Abdominal tuberculosis in adult – 10-year experience in a teaching hospital in central Taiwan

成人腹腔內結核: 中台灣教學醫院之 10 年經驗分析

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Abstract

Background

Tuberculosis is an important communicable disease worldwide. The clinical presentation of abdominal tuberculosis often mimics various gastrointestinal disorders and may delay accurate diagnosis. Here, we conduct this 10-year retrospective study to investigate the clinical manifestations, treatment response and outcome of abdominal tuberculosis.

Materials

This retrospective study recruited patients presenting between January 1998 and December 2007; all patients≧18 years of age with the diagnosis of abdominal tuberculosis were enrolled. Patients' charts were thoroughly reviewed and clinical specimens were processed in the laboratory by BBL™ MycoPrep™ System and BACTEC™ MGIT™ 960 Mycobacterial Detection System. *Mycobacterium tuberculosis* complex was confirmed by acid fast stain and BD ProbeTec^{TM} ET System.

Results

During the study period, 34 patients were diagnosed with abdominal tuberculosis. The mean age was 55 ± 18 years. Fourteen patients (41%) had no risk factor; however, twenty 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. 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 attributable mortality rate was 3%.

Conclusion

In an endemic area like Taiwan, regardless of whether a patient has risk factors for tuberculosis, abdominal tuberculosis should be seriously considered in the differential diagnosis when patients present with gastrointestinal symptoms and unexplained ascites.

Key words

Tuberculosis, abdomen, peritoneum, granuloma, Taiwan

Introduction

Tuberculosis (TB) is an important communicable disease worldwide. According to the global report 2009 published by the World Health Organization (WHO), 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 the 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 and 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]. Currently, approximately 350 to 400 new cases of TB are diagnosed at our institution annually and one-third of them belong to the category of extrapulmonary TB (3% with intra-abdomen involvement). Various intra-abdominal organs could be affected by tuberculosis, such as the intestines, peritoneum, solid organs and mesenteric lymph nodes. Three different imaging findings of peritoneal tuberculosis have been described in the literature: wet type with ascites, encysted (loculated) type with a localized abdominal swelling and fibrotic type with abdominal masses [7]. The postulated mechanisms of acquiring GI tract TB include hematogenous spread from primary pulmonary lesion, ingestion of infected sputum, or spreading from contiguous tissues with tuberculous infection [7]. The clinical manifestations of abdominal TB are protean and

can mimic other disease process and this phenomenon may delay accurate diagnosis. Several articles on abdominal TB were published in the past years in Taiwan, an endemic area for TB [8-11], but the prevalence of abdominal TB, detailed description of patient's characteristics and the differences in diagnostic yield rates among various methodologies in different population are seldom mentioned. Therefore, we conduct this 10-year retrospective study in light to answer these clinically relevant questions.

Materials and Methods

Patient selection

Patient's information was obtained from China Medical University Hospital (a 2000-bed tertiary teaching hospital in central Taiwan). Between January 1998 and December 2007, the medical records of all patients≧18 years of age diagnosed as 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 outcome were recorded. Otherwise, susceptibility of clinical isolates was also reviewed. The 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 *Mycobacterium 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 decontaminated initially by 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 by BD ProbeTec™ ET System (Becton Dickinson Diagnostic, Sparks, MD, USA).

Statistical analysis

The results were expressed as mean values ± standard deviation, range, median or percentages. For continuous variables, Mann-Whitney *U* test was used. Categorical data were analyzed by chi-square test where appropriate. A 2-tailed *p* value of < 0.05 was considered statistically significant. All statistical calculations were done using the Statistical Package for the Social Sciences for Windows (Version 12.0; SPSS, Chicago, IL, USA)

Results

During the study period, a total of 34 patients were diagnosed with abdominal TB. The demographic characteristics of these patients were summarized in table 1. There were 19 male patients and 15 female patients with a mean age of 55 ± 18 years, ranging from 20 to 82 years old. Twenty (59%) patients had risk factors, such as liver cirrhosis (32%), end stage renal disease (ESRD) underwent continuous ambulatory peritoneal dialysis (CAPD) (15%) and diabetes mellitus (DM) (9%). No risk factor could be identified in fourteen (41%) patients, and their average age was 48 years old, predominantly younger than those patients with risk factors (60 years old). The median elapsed time between onset of symptoms to the diagnosis of abdominal TB was 58 days (range, 10-175 days), 73.5% patients had symptoms lasting for more than 1 month. The median duration of hospitalization was 18 days (range, 3-213 days). In the patients without risk factor, the median duration between onset of symptoms and diagnosis was 59 days (range, 10-172 days), which was similar (p=0.90) to those with risk factors (58 days, range 13-175 days). Otherwise, there was no significant difference in the duration of hospitalization between patients with risk factors compared to those without (18 days *vs.* 15 days, p=0.55).

