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Original Article

Diagnosis of Intestinal Tuberculosis at Viet Duc Hospital (2004-2009)

Nguyen Duc Chinh*
Do Duc Van*
Do Son Ha*
Nguyen Van Xuyen*
Nguyen Quang*
Ninh Viet Khai*
Pham Hai Bang*
Michel Huguier**

**Department of Septic Surgery, Viet Duc Hospital, Hanoi, Vietnam*
***Hospital Tenon, Paris France*

Abstract

Purpose: **Gastrointestinal tuberculosis, especially complicated intestinal tuberculosis (ITB) is still an ongoing challenge for physicians and radiologists. This study aimed to assess the clinical features and related factors which might help the diagnosis and direct proper management.**

Materials and Methods: **This was a retrospective study of all ITB diagnosed in patients over 16 years of age who were treated at Viet Duc Hospital from 2004 to 2009. ITB was confirmed by histopathological examination or PCR assay of the biopsies or surgical specimens.**

Results: **There were 85 cases of ITB patients including 61 men and 24 women. Common symptoms were abdominal pain (90%), diarrhea (82%), weight loss (61%) and fever (55%). A medical history of TB was found in 41% of cases. The complications most commonly observed were bowel obstruction (38.8%) and peritonitis (25.5%). Ultrasound and CT scan findings were ascites, ileo-cecal bowel wall thickening, proximal dilatation of bowel loops and cecal mass. Colonoscopy with biopsy confirmed the diagnosis in 66.7% whereas PCR assay was positive in 53.9%. A pre-operative diagnosis was established in 39% of patients, while the diagnosis was established intra-operatively in 83.5%. There were surgical indications to make a diagnosis in 13.9%.**

Conclusion: **ITB has diverse and non-specific symptoms and is an ongoing diagnostic dilemma for both physicians and radiologists. X-ray and endoscopy with biopsy are the most helpful means for establishing a definitive diagnosis.**

Keywords: **acute abdomen, colonoscopy, intestinal tuberculosis, PCR assay**

Introduction

Intestinal tuberculosis (ITB) was relatively common in the world in the first half of the twentieth century when it had an 80% mortality associated with pulmonary tuberculosis.[1] Since the effective anti-tuberculous chemotherapy was introduced and the standard of living improved, the frequency of ITB has decreased. Most recently, however, the incidence of ITB has increased again due to the widespread immigration and increased prevalence of human immunodeficiency virus (HIV) infection. Approximately one of eight of total TB cases are extra

Correspondence address : *Nguyen Duc Chinh, MD, Chief, Department of Septic Surgery, Viet Duc Hospital, 40 Trang Thi, Hanoi, Vietnam, Telephone: 00844 3 8250783, Fax: 00844 3 8248308; E-mail: duc_chin1960@yahoo.com*

pulmonary, of which ITB accounts for 11-16%. ITB may be enteric (intestine involved itself), peritoneal, nodal (with lymph nodes involvement) and solid visceral TB (such as hepatic, spleen and renal disease). In HIV-positive patients the incidence of ITB is up to 50%.[1-3]

Diagnosis of ITB is difficult because its clinical features are usually vague and non-specific, especially in complicated intestinal tuberculosis. Furthermore, other diseases often mimic ITB, such as Crohn's disease, abdominal lymphoma and solid organ malignancy. These complexities of diagnosing may often delay its diagnosis and treatment, particularly in settings with limited resources. This delay contributes to its high mortality rate.[2,4,5]

The aims of this study were to review the patients diagnosed with ITB treated in our hospital and to assess the value of the clinical, physical and laboratory findings in establishing an early diagnosis in order to reduce its morbidity and mortality.

Material and Methods

The retrospective study included all patients with acute intestinal tuberculosis aged over 16 years who were treated at Viet Duc Hospital during a 5-year period from January 2004 to May 2009. The sex, age, occupation, medical history, symptoms and physical findings of patients were recorded. The diagnosis of ITB was confirmed by histopathology examination and other specific tests such as TB PCR.

All data was analyzed using SPSS (version 13.0 for Windows; SPSS; Chicago; IL) for analysis. Qualitative and quantitative variables were analyzed.

