



# Clinical Presentation in a Series of Eight Children with Abdominal Tuberculosis: Experience of a Single-Center in Turkey

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Received 2016 November 22; Revised 2017 February 16; Accepted 2017 April 25.

## Abstract

**Background:** Abdominal tuberculosis, the sixth commonest extrapulmonary tuberculosis, is easily misdiagnosed due to nonspecific gastrointestinal symptoms. The diagnosis is highly dependent on clinician's suspicion of the disease; therefore to increase awareness we retrospectively reviewed clinical features of eight children in a four year-period.

**Methods:** The medical records of children with abdominal TB were retrospectively reviewed. The diagnosis of abdominal TB was defined as Mycobacterium tuberculosis infection of gastrointestinal tract along with peritoneal or solid organ involvement.

**Results:** There were six girls and two boys with a mean age of  $13.6 \pm 2.8$  years (range, 7 - 16 years). Abdominal pain and weight loss were common complaints in all patients (100%) at presentation; fever was present in four (50%) patients and abdominal distension in two (25%) patients. Mean duration of symptoms before diagnosis was  $2.5 \pm 1$  months. Laparotomy performed in six patients, and the peritoneum was the most common infection site (in 5 patients). Chest X-rays of 7 patients indicated lung involvement. The most common abdominal computed tomography and ultrasonography finding was ascites. Bowel wall thickening was recorded in 2 patients and ileal thickening in 1 patient. Inguinal lymphadenopathy and multiple mesenteric lymphadenitis were present as single cases.

**Conclusions:** The abdominal tuberculosis should be suspected in children with ongoing abdominal pain, fever, and abdominal distension, laparoscopy or laparotomy could be useful in the differential diagnosis and utilizing imaging techniques, invasive methods with clinical suspicion may prevent delay of the diagnosis.

**Keywords:** Abdominal Tuberculosis, Clinical Manifestations, Diagnosis, Children

## 1. Background

The incidence of tuberculosis (TB) is increasing worldwide. The world health organization (WHO) published global TB data. In 2015, there were an estimated 10.4 million new incidents of TB cases worldwide, of which 1.0 million (10%) occurred in children (1). There are several reasons for high morbidity rate of this preventable disease such as poor treatment adherence, acquired drug resistance, treatment failure, and development of Mycobacterium tuberculosis infection without any clinical symptoms, which increases the risk of progression and extrapulmonary manifestations (2-5). Abdominal TB is the sixth commonest extrapulmonary TB after lymphatic, genitourinary, bone and joint, miliary, and meningeal forms, constituting 5% of all

TB cases (6, 7). It occurs via the infection of gastrointestinal tract through hematogenous spread from a primary lung focus, or via lymphatics from infected nodes, ingestion of bacilli either from the sputum or from contaminated milk products, or by direct spread from adjacent organs (3, 8, 9). Pathogenesis usually involves peritoneum and pancreatobiliary system, most commonly observed in ileocecal area and results in granuloma formation, caseation, mucosal ulceration, fibrosis, and scarring (8). Abdominal TB is relatively well described in its most common age group of adults (25 to 45 years old); however, it is quite rare in children (8, 10, 11). The incidence in children was reported to be around 10%, of which over 50% have extra-abdominal manifestations such as meningitis that can lead to more severe

disease with higher rate of morbidity and mortality (11, 12). The actual number of children with abdominal TB may even be higher than previously reported due to incorrect diagnosis. For example, Ridaura-Sanz et al. (13) reported in their study with autopsy cases of children who died from TB, that 15.7% of all cases had peritoneal/intestinal disease.