Table 2 summarized 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%). Among these enrolled patients, 14 patients (41.2%) were initially diagnosed as peritoneal carcinomatosis without known origin. Another 11 patients

were regarded as having spontaneous bacterial peritonitis despite of monocyte-predominant ascites data.

Clinical specimens was available for further evaluation with acid fast stain (AFS) and mycobacterial culture in 30 patients (26 ascites and 4 tissues). Eighteen patients were smear- and culture-positive, and 2 were smear-negative and culture-positive. Patients with risk factors had a significantly higher positive rate of AFS (p=0.02) and mycobacterial culture (p=0.05). Pathologic examination was performed in 20 patients, and all had characteristic pathologic changes of TB, including positive AFS (n=10), Langhan's giant cells (n=16), caseous necrosis (n=15) or granulomatous inflammation (n=19).

Numerous intra-abdominal sites could be infected by TB and these data are showed in table 3. Among these 34 patients, 30 (88%) patients had peritoneal involvement and 7 of these patients had additional intra-abdominal organs involvement (1 duodenum, 2 ileocecum, 1 large bowel**,** 2 ovary and 1 mesenteric lymph nodes); it was evident that peritoneum was the most frequently involved site. There was no evidence of peritoneal involvement in 4 patients; 2 had hepatic tuberculosis diagnosed by liver biopsy, 1 had anal ulceration and the remaining one with ileocecal area involvement. All patients received chest plain film examination, but 17 patients demonstrated abnormal radiographic findings, including cavitary lesions, alveolar processes, and pleural effusion. Pulmonary TB was confirmed in 8 of these 17 patients by positive sputum AFS and mycobacterial culture. Table 4 showed the ascites profile data of 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 these findings were statistically significant (AFS, p =0.05; TB culture, p =0.01).

Twenty TB isolates from abdominal specimen were submitted for susceptibility test, and all were susceptible to the current first-line anti-TB drugs. Treatment strategies were based on the guideline 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, ranging from 180 to 360 days. Among those patients (n=30) whom completed the treatment, 15 were regularly followed up at our outpatient setting. The median duration of follow-up was 303 days, ranging from 34 to 956 days. No relapse was detected during the period of follow-up. During treatment, 7 patients experienced adverse drug effects, such as hepatitis, gastrointestinal upset, skin rashes and peripheral neuropathy. Among those patients who did not complete the treatment course, 3 patients died during therapy and 1 was lost to follow-up. Only one patient's death was attributable to abdominal tuberculosis. This patient suffered from ileocecal TB enteritis complicated with intestinal perforation and septic shock. The crude mortality rate was 9% and the attributable mortality was 3%.

Discussion

In the present study, male and female patients were nearly equally affected by abdominal tuberculosis (male/female ratio: 1.26) and this result was similar to that reported by the CDC of Taiwan (male/female ratio: 2) and Chen et al. (male/female: 1.62) [11]. However, this finding was different from other earlier studies in Taiwan [8, 9]. In those studies, male patients occupied a significant portion of the affected population (ratio from 2.5:1to 4.9:1). Possible explanations for these discordant results may arise from the changing gender composition of the general population in Taiwan since early 1990s [13] and sampling bias from those studies [8, 9].

Abdominal TB can influence any age group. In the study conducted by Sharma et al. [7], the most affected patients were between 21 and 45 years of age. This result was obviously different from the current study. The mean age of patients in our study was 58 ± 18 years (range, 20 to 82 years) and this observation was similar to other reports from Taiwan [8, 11]. Liver cirrhosis, especially caused by alcoholism, is a well-known risk factor for acquiring TB peritonitis [11, 14]. In our study, 32% of the patients suffered from liver cirrhosis and this was also the leading risk factor of abdominal TB. Other risk factors, such as ESRD with CAPD, malignancy and DM, were also recorded. Interesting to note in the present study was that 14 patients (41%) had no identifiable risk factor. This observation has never been described in other studies. How these patients acquire abdominal TB requires further investigation.

