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Original Article

Abdominal Tuberculosis in Adult: 10-Year Experience in a Teaching Hospital in Central Taiwan

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BACKGROUND/PURPOSE: Tuberculosis (TB) is an important communicable disease worldwide. The clinical presentation of abdominal TB often mimics various gastrointestinal disorders and may delay accurate diagnosis. In this study, we conducted a 10-year retrospective study to investigate the clinical manifestations, treatment responses and outcomes of abdominal TB.

METHODS: This retrospective study recruited patients presenting between January 1998 and December 2007; all patients ≥ 18 years of age with a diagnosis of abdominal TB were enrolled. Patient charts were thoroughly reviewed and clinical specimens were processed in the laboratory using the BBL MycoPrep System and BACTEC MGIT 960 Mycobacterial Detection System. *Mycobacterium tuberculosis* complex was confirmed by acid fast stain and the BD ProbeTec ET System.

RESULTS: During the study period, 34 patients were diagnosed with abdominal TB. The mean age was 55 ± 18 years. Fourteen patients (41%) had no risk factors; however, 20 patients (59%) had at least one risk factor. Abdominal pain (94.1%), abdominal fullness (91.2%), anorexia (88.2%) and ascites (76.5%) were the most common presenting symptoms. The peritoneum (88%) was the most commonly involved site. Patients with risk factors such as liver cirrhosis, end-stage renal disease and diabetes mellitus had a higher positive rate of acid-fast stain and mycobacterial culture from abdominal specimens ($p=0.02$ and 0.05 , respectively). The crude mortality rate was 9% and the attributed mortality rate was 3%.

CONCLUSION: In an endemic area like Taiwan, regardless of whether a patient has risk factors for TB, abdominal TB should be seriously considered as a differential diagnosis when a patient presents with gastrointestinal symptoms and unexplained ascites.

KEYWORDS: abdomen, granuloma, peritoneum, Taiwan, tuberculosis

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Introduction

Tuberculosis (TB) is an important communicable disease worldwide. According to a global report published in 2009 by the World Health Organization, nearly one-third of the population of the world is infected with TB and 9.27 million new cases of TB were diagnosed in 2007 (139 per 100,000 population).¹ Based on data from the Centers for Disease Control (CDC) of Taiwan, about 15,000 patients with TB are diagnosed annually, and one-fifth of them are

from central Taiwan.² Any organ system may be affected by this pathogen, but pulmonary TB (80%) is the most common clinical manifestation.³ Prior to the development of anti-TB drugs, 50–90% of the patients with pulmonary TB also had gastrointestinal (GI) tract involvement. With the introduction of effective anti-TB drugs, the incidence of GI tract TB decreased to 25% and is even rarer at this time.^{4–6} At present, approximately 350–400 new cases of TB are diagnosed at our institution annually and one-third of them belong to the category of extra-pulmonary TB (3% with intra-abdominal involvement). Various intra-abdominal organs could be affected by TB, such as the intestines, peritoneum, solid organs and mesenteric lymph nodes. Three different imaging findings of peritoneal TB have been described in the literature: a wet type with ascites, an encysted (loculated) type with localized abdominal swelling and a fibrotic type with abdominal masses.⁷ The postulated mechanisms of acquiring GI tract TB include hematogenous spread from a primary pulmonary lesion, ingestion of infected sputum or spread from contiguous tissues infected by *Mycobacterium tuberculosis*.⁷ The clinical manifestations of abdominal TB are protean and can mimic other disease processes, a phenomenon that may delay accurate diagnosis. Several articles on abdominal TB have been published in Taiwan (an endemic area for TB) over the past years,^{8–11} but the prevalence of abdominal TB, detailed descriptions of patient characteristics and differences in diagnostic yield rates among various methodologies in different populations are seldom mentioned. Therefore, we conducted this 10-year retrospective study to answer these clinically relevant questions.

Methods

Patient

Patient information was obtained from China Medical University Hospital (a 2,000-bed tertiary teaching hospital in central Taiwan). Between January 1998 and December 2007, the medical records of all patients ≥ 18 years of age diagnosed with abdominal TB, including GI tract, peritoneum, mesenteric lymph nodes, or other intra-abdominal solid organs, were reviewed. The demographic data, underlying diseases, clinical manifestations, laboratory data, diagnostic methods and outcomes were recorded. The susceptibility of the clinical isolates was also reviewed.