Results

Demographics and Clinical Characteristics

From January 2004 to May 2009 a total of 85 patients were diagnosed with ITB including 61 (71.8%) males and 24 (28.2%) females. Ages of the patients ranged from 17 to 83 years with a mean age of 42.24 years.

The most frequent symptoms were pain in 77 patients (90.6%), constipation associated with diarrhea in 70 patients (82.4%), diarrhea in 31 patients (36.5%), vomiting in 39 patients (45.9%), fever in 47 patients (55.3%), weight loss in 52 patients (61.2%), anorexia in 45 patients (52.9%) and bloody diarrhea in 6 patients (7.1%). Thirty five patients (41.2%) had a past history of treatment for tuberculosis, including 25.7% with lung TB and 28.6% with other sites of abdominal TB.

Complications of ITB included subacute intestinal obstruction in 44 patients (52.8%), fistula in 18 patients (21.2%), entero-bladder fistula in two patients (2.4%), peritonitis in 19 patients (22.4%), intra-abdominal abscess in three patients (3.5%) and hemorrhage in one patient (1.2%).

Hematological and biochemical analyses commonly showed non-specific changes that might be important evidences of malnutrition and infection. Our series showed that the hematological and biochemical examinations were often normal, except ESR (mm/1st hour) was higher than 50 in all patients with the mean ESR of 56.3.

Abdominal ultrasound findings were normal in 5 patients (6%), ascites was present in 50 patients (59.5%), intestinal obstruction in 28 patients (33.3%), enlarged mesenteric lymph nodes in 7 patients (8.3%), tumor in 10 patients (11.9%) and omental thickening in 6 patients (7.1%).

Colonoscopy was performed in 15 patients and revealed a fistula in one patient (5.6%), polyps in 5 patients (27.3%), a deformed cecum in 7 patients (38.9%), intestinal ulcerations in 12 patients (66.7%) and an irregular lesion in 2 patients (11.1%). Results

Table 1 Significant Findings from CT Scan of the Abdomen

Findings	N (33)	%
Loop wall thickening	15	45.5
Peritoneum inflammation	13	39.4
Enlarged mesenteric lymph nodes	8	24.2
Calcified lymph node	1	3.0
Dilation bowel loop	4	12.1
Ascites	8	24.2
Tumor of colon	8	24.2
Huge intra-abdominal mass	2	6.1
Hepatosplenomegaly	5	15.2
Ovarian mass	2	6.1

Table 2 Barium enema results

Findings	N (11)	%
Normal	1	9.1
Fistula	1	9.1
Deformed cecum	2	18.2
Colon tumor	7	63.6

of biopsies obtained by colonoscopy confirmed the diagnosis of TB in 10 patients (66.7%).

Other laboratory tests

AFB were found on abdominal fluid collected in 29 patients, however the results were positive in only three patients (10.3%). PCR was positive in 53,9% of ascitic fluid.

Among 85 patients admitted with ITB 79 patients required an abdominal operation. Pre-operative diagnosis was established in 31 patients (39.2%), diagnosis was made intra-operatively in 66 patients (83.6%). Frozen sections were performed in 14 patients, confirming the diagnosis of TB in 13 cases (92.9%).

Discussion

Tuberculosis continues to be an important medical, social and economic problem in many developing countries where public health and sanitation are limited. While pulmonary tuberculosis is the most common site of disease, gastrointestinal tract involvement is very rare and difficult to diagnose clinically due to its vague and non-specific clinical features. Complicated and acute intestinal tuberculosis are particularly difficult to diagnose.[1,2,6,7]

Typically, the diagnosis of ITB is based upon the analysis of clinical features and past history, results of microbiological investigations [Acid Fast Bacilli (AFB) smears or culture], histopathology from biopsies tissues obtained by colonoscopy showing tubercular granuloma (with or without caseation) and imagings (such as ultrasound, CT scanner, barium enema, including chest X ray). Patients with a high index of clinical suspicion and negative diagnostic workup may be diagnosed with ITB if they show a good response to therapeutic trial of anti TB medicines[2].

Smear and culture are usually performed, however smear has a low sensibility and specificity while culture takes time to confirm the diagnosis. This limitation often delays the confirmation of a diagnosis in complicated ITB.

