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Clinical features of and diagnostic approaches for abdominal tuberculosis: 5-year experience from a non-tuberculosis-designated hospital in China

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Abstract

Background and purpose: Abdominal tuberculosis (TB) is a common form of extrapulmonary TB but is still a diagnostic dilemma in clinical practice. We are aimed

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to highlight the clinical features of and diagnostic approaches for abdominal TB.

Methods: Seventy cases of diagnosed abdominal TB were retrospectively collected between 1 August 2015 and 30 June 2020. They were classified as peritoneal TB, lymph node TB, gastrointestinal TB, visceral TB, or mixed TB.

Results: Eighteen patients were diagnosed with peritoneal TB, 9 with lymph node TB, 5 with gastrointestinal TB, 2 with visceral TB, and 36 with mixed TB. More than sixty-five percent of the patients had tuberculosis of other sites except abdomen. The median diagnosis time was 60 days. Ascites (58.6%), abdominal distension (48.6%), weight loss (44.3%) and fever (42.9%) were the most common symptoms. The overall microbiological and histological detection rates were 70.0% and 38.6% respectively. The non-ascites samples yielded a higher microbiological confirmation rate (63.6%) than the total samples (40.8%). Diagnosis was confirmed histologically in 18 patients (69.2%). Forty-five cases (64.3%) were clinically diagnosed. Invasive procedures such as surgery (6/7), percutaneous biopsy (7/7) and endoscopy in lymph node TB (4/5) had high confirmation rates.

Conclusions: The diagnosis of abdominal TB should be reached by a combination of clinical, laboratorial, radiographic, microbiological, and pathological findings.

Key words: Abdominal tuberculosis. Clinical features. Diagnostic approaches.

Introduction

Tuberculosis (TB) is a communicable disease that is one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent. In 2019, an estimated 10.0 million people were infected with TB, and 1.2 million TB deaths occurred among HIV-negative individuals. In the South-East Asia region, 17% of the TB cases reported to the WHO were extrapulmonary TB (EPTB) (1). Abdominal TB is one of the most common forms of EPTB, constituting approximately 10% of EPTB cases (2,3).

The diagnosis of abdominal TB is still a dilemma due to the involvement of multiple organs and the nonspecific symptoms and signs (4,5). Furthermore, it mimics many diseases seen in the fields of gastroenterology and surgery, including abdominal

malignancy and Crohn's disease (6,7).There is a paucity of data concerning EPTB and even less pertaining to abdominal TB. Suspected abdominal TB has always been overlooked and delayed. Here, we retrospectively reviewed 70 cases to evaluate the clinical, laboratorial, and radiological features of and the diagnostic approaches for abdominal TB.

Materials and Methods

Study design and subjects

Our study is a retrospective cohort study. We enrolled patients aged >18 years diagnosed with abdominal TB from the Department of Infectious Diseases, Zhongshan Hospital in Shanghai, China, between 1 August 2015 and 30 June 2020. An ethical review application was validated by the Ethical Review Committee of Zhongshan Hospital, Fudan University, Shanghai, China.

Definitions and classification

The diagnostic criteria of abdominal TB consisted of at least one of the following: (a) positive acid fast bacteria (AFB) smear or culture from ascites, pus or biopsy tissues; (b) positive nucleic acid testing from ascites, pus, biopsy tissues, or pathological sections; (c) histopathological demonstration of granulomatous inflammation (with or without caseation); (d) high suspicion of abdominal TB with clinical and radiologic evidence and microbiologically confirmed TB in another site; and (e) lymphocytic exudate of ascitic fluid with elevated ascitic adenosine deaminase (> 33 IU/L) and a good response to anti-TB agents. According to the clinical and radiological findings, we classified cases into five different categories (6): mixed TB, peritoneal TB [wet or dry], lymph node TB, gastrointestinal TB, and visceral TB. Gastrointestinal TB included oesophageal, gastric, duodenal, jejunal, ileocecal, and colorectal TB. Visceral TB included hepatic, splenic, adrenal, and genitourinary TB.

Imaging features of peritoneal TB

Peritoneal TB is the common form of abdominal TB in our study, which has a lack of specificity in imaging. We collected the imaging features of abdominal CT and

Positron Emission Tomography-Computed Tomography (PET/CT) and compare the radiologic diagnostic value in peritoneal TB.

Statistical analysis

Continuous variables with a normal distribution are presented as the mean ± standard deviation, and continuous variables that deviated from a normal distribution are presented as the median (25th and 75th percentiles). Categorical variables are presented as frequencies and percentages. Comparative analysis was conducted by Pearson's test or the Kruskal-Wallis test for discrete variables or categorical variables where appropriate. Data analysis was performed with SPSS 22.0 (IBM SPSS Statistics). P values less than 0.05 were considered significant, and all tests were two tailed.