Diagnosis of abdominal TB in children is challenging due to nonspecific clinical features depending on host factors such as age and immunological status; and in most cases, pulmonary TB is absent making it difficult to establish the diagnosis (6, 14-18). Less than half of the patients can be diagnosed with abdominal TB when the only clinical presentation is abdominal complaint such as pain (3). When diagnosis is delayed, the rate of complications, therefore, mortality increases (10, 19, 20). The diagnostic modules are multiple; a positive tuberculin skin test, results of chest radiography, epidemiological link to a known source and exclusion of all other possible pathologies with similar clinical features like inflammatory bowel disease, malignancy, and other infectious diseases (3, 7, 17). The diagnosis of abdominal TB in a pediatric patient is, therefore, highly dependent on the clinician's awareness of nonspecific clinical features to become suspicious of the disease (3, 7, 17).

## 2. Objectives

Here, we aimed to present our four-year experience on the clinical features of abdominal TB in children followed up in our hospital.

## 3. Methods

### 3.1. Study Design and Patients

This was a descriptive case-series study. The medical records of children with abdominal TB who were followed up at pediatric Infection and pediatric gastroenterology departments of Sisli Hamidiye Etfal research and training hospital (Istanbul/Turkey) from 2010 to 2014 were retrospectively reviewed. The diagnosis of abdominal TB was defined as *Mycobacterium tuberculosis* infection of gastrointestinal tract along with peritoneal or solid organ involvement. The exact diagnosis was based on 1) bacteriological identification of *Mycobacterium tuberculosis* with Ziehl-Neelsen acid-fast staining and/or inoculation on Lowenstein-Jensen medium, 2) histopathological evidence of caseous necrosis and epithelioid granuloma on biopsy specimens, and/or 3) clinical and radiological evidence compatible with TB and elimination of all other possible pathologies with similar clinical features.

### 3.2. Follow-Up and Management of Patients

Abdominal TB was identified in eight children whose data including demographic characteristics (age, gender, and ethnicity), medical history, presenting symptoms and their duration, physical evaluation, laboratory data, radiological findings, diagnosis, treatment, and clinical outcome were collected. Records of selected patients were reviewed in detail for Bacillus Calmette-Guerin (BCG) vaccination, history of contact with an adult with TB, results of physical evaluation (fever, weight loss, night sweat, poor appetite, abdominal pain, diarrhea and constipation), clinical evidence (abdominal swelling, abdominal mass, ascites and lymph node enlargement), biochemical profile (erythrocyte sedimentation rate), radiological evidence (chest radiographs, abdomen ultrasonography, chest and abdominal tomography, when available), laparoscopy operation notes and results, treatment and clinical outcome. Tuberculin skin tests were performed using the purified protein derivative (PPD) with intradermal injection of 5 tuberculin units. Results were interpreted after 72 hours where an induration of 15 mm or more in children with BCG vaccination, or an induration of at least 10 mm in those without BCG vaccination, was referred as positive.

Patients were treated with antituberculous drugs; rifampin, isoniazide, pyrazinamide, streptomycin/ etambutol at pediatric doses. The combination treatment was terminated at the end of second month, maintenance with rifampin, isoniazide was continued for 7 months. Patients with tuberculous peritonitis were also given methylprednisolone (2 mg/kg per day) for the first six weeks. The duration of the therapy was twelve months in the patient with disseminated involvement.

### 3.3. Statistical Analysis

Study data were summarized using descriptive statistic (e.g., mean, standard deviation, frequency, percentage). Analysis was performed by statistical software statistical package for social sciences version 15.0 (SPSS Inc, Chicago, IL, USA).

## 4. Results

### 4.1. Demographic and Clinical Characteristics of Patients

Eight patients were diagnosed with abdominal TB six girls and two boys with a mean age of  $13.6 \pm 2.8$  (range, 7 - 16) years (Table 1). One of the patients was of Syrian origin; others had been born in Turkey. The history of exposure to TB from a known source was found in three patients (Table 1). At presentation, abdominal pain and weight loss were common complaints in all (100%) patients. Abdominal distension was present in two (25%) patients, while four