The most frequent symptoms clinically at presentation ITB were abdominal pain, fever and weight loss. In one study by Rustam Khan[2] common symptoms included abdominal pain 93%, fever 64%, night sweats 48%, weight loss in 47% and vomiting associated with constipation or diarrhea (36%). VKS Leung[4] showed that abdominal pain occurred in 84%, diarrhea in 55%, weight loss 55% and fever in 45% of patients. In our series, the most common symptoms were abdominal pain (90.6%) and constipation associated with diarrhea (82%), fever (55%) and weight loss (61%).

Current series of ITB patients without HIV have highlighted several important considerations. Young, female predominance was shown as one characteristic feature of ITB in several studies in the past, contributing up to 59%.[2,3] In contrast, our study showed most patients with ITB but without HIV were male, with a mean age of 42.2 years. Past history of TB supported a diagnosis of ITB. In our series, the history of previous TB was present in 41% of patients, of which 92 % had previously received anti TB therapy. In another reviews, the history of past TB, especially lung TB was up to 60%. Other studies report similar findings.[2,6]

Intestinal obstruction and peritonitis were most common complications of ITB in the literatures.[4,7,8] In our study, sub-acute intestinal obstruction was seen in 38.8%, peritonitis in 25.8% respectively. Initially, AFB smears and culture are helpful for diagnosis of ITB. In the literature, results of microscopic examinations of ascitic fluid from patients with ITB were positive for AFB in less than 5% of cases and cultures were positive in 20 to 85% of patients.[9] However, cultures often take more than six weeks, which delays diagnosis. When a peritoneal fluid specimen is collected or ≥ 1L of ascitic fluid is aspirated and sent for AFB smears and culture, the sensitivity rate for ITB exceeds 80%. In our series only 10.3 % of ascitic fluid collected in ITB patient was positive for AFB.

In recent years, the polymerase chain reaction (PCR) has been more widely introduced in making a diagnosis of TB. PCR is positive in up to 80% with reported specific and sensitivity rates of 95 % and 98% respectively. PCR from tissue collected from biopsy or operative specimens can contribute to the diagnosed ITB.[2,6] However, in this study, the PCR from abdominal fluid was positive in 53.9%. The tissue PCR was not available in our hospital.

Radiography is generally a safe and helpful procedure for diagnosing ITB, and some authors have suggested that the carefully x ray analysis can confirm the ITB diagnosis. Barium meal studies have been considered as the gold standard for diagnosis of ITB by many physicians globally[10] and in Pakistan. Le Van

Hoanh[1] reported that x-ray could establish the diagnosis of ITB in early disease by specific findings, e.g. the radiographic sign of Stierlin which shows the deformed and irregular wall of the cecum with proximal dilation of the small bowel (Figure 1). Hablani and Rustam[2,11] found that the particular images of ITB on barium enema were luminal narrowing with proximal dilation bowel and deformity of the cecum, which can cause the bowel obstruction. In the series of Rustam, there were up to 90% of barium enemas showed the intestinal wall thickening and narrowing of the colon wall with dilation of small bowel. Some other studies have shown that the x-ray was not helpful in early disease and seldom helpful in advanced disease.[10] Diagnosis made on the basis of radiography is rapid, easy and less expensive but it is presumptive and cannot completely exclude other diseases such as Crohn's disease, malignancies and other disease of digestive tract. In our series, the most common findings were deformed cecum with thickening of bowel wall in 81.8% of patients.

Common features of computerized tomography (CT) and ultrasound of the ITB were bowel wall thickening, enlarged mesenteric lymph nodes, ascites, omental thickening or rarely central necrosis.[12] In the series of Rustam,[2] the CT scanner findings were ascites in 79%, enlarged lymph nodes in 35%, and 25% of patients had bowel wall thickening (Figure 2). The pulmonary tuberculosis on x-rays chest also were found in 64% and had radiological features of active pulmonary TB in 4.8%. Among 33 patients undergoing the CT scan in our study, the most findings were the bowel wall thickening in 45.5%, ascites in 43.5%, enlarged lymph nodes in 24%. The common ultrasound findings were ascites (60%), bowel dilation (33%), and bowel wall thickening (25%).

