation in remaining 11(36.66%). 6 resected specimens were having mesenteric lymph nodes enlargement which also showed presence of caseating granulomas.

Table 1: Age distribution in 30 cases of intestinal TB

Age (years)	No of Cases	Percentage (%)
1-10	00	00
11-20	04	13.3
21-30	10	33.3
31-40	06	20.0
41-50	05	16.8
51-60	01	3.33
61-70	04	13.3
Total	30	100%

Table 2: Presenting symptoms in 30 cases of intestinal TB

Symptoms	Number of Cases	Percentage (%)
Abdominal Pain	22	73.33
Nausea	18	60.00
Vomiting	15	50.00
Diarrhoea	08	26.66
Constipation	10	33.33
GI bleed	05	16.66
Lump in abdomen	04	13.33
Fever	20	66.66
Weight loss	15	50.00

Table 3: Site-wise distribution of cases of intestinal TB

Site	No. of Cases	Percentage (%)
Ileum	16	53.33
Caecum	02	6.66
Ileo-caecal junction	06	20.00
Appendix	02	6.66
Colon & Rectum	02	6.66
Anal Canal	01	3.33
Total	30	100%



Fig. 1: Gross appearance of ulcerative mucosa of bowel

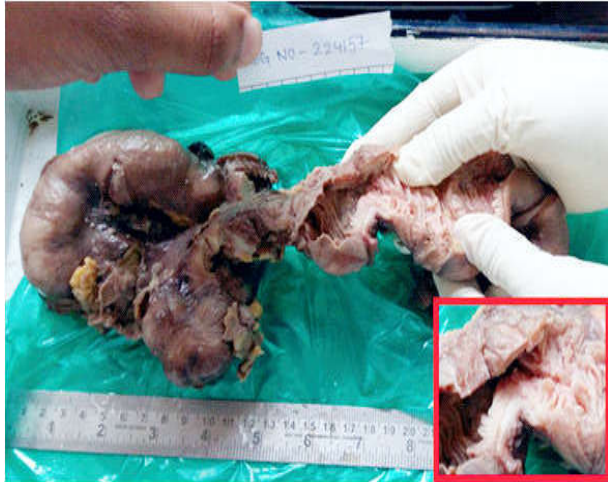


Fig. 2: Gross appearance of stricture in the wall of ileum

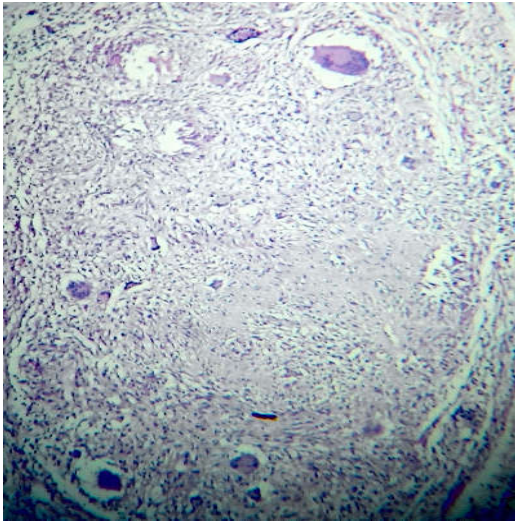


Fig. 3: Section showing multiple caseating granulomas in the submucosa of ileum. H&E (10X)

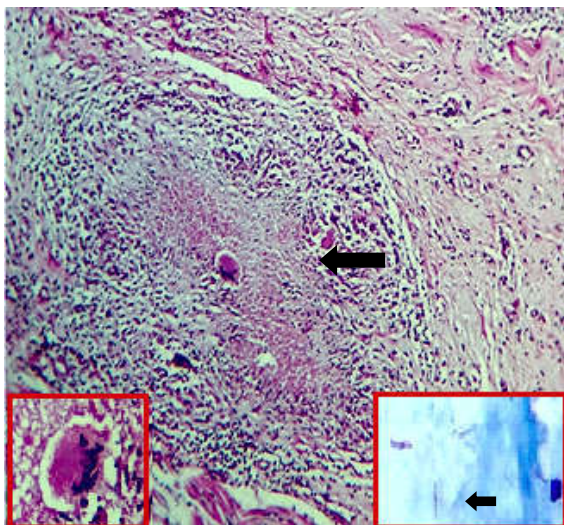


Fig. 4: Section showing Epithelioid granuloma with central caseation necrosis H&E (10X). Rt. Inset shows AFB positive bacillus (100X). Lt. inset shows Langhans' giant cell (40X)

ZN staining for demonstration of AFB was performed on tissue sections of all 30 cases. AFB were demonstrated in 9 (30%) cases (Figure 4).

Patients with histopathological diagnosis of intestinal TB were referred to the Department of TB and Chest diseases of the Hospital where they were started with Combined Anti Tubercular (CAT) therapy.

Discussion

Pulmonary as well as extra-pulmonary tuberculosis (TB) has made a global comeback [6]. India is the highest TB burden country in the world with a current prevalence of 2.8 million cases [7]. 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 male preponderance. Age and sex occurrence of the present study correlated with that of other studies [8,9].

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 military TB, (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. 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 [10]. Reinfection plays an important role in regions of high contagion. However, as culture studies were not done, causative organism could not be confirmed in our cases.

Intestinal obstruction was the most common mode of presentation in our study and also observed by other workers [11,12]. In our study, maximum number of patients were presented with abdominal pain which was non-specific, which was in concordance with poffe et al [13].

The preoperative diagnosis of abdominal tuberculosis is difficult. Routine haematological and biochemical tests are of no diagnostic value. 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. In the past, numerous

reports in the literature have stressed the need for surgical intervention to establish the diagnosis [14].

Although TB can involve any part of GIT, the most frequent site of involvement was ileum and ileocaecal region of small intestines followed by appendix and colon in present as well as other studies [8,15]. 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 permits free contact of the organisms with the mucosal lining and an abundance of lymphoid tissue at the site [16].

The ulcerative gross morphologic type commonly affects the ileum and ileo-caecal junction and is characterised by a single or multiple superficial, transverse ulcers, the healing of which may lead to stricture formation.

Classically, the diagnosis of tuberculosis is based on the demonstration of caseating granuloma, but a significant number of granulomas may not show caseation. Several workers [14,17] have reported non caseating granuloma in patients with tuberculosis. In the present study, classical caseating granulomas were seen in 19 (63.33%) and granulomas without caseation in remaining 11 (36.66 %). Few other studies also observed tubercular lesions showing granulomas without caseation [18]. Demonstration of acid fast bacilli in tissue sections is a definitive diagnostic method for tuberculosis. Alvarez et al [19] found AFB positivity in 5% cases of colonic tuberculosis.

Patel et al [20] demonstrated AFB smear positivity in 40.5% cases of ITB in tissues from luminal sources. Thus even though it is an important diagnostic test for tuberculosis, the sensitivity of AFB detection in tissues is very low ranging from about 10 to 50%. In our study, AFB were demonstrated in 9 (30%) cases. Thus, the absence of acid fast bacilli does not always rule out tuberculosis completely. Anti-TB therapy remains mainstay of treatment in ITB, before and after surgery [18].

Conclusion

Change in disease presentation, non-specific clinical picture and radiological 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.

TB is an endemic disease in our country. Hence, it is advisable to send every specimen of the bowel for histopathological examination. Timely diagnosis and management of the patient with anti-tubercular regime prevents complication such as stricture formation and spread to other organs. This ensures prevention of complications and complete cure.

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