(50%) patients had fever and one (12.5%) patient had rectal bleeding (Table 1). Mean duration of symptoms before diagnosis was  $2.5 \pm 1$  months (range, 1 - 4 months) (Table 1). All patients had BCG scars. TST was not given to one patient, and six out of the remaining seven patients had negative test with an induration ranging from 10 - 15 mm (Table 1). Quantiferon was positive in four (50%) patients of the patients (Table 1). Erythrocyte sedimentation rate varied, but was relatively high in most patients (Table 1). Anemia was present in six (75%) patients. Positive bacterial sputum cultures were present in two patients, whereas growth was observed only in one patient on gastric fluid culture (Table 1). Laparotomy was performed in five patients and histopathological evidence indicated abdominal tuberculosis in six patients (Table 1). The peritoneum was the most common infection site (five patients), followed by small intestine (two patients). One patient had co-existent intestinal and lymph node infection, and another patient had peritoneal and lymph node infection (Table 1).

#### 4.2. Radiological Evaluation

Chest X-ray was performed in seven patients, and all indicated lung involvement including miliary TB (one patient), pleurisy (one patient), mediastinal lymphadenopathy (three patients, one along with tree-in-bud sign), and cavitory and calcific nodules at one lung (three patients) (Table 2). Chest computed tomography results were similar to chest X-ray results except for one patient (patient number 8) where CT results indicated normal appearance (Table 2). The most common abdominal tomography and ultrasonography finding was ascites (Table 2). Abdominal CT indicated omental cake in two patients and fluid in the pouch of Douglas in two other patients (Table 2). Bowel wall thickening was observed in two patients and ileal thickening in another patient (Table 2). Inguinal lymphadenopathy, multiple mesenteric lymphadenitis and inflammation of the cecum were present as single cases (Table 2).

#### 4.3. Outcomes

All patients completed the therapy. Drug reaction was noted in two patients. Drug reactions were mildly elevated liver enzymes and at follow-up with dose modification liver enzymes became normal. One patient developed sequelae with neurological involvement at the follow-up. The disseminated involvement was seen in this patient.

## 5. Discussion

According to the WHO's latest report in 2016, there are an estimated 14,000 TB cases in Turkey. Among new and re-

lapse cases; 4% of them were under 15 years old (1). Abdominal TB is mostly seen in patients aged between 25 and 45 years, and relatively uncommon in children (10, 21). Lack of the diagnostic tests and challenges in the setting of the diagnosis may be the factors of the low incidence of abdominal TB in children. Forssnohm et al. (22) reported the incidence of peritoneal TB cases in children under 14 years old as 5% in Germany, and Starke et al. (23) indicated that peritoneal TB in children less than 20 years old (mean age of 13 years) was recorded only in 0.3% of population in US. The frequency of abdominal TB is also rare in Turkey; in the present study there were only eight children in a four-year period which is similar to a previous report where Dinler et al. (10) followed nine children in a five year period in the Black sea region of Turkey. Kilic et al. (24) reported 35 children diagnosed with abdominal TB in a fifteen year period. The mean age of our study population was  $13.6 \pm 2.8$  (range, 7 - 16) years, which is in compliance with the literature. The youngest patient was a boy of seven years.

Abdominal TB is a clinically complex disease, and diagnosis is often delayed due to nonspecific symptoms (9). Most common clinical signs and symptoms are fever, weight loss, abdominal pain, abdominal swelling, hepatomegaly, diarrhea and constipation, fatigue and malaise (3, 10, 11, 25). The most common symptoms reported in various studies were fever (73% - 75%) (12, 26), weight loss (46.9% - 81%) (12, 27), fatigue (81%) (27), and abdominal pain (51.2% - 93%) (12, 24, 28, 29). In agreement with the literature the clinical symptoms of the study patients were similarly nonspecific; the most common of which was abdominal pain observed in all patients, followed by fever (50%) and abdominal distension (25%).

The clinical manifestations of abdominal tuberculosis are protean and can mimic many other disease processes causing delay in diagnosis. When the disease is not suspected clinically, significant morbidity and mortality can be observed. Time to diagnosis of abdominal TB in the study patients was  $2.5 \pm 1$  (range, 1 - 4) months, which was similar to the diagnosis of 63% of the patients in more than six weeks as reported by Muneef et al. (26). Kilic et al. (24) reported mean 109 days as the duration of complaints at the time of presentation.