Colon and terminal ileum are the most common sites of involvement in the intestinal variety of tuberculosis and in this regards colonoscopic images and biopsies are considered a quick and accurate diagnostic tool. Colonoscopy also helps in differentiating the colonic tuberculosis from Crohn's disease and other diseases. In the series of Rustam,[2] the most common lesions of ITB on colonoscopy were deformed cecum in 91%, and irregularity of ileocaecal valve in 80% and mucosal ulcers in 80%. Nodules were present in 31% of colonoscopies performed and colon strictures were present in 17%. In the present series, the colonoscopic biopsies were helpful in making a rapid and accurate diagnosis. In the report of Rustam, colonoscopy biopsies were positive in 83% compared with 62% in Nguyen Duc Chinh's study.[2,13] Yilmaz and Geraldine[7,9] reported that the colonoscopic biopsy was very useful in the diagnosis of colonic and ileocolic tuberculosis. The most common colonoscopic features

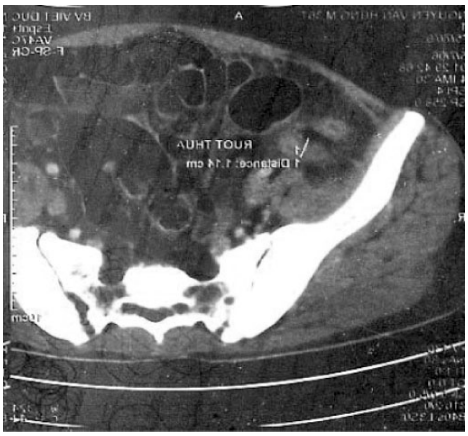


Figure 2 Abdominal CT scan showed ascites and bowel wall thickening



Figure 1 Barium enema showed sign of Stierlin



Figure 3 Colonoscopy showed ileocecal valve ulcers

are ulcers, nodules and a deformed cecum and ileocecal valves. Colonoscopy with direct biopsy may provide rapid diagnosis for large bowel and ileocecal TB. This technique may be unsuccessful if bowel preparation is inadequate and if there is marked angulation of the splenic flexure or significant bleeding. If the histopathology does not show a typical granuloma with caseation then the patient may be mistakenly diagnosed with Crohn's disease. In the literatures, the histopathology can be non-diagnostic in up to 10% of patients due to the nonspecific features.[4,11] In our series, the most common features were nodule-ulcers (66.7%) and deformity of the ileocecal valves (38.9%).

Many authors advocated a trial of therapeutic anti-tubercular medications, however we believe that this should not be encouraged routinely as it may delay the diagnosis of malignancy, lymphoma and Crohn's disease. The therapeutic trial of anti TB drugs should not be taken more than 3 weeks before reviewing the diagnosis. Some studies reported that a presumptive diagnosis by therapeutic trial can be made in up to 40% of cases of ITB.[6,8] In the study of Rustam, 76% patients responded to medical treatment alone and only 17% patients with complication at admission required additional surgical intervention. This was consistent with the findings of Quang Van Tri.[5]

In cases where other diseases are suspected or the patient has not responded to a therapeutic trial of anti TB drugs, then laparoscopy and biopsy are generally safe and may help in establishing the diagnosis of ITB. In different studies, laparoscopy was found helpful in the diagnosis between 87% and 92% of cases. Peritoneal biopsy via mini-laparotomy should also be considered if laparoscopy is non-diagnostic.[1,2,7] In our study, 14% of exploratory laparotomy was diagnostic.

Conclusion

Intestinal tuberculosis has diverse and non-specific symptoms. No single test alone is insufficient for reaching a diagnosis, particularly in cases of complicated ITB. Currently, the diagnosis of ITB should be based upon the analysis of the clinical features, results of positive acid fast bacilli (AFB) smears or culture, histopathology from biopsies tissues obtained by colonoscopy or operative specimens, imaging investigations such as ultrasound, CT scanner, barium enema and including chest X ray. Colonoscopic biopsy is a highly specific and sensitive tool for diagnosing ITB. Finally if there is a high index of clinical suspicion despite a negative diagnostic workup, the diagnosis can be based upon a good response to therapeutic trial of anti TB medicines. Until the time when we have a more specific test for diagnosis of ITB, this remains a considerable challenge for physicians.

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