A diagnosis of abdominal TB was made in patients with compatible symptoms, such as abdominal pain, fullness or distention, and if one of the following criteria was met: (1) positive culture of *M. tuberculosis* from ascites or biopsy specimens; or (2) demonstration of caseating granuloma on histological assessment of biopsy specimens and response well to anti-TB agents.

Laboratory methods

Specimens obtained from patients for *Mycobacterium* culture were initially decontaminated using the BBL MycoPrep System (Becton Dickinson Diagnostic Systems, Sparks, MD, USA). The processed material was incubated in BACTEC MGIT 960 Mycobacterial Detection System (Becton Dickinson Microbiology Systems, Sparks, MD, USA) and BBL Lowenstein-Jensen Medium (BBL/Becton Dickinson Microbiology Systems, Sparks, MD, USA). The isolated *Mycobacterium* species was further confirmed as *M. tuberculosis* complex using the BD ProbeTec ET System (Becton Dickinson Diagnostic, Sparks, MD, USA).

Statistical analysis

The results were expressed as mean \pm standard deviation, ranges, median or percentages. For continuous variables, the Mann-Whitney *U* test was used. Categorical data were analyzed using the χ^2 test where appropriate. A two-tailed *p* value < 0.05 was considered statistically significant. All statistical calculations were done using the Statistical Package for the Social Sciences version 12.0 (SPSS Inc., Chicago, IL, USA).

Results

During the study period, 34 patients were diagnosed with abdominal TB. The demographic characteristics of these patients are summarized in Table 1. There were 19 male patients and 15 female patients with a mean age of 55 ± 18 years (range, 20–82 years). Twenty (58.8%) patients had risk factors such as liver cirrhosis (32.4%) and end-stage renal disease (ESRD), and were undergoing continuous ambulatory peritoneal dialysis (CAPD) (14.7%), and diabetes mellitus (DM) (8.8%). No risk factor could be identified in 14 (41.2%) patients (average age = 48 years) who were predominantly younger than those patients with risk factors (average age = 60 years). The median elapsed time between onset of

Table 1. Demographic characteristics and risk factors of 34 patients with abdominal tuberculosis^a

Characteristic	
Age	
Mean \pm SD	55 \pm 18
Median (range)	58 (20–82)
Sex	
Male:female	19:15
Risk factor	
Liver cirrhosis	11 (32.4)
ESRD on CAPD	5 (14.7)
Diabetes mellitus	3 (8.8)
Malignancy	4 (11.8)
Previous gastrectomy	3 (8.8)
Prolonged steroid (>7 d)	1 (2.9)
No major systemic disorders	14 (41.2)
Duration of diagnosis (d)	
Mean	63
Median (range)	58 (10–175)

^aData presented as mean \pm standard deviation, median (range) or *n* (%). SD=Standard deviation. ESRD=end-stage renal disease; CAPD=continuous ambulatory peritoneal dialysis.

symptoms to diagnosis of abdominal TB was 58 days (range, 10–175 days). In patients without risk factors, the duration of symptoms before TB diagnosis was similar ($p=0.90$) to those with risk factors [59 days (range, 10–172 days) *vs.* 58 days (range, 13–175 days), respectively]. Otherwise, there was no significant difference in the duration of hospitalization between patients with risk factors compared with those without (18 days *vs.* 15 days; $p=0.55$).

Table 2 summarizes the clinical manifestations of the affected patients. Abdominal pain (94.1%) was the most common clinical presentation, followed by abdominal fullness (91.2%), anorexia (88.2%), ascites (76.5%) and fever (52.9%). Of these enrolled patients, 14 (41.2%) were initially diagnosed with peritoneal carcinomatosis of unknown origin. Another 11 patients were regarded as having spontaneous bacterial peritonitis despite monocyte-predominant ascites data.

Clinical specimens from 30 patients (26 ascites and 4 tissues) were available for further evaluation with acid-fast stain (AFS) and mycobacterial culture. Eighteen patients were smear-positive/culture-positive and two were smear-negative/culture-positive. Patients with risk factors

Table 2. Clinical features in 34 patients with abdominal tuberculosis

Symptoms	<i>n</i> (%)
Abdominal pain	32 (94.1)
Abdominal fullness	31 (91.2)
Anorexia	30 (88.2)
Ascites	26 (76.5)
Fever	18 (52.9)
Night sweating	14 (41.2)
Nausea/vomiting	12 (35.3)
Tenesmus	10 (29.4)
Body weight loss	10 (29.4)
Cough	9 (26.5)
Constipation	8 (23.5)
Diarrhea	6 (17.6)
Ileus	5 (14.7)
Bloody stool	4 (11.8)
Bowel perforation	1 (2.9)

had a significantly higher positive rate of AFS ($p=0.02$) and mycobacterial culture ($p=0.05$).