Clinical manifestation of abdominal TB is 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 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 cough reported by other authors ranged from 4-27% [8-10, 16, 17]. No specific physical signs could be ascribed to abdominal TB; the classical "doughy" abdomen is seldom reported in the 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%) had abnormal chest film (CXR) findings and 8 of them had positive sputum culture for TB. Compared with patients with co-morbidities, those without risk factor had higher proportion of abnormal CXR (p =0.001), but statistically insignificant in the positive rate of sputum AFS and TB culture (p =0.42). However, 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, end-stage renal disease and diabetes mellitus has been perceived and well documented by investigators [20-22] and the main immunological response to TB is via the innate cellular immunity [23]. Impaired immunological response in the patient group with co-morbid diseases might facilitate the replication of this pathogenic mycobacterium and this phenomenon could result in higher positive culture rate and AFS rate in this population. As seen in prior studies [24-27],

lymphocytes were the predominant cells in ascites of TB peritonitis, but in the cases receiving CAPD, the predominant cells were neutrophils (80% patients); this observation had also been described in previous studies [28-30].

With adequate and appropriate treatment, most patients with abdominal TB will have good response and prognosis [4, 8-11]. In our study population, good prognosis was observed in patients whom completed the whole treatment course. Twenty percent of the 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 those conducted in Taipei in the 1990s (14.8%, 13.2%) [8, 9], and that in Southeastern Taiwan (20.8%) [11]. The possible explanations for the lower mortality rate in this study could be attributed to inadequate drug therapy in the early era, different underlying conditions, different patient population and particularly for Southeastern Taiwan, the limited access to the healthcare system.

This retrospective study has some unavoidable limitations, such as incomplete examination in all patients and patient's recall bias, but there are still several important points that should be kept in mind during daily clinical practice. In term of protean clinical manifestations of abdominal TB and easiness of delayed diagnosis, high index of suspicion is always required. In an endemic area like Taiwan, regardless of whether patients had risk factors for tuberculosis, abdominal tuberculosis should be vigilantly considered and carefully monitored in the differential diagnosis in patients with gastrointestinal symptoms and unexplained ascites.

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

Characteristic	**Patients (%, n = 34)**
Mean age (years ± SD) (median; range)	55 ± 18 (58; 20-82)
Gender, male: female	19:15
Risk factor	
Liver cirrhosis	11 (32%)
ESRD on CAPD	5 (15%)
Diabetes mellitus	3 (9%)
Malignancy	4 (11%)
Previous gastrectomy	3 (9%)
Prolonged (>7days) steroid	1 (2%)
No major systemic disorders	14 (41%)
Mean diagnosis duration, (days) (median; range)	63 (58; 10-175)

Abbreviations: SD = standard deviation; ESRD = end stage renal disease;

CAPD = continuous ambulatory peritoneal dialysis; HIV = human immunodeficiency virus

Table 2.Clinical features in 34 patients with abdominal tuberculosis

Symptoms	Number (%, n = 34)
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%)

Table 3 Anatomical location of lesion in 34 patients with abdominal tuberculosis

Site	No. (%) of patient	
	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	1 (7.1%)
Ileocecum	1 (5.0%)	1 (7.1%)
Large bowel	0	1 (7.1%)
Ovary	0	2 (14.3%)
Mesenteric LNs	0	1 (7.1%)
Non-peritoneal involvement	2 (10.0%)	2 (14.3%)
Liver	0	2 (14.3%)
Anus	1 (5.0%)	0
Ileocecum	1 (5.0%)	0

*Risk factors: liver cirrhosis, ESRD, diabetes mellitus, malignancy, gastrectomy and prolonged (>7days) steroid use

Table 4. Ascites analysis in 26 patients with abdominal TB and present with ascites

Ascites analysis	No. (%) of patient		
	With risk factors (n=14)	Without risk factors (n=12)	*p*
Neutophil predominant	7 (50%)	2 (16.7%)	0.11
Monocyte predominant	7 (50%)	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

*Risk factors: liver cirrhosis, ESRD, diabetes mellitus, malignancy, gastrectomy and prolonged (>7days) steroid use