Inadequate diagnostic modules are another factor for the difficulties in diagnosis of abdominal TB (3, 9). Tuberculin skin test, for example, was reported to be positive only in 18% - 27% of the patients, although the results can vary between the studies (10, 19, 26). Similarly, in the present study there was only one positive result out of seven (28.5%) patients given the tuberculin skin test. Common diagnostic methods for microbiological confirmation of abdominal TB were reported to have very low sensitivity (3, 6, 18, 29). In this study, positive results were

**Table 1.** Demographic Profile and Clinical Findings of the Patients

	1	2	3	4	5	6	7	8
<b>Age (years)</b>	13	15	14	13	14	16	7	15
<b>Gender</b>	Female	Female	Female	Female	Male	Female	Male	Female
<b>Clinical presentation</b>	Abdominal pain, weight loss	Abdominal pain, abdominal distension, weight loss	Abdominal pain, weight loss, fever	Abdominal pain, abdominal distension, weight loss	Abdominal pain, weight loss, fever	Abdominal pain, weight loss, fever	Abdominal pain, weight loss, rectal bleeding	Abdominal pain, weight loss, fever
<b>Duration of symptoms (months)</b>	3	1.5	2	1	2	3.5	3	4
<b>Type of abdominal tuberculosis</b>	Intestinal+lymph node	Peritoneal	Peritoneal	Peritoneal	Intestinal	Peritoneal	Peritoneal+lymph node	Intestinal
<b>History of contact</b>	Yes	No	Yes	No	No	No	No	Yes
<b>BCG/TST (scar/mm)</b>	Positive/10	Positive/12	Positive/15	Positive/10	Positive/13	Positive/11	Positive/10	Positive/-
<b>Quantiferon</b>	Positive	Negative	Positive	Negative	Negative	Positive	Positive	Negative
<b>ESR (mm/h)</b>	57	72	55	61	42	71	37	31
<b>Bacterial sputum culture</b>	Yes	No	No	No	No	No	No	Yes
<b>Inoculation on culture media</b>	Positive	Negative	Negative	Negative	Negative	Negative	Negative	Negative
<b>Laparotomy</b>	Yes	Yes	No	Yes	No	Yes	Yes	No
<b>Histopathology</b>	Positive	Positive (Peritoneum biopsy)	None	Positive (Peritoneum biopsy)	None	Positive (Plastrone appendicitis)	Positive (Lymph node)	Positive (by colonoscopy)

Abbreviations: BCG, Bacillus Calmette-Guerin vaccination; ESR, erythrocyte sedimentation rate; TST, Tuberculosis skin test.

obtained only in two patients with bacterial sputum culture, and there were only one positive growth on culture media. A peritoneal biopsy via laparoscopy or laparotomy is highly suggested for diagnostic purposes in patients with clinical presentations suggesting abdominal TB to decrease complications and mortality (8, 14, 17). The observation of thickened peritoneum, multiple tubercles in peritoneum, adhesions, and granulomatous changes observed in biopsy specimens confirms abdominal TB (8, 17). Sotoudehmanesh et al. (30) established the diagnosis by laparotomy or laparoscopy in 74% of their cases (n=50). Kilic et al. (24) established the diagnosis by pathological examination of specimens obtained by laparotomy, laparoscopy, or fine-needle aspiration. As suggested, laparotomy was performed in five patients in this study and histopathological analysis indicated abdominal TB in 75% of these patients.