Pathological examination was performed in 20 patients and all had characteristic pathological changes consistent with TB, including positive AFS ($n=10$), Langhans giant cells ($n=16$), caseous necrosis ($n=15$) or granulomatous inflammation ($n=19$).

Numerous intra-abdominal sites may be infected by TB (Table 3). Of the 34 patients with evidence of intra-abdominal involvement, the peritoneum was the most frequently involved site (30 patients, 88.2%). In seven of these patients, the intra-abdominal organs were also involved (1 duodenum, 2 ileocecum, 1 large bowel, 2 ovary and 1 mesenteric lymph nodes). There was no evidence of peritoneal involvement in four patients; two had hepatic TB diagnosed by liver biopsy, one had anal ulceration and the remaining one had ileocecal involvement. All patients received plain film chest radiographs (CXR), and 17 patients had abnormal radiographic findings including cavitory lesions, alveolar processes and pleural effusion. Pulmonary TB was confirmed in 8/17 patients by positive sputum AFS and mycobacterial culture. Table 4 shows the ascites profile data from 26 patients: 14 with risk factors and 12 without. Higher diagnostic yields of AFS and mycobacterial culture were found in patients with risk factors, and

Table 3. Anatomical location of lesion in 34 patients with abdominal tuberculosis^{a,b}

Site	With risk factors (n=20)	Without risk factors (n=14)
Peritoneal involvement	18 (90.0)	12 (85.7)
With other intra-abdominal organ	1 (5.0)	6 (42.9)
Duodenum	0 (0)	1 (7.1)
Ileocecum	1 (5.0)	1 (7.1)
Large bowel	0 (0)	1 (7.1)
Ovary	0 (0)	2 (14.3)
Mesenteric lymph nodes	0 (0)	1 (7.1)
Non-peritoneal involvement	2 (10.0)	2 (14.3)
Liver	0 (0)	2 (14.3)
Anus	1 (5.0)	0 (0)
Ileocecum	1 (5.0)	0 (0)

^aData presented as *n* (%); ^brisk factors included liver cirrhosis, end-stage renal disease, diabetes mellitus, malignancy, gastrectomy and prolonged steroid use (>7 days).

Table 4. Ascites analysis in 26 patients with abdominal tuberculosis and present with ascites^{a,b}

Ascites analysis	With risk factors (n=14)	Without risk factors (n=12)	<i>p</i>
Neutrophil predominant	7 (50.0)	2 (16.7)	0.11
Monocyte predominant	7 (50.0)	10 (83.3)	0.11
Positive AFS	11 (78.6)	4 (33.3)	0.05
Positive TB culture	12 (85.7)	4 (33.3)	0.01

^aData presented as *n* (%); ^brisk factors included liver cirrhosis, end-stage renal disease, diabetes mellitus, malignancy, gastrectomy and prolonged steroid use (>7 days). AFS=Acid-fast stain; TB=tuberculosis.

these findings were statistically significant (AFS, $p=0.05$; TB culture, $p=0.01$).

Twenty TB isolates from abdominal specimens were submitted for susceptibility testing and all were susceptible to currently used first-line anti-TB drugs. Treatment strategies were based on the guidelines proposed by the CDC of Taiwan and the therapeutic regimen consisted of isoniazid, rifampicin, ethambutol, streptomycin and pyrazinamide in various combinations for 6–12 months.¹² Thirty patients completed the course of anti-TB therapy. The mean duration of treatment was 225 ± 56 days (range, 180–360 days). Of the patients ($n=30$) that completed the treatment, 15 were regularly followed up at our outpatient clinic. The median duration of follow-up was 303 days (range, 34–956 days). No relapse was detected during the follow-up period. During treatment, seven patients experienced adverse drug effects such as hepatitis, gastrointestinal upset, skin rashes and peripheral neuropathy. Of those patients who did not complete the treatment course,

three died during therapy and one was lost to follow-up. Only one death was attributable to abdominal TB. This patient suffered from ileocecal TB enteritis complicated by intestinal perforation and septic shock. The crude mortality rate was 9% and the attributed mortality was 3%.

Discussion

In this study, male and female patients were nearly equally affected by abdominal TB (male to female ratio=1.26), a result similar to that reported by the CDC of Taiwan (male to female ratio=2) and Chen et al (male to female ratio=1.62).¹¹ However, this finding was different from other earlier studies in Taiwan.^{8,9} In those studies, male patients comprised a significant proportion of the affected population (ratio=2.5:1 to 4.9:1). Possible explanations for these discordant results may be the changing gender composition of the general population in Taiwan since early 1990s¹³ or sampling bias in those studies.^{8,9}

Abdominal TB can affect any age group. In a study conducted by Sharma et al,⁷ most affected patients were between 21–45 years of age. This result was clearly different from that of the current study. The mean age of the patients in our study was 58 ± 18 years (range, 20–82 years) and this is similar to other reports from Taiwan.^{8,11} Liver cirrhosis, especially caused by alcoholism, is a known risk factor for TB peritonitis.^{11,14} In our study, 32.4% of the patients suffered from liver cirrhosis and this was also the leading risk factor for abdominal TB. Other risk factors, such as ESRD with CAPD, malignancy and DM, were also recorded. Interestingly, 14 patients (41.2%) had no identifiable risk factors. This observation has never been described in other studies. The reason that these patients acquired abdominal TB needs further investigation.

The clinical manifestations of abdominal TB are quite protean. Similar to previous reports,^{7,15} abdominal pain (94.1%) was the most common clinical presentation in this study, followed by abdominal fullness (91.2%) and anorexia (88.2%). According to a study performed in India,⁷ fever was recorded in half of the patients. In our study, the majority of the symptoms (Table 2) were confined to the GI tract, with the exception of cough, which was observed in 26.5% patients with abdominal TB. The proportion of patients with a cough reported by other studies ranges from 4% to 27%.^{8–10,16,17} No specific physical signs could be ascribed to abdominal TB; the classical “doughy” abdomen is seldom reported in clinical practice.¹⁸ None of our patients had this characteristic sign.

Routine laboratory tests have limited value in the diagnosis of abdominal TB.^{8,9,11,19} Among the study cases, 17 patients (50.0%) had abnormal findings on CXR and eight of them had a positive sputum culture for TB. Compared with patients with co-morbidities, those without risk factors had a higher proportion of abnormal CXR ($p=0.001$), but statistically insignificant differences in the positive rate of sputum and AFS and TB culture ($p=0.42$). However, a higher proportion of positive AFS and TB culture results from specimens other than sputum were noted in the patients with risk factors (AFS, $p=0.02$; TB culture, $p=0.05$). Impaired cellular immunity in patients with liver cirrhosis, ESRD and DM has been documented by investigators,^{20–22} and the main immunological response to TB is through innate cellular immunity.²³ Impaired immunological responses in patients with co-morbid diseases

might facilitate the replication of this pathogenic mycobacterium and this phenomenon could result in higher positive culture rate and AFS rates in this population. As seen in prior studies,^{24–27} lymphocytes were the predominant cell-type in the ascites of patients with TB peritonitis; however, in cases receiving CAPD, the predominant cells were neutrophils (80% of patients). This observation had also been described in previous studies.^{28–30}

With adequate and appropriate treatment, most patients with abdominal TB show good responses and have a good prognosis.^{4,8–11} In our study population, a good prognosis was observed in patients that completed the whole treatment course. Twenty percent of patients experienced adverse drug effects. In contrast to other local studies previously done in Taiwan, the mortality rate (9%) determined in our study was lower than that from studies conducted in Taipei in the 1990s (14.8% and 13.2%)^{8,9} and in southeastern Taiwan (20.8%).¹¹ Possible explanations for the lower mortality rate in this study are inadequate drug therapy during the 1990s, different underlying conditions, different patient populations and limited access to the healthcare system (particularly in southeastern Taiwan).

This retrospective study has some unavoidable limitations, such as incomplete examination in all patients and patient recall bias; however, there are still several important points that should be kept in mind during daily clinical practice. In terms of protean clinical manifestations of abdominal TB and the ease of delayed diagnosis, a high index of suspicion is always required. In an endemic area like Taiwan, regardless of whether patients have risk factors for TB, abdominal TB should be actively considered as a differential diagnosis in patients with gastrointestinal symptoms and unexplained ascites.

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