Chest radiographs were reported to be abnormal in 50% to 75% of abdominal TB patients (3, 10, 31). In the present study, the chest radiographs of seven patients (one

had no chest radiograph) clearly indicated lung involvement of TB. Kilic et al. (24), reported active pulmonary tuberculosis in 34.1% of their cases. Our results indicated more pulmonary involvement when compared with literature. Computed tomography is the best choice for diagnosis of abdominal TB where the infection can be visualized as peritoneal thickening, ascites with fine septations, mesenteric disease, lymphadenopathy, caseation within lymph nodes, fibrous bands, fistulae, pseudopolyps, ileocecal valve deformities, bowel wall thickening, omental caking, or bowel obstruction (3, 8). Chest computed tomography results of the study patients were quite similar to the chest radiograph results and in one case (patient no. 8) indicated normal appearance where mediastinal lymphadenopathy was observed on radiography. Abdominal CT, on the other hand, clearly indicated bowel and ileal wall thickening and omental cake appearance; all diagnostic evidences for abdominal TB. Ultrasonography is a non-invasive tool which is helpful to visualize the loculations and stranding in ascitic fluid, to demonstrate

**Table 2.** Radiological Findings of the Patients

Patient no.	1	2	3	4	5	6	7	8
<b>Chest X-ray</b>	Miliary tuberculosis	Pleurisy	Mediastinal lymphadenopathy, cavitory nodule at right lung	Calcific nodule at right lung	Mediastinal lymphadenopathy, tree-in-bud sign at left lung	Cavitory nodule at bottom side of right lung	Not evaluated	Mediastinal lymphadenopathy
<b>Chest CT</b>	Hilar lymphadenopathy, miliary tuberculosis	Pleurisy and pleural thickening	Mediastinal lymphadenopathy, nodule at right lung, cavitory lesion	Calcific nodule at right lung	Mediastinal lymphadenopathy, tree-in-bud sign at left lung	Cavitory nodule at bottom side of right lung	Not evaluated	Normal
<b>Abdominal CT</b>	Gallbladder stone, fluid in the pouch of douglas, inflammatory mass, paraaortic lymph nodes, inflammation of the cecum	Ascitic fluid	Ascitic fluid, inguinal lymphadenopathy	Gallbladder stone, ascitic fluid, omental cake	Bowel wall thickening	Gallbladder stone, ascitic fluid omental cake	Not evaluated	Ileal thickening, minimal fluid in the pouch of douglas
<b>Abdominal US</b>	Gallbladder stone, ascitic fluid, inflammatory mass	Ascitic fluid	Ascitic fluid, bowel wall thickening	Ascitic fluid	Bowel wall thickening	Ascitic fluid	Not evaluated	Cecal wall thickening, multiple mesenteric lymphadenitis

Abbreviations: CT, computed tomography; US, ultrasonography.

retroperitoneal or mesenteric adenopathy, abscesses or hepatosplenic nodules and to detect ancillary findings such as bowel wall thickening, omental mass, and solid organ involvement (3, 8, 29). So radiological examinations (chest X-ray, ultrasound, and CT) constituted main diagnostic modalities when we suspected abdominal TB as the diagnosis. Khan et al. (28), found that the most common findings were ascites (79%), lymphadenopathy (35%), omental thickening (29%), and thickening of the intestinal loops (25%) in abdominal ultrasound and CT. In this present study, ascites, the most common finding, was observed in five patients, and bowel wall thickening in two patients.

Limitations of our study include its retrospective property and small number of patients but our study period was 4 years.

Since the clinical presentations of abdominal tuberculosis are very non-specific and vague, and the diagnostic criteria are limited, the diagnosis has to be supported by additional tests and retrospective analysis with reference to clinical patterns, underlying diseases and X-ray findings. The histopathological examination in establishing the diagnosis in poor resource settings is also very important (32).

In conclusion, it is important to consider TB in the differential diagnosis of pediatric patients with chronic abdominal pain, weight loss and fever, even if there are no other signs to support diagnosis of TB in the initial evaluation as different forms of abdominal tuberculosis, especially in developing countries, may present with non-specific signs and laparoscopy or laparotomy could be useful in the differential diagnosis and utilizing imaging techniques, invasive methods with clinical suspicion may prevent delay of the diagnosis.

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