Results

Demographics and clinical characteristics

A total of 70 patients were diagnosed with abdominal TB. The demographic information is listed in Tab. 1. The average age of the 70 patients was 43.1 years. Male sex accounted for 60.0%. The median diagnosis time was 60 days. Only one patient with systemic lupus erythematosus using glucocorticoids and immunosuppressants had a negative T-SPOT result. Sixty-one patients (87.1%) had no underlying disease, and 66 (94.3%) had no history of TB. More than half of the patients had lymphocytopenia and $CD4^+$ T-lymphocytopenia, 52.9% and 51.6%, respectively. Although the majority of patients had a normal serum albumin level and BMI, sixty-two (88.6%) had decreased serum prealbumin levels.

As shown in Tab 2, ascites (58.6%), abdominal distension (48.6%), weight loss (44.3%) and fever (42.9%) were the most common symptoms. Ascites was common in the mixed group and peritoneal group associated with peritoneal involvement. The incidence of abdominal distension was significantly lower in the lymph node group than in the mixed and peritoneal groups. However, there were no significant differences in the frequencies of other symptoms among the 5 study groups. Eight patients (11.4%) had no symptoms.

Types of abdominal TB and other sites of TB involvement

Eighteen patients (25.7%) were diagnosed with peritoneal TB, 9 (12.9%) with lymph node TB, 5 (7.1%) with gastrointestinal TB, 2 (2.9%) with visceral TB, and 36 (51.4%) with mixed TB. The sites of involvement in the mixed group are listed in Fig 1a. The porta hepatis (54.5%, 12/22) and genitourinary tract (55.6%, 10/18) were the most frequently involved sites in patients with lymph node and visceral TB, respectively. Twenty-four patients (34.3%) had only abdominal TB, while 7 (10.0%) had abdominal TB combined with PTB, 19 (27.1%) combined with EPTB in one or more sites, and 20 (28.6%) combined with both PTB and EPTB in other sites (Fig 1b).

Diagnostic methods

The overall aetiological diagnosis rate of abdominal TB was low, and most cases were clinically diagnosed (64.3%, 45/70). Among the 70 patients, the total pathogenic detection rate (including culture, smear, or nucleic acid tests) was 70.0% (49/70), and the total histological detection rate was 37.1% (26/70). Diagnosis was confirmed microbiologically in 20 patients (40.8%, 20/49) and histologically in 18 patients (69.2%, 18/26). The rate of microbiologically confirmed abdominal TB in the non-ascites sample was 63.6% (14/22), which was much higher than that in the total sample.

Among the patients, seven underwent surgery, and another seven underwent percutaneous biopsy for the diagnosis of suspected abdominal TB; the confirmation rates of both were high (85.7% and 100%, respectively). Twelve patients (17.1%) underwent endoscopy or colonoscopy, with confirmation in only 50.0% of them. The rate of endoscopically detected lymph node TB was high because most cases involved the porta hepatitis and peripancreatic region. Paracentesis was performed in 34 patients (48.6%), in whom only six were bacterially confirmed by ascites. Tab. 3

Peritoneal TB

A total of 68.6% of patients (48/70) had peritoneal TB, 40 with wet and 8 with dry type; thus, the radiologic findings were analysed separately and are shown in Fig. 2.

The aetiological diagnosis rate of peritoneal tissue was superior to that of ascites, although the sample size of peritoneal biopsy was small. PET/CT had advantages over abdominal CT in differentiating peritoneal TB from malignancy, while 53.8% (14/26) and 29.2% (14/48) of patients had a tentative diagnosis of abdominal TB. The most common findings on abdominal CT were ascites (85.4%), peritoneal thickening (75.0%) and omental thickening (62.5%). Pictures and radiography images of wet and fry peritoneal TB are shown in Fig. 3.

Discussion

TB is a major public health issue in developing countries, including China. Abdominal TB is one of the common types of EPTB; however, it involves the peritoneum, lymph nodes, solid organs, and all parts of the gastrointestinal tract (4). It has a varied clinical presentation, often mimicking other common and rare diseases. Therefore, the diagnosis of abdominal TB is a great challenge even for experienced clinicians. In the current study, we reviewed the clinical features of abdominal TB in a tertiary hospital in China.

The average age of our patients was 43.1 years, which is not as young as that in research in India (2). Most of our patients did not have underlying diseases or previous TB onset. More than half of them had lymphocytopenia and $CD4^+$ T-lymphocytopenia, which was consistent with a recent study of HIV-negative TB patients in Uganda (8), suggesting that these patients have impaired immune responses to *M. tuberculosis.* However, others have suggested that TB is the cause of T-lymphocytopenia in contrast to $CD4^+$ T-lymphocytopenia as a risk factor for TB due to improvements after anti-TB therapy (9,10). We found that 88.6% of our patients had decreased serum prealbumin levels, which was superior to albumin in assessing an individual's recent nutritional intake and current nutritional state (11). Since serum prealbumin is a good marker of nutritional status, we believe that improved nutritional status may be of great importance for preventing TB.

Symptoms of abdominal TB usually lack specificity, as some patients have mild symptoms or are asymptomatic, and some have severe abdominal pain or experience septic shock onset (12,13). The most common symptoms we observed

were ascites and abdominal distension, which were related to the presentation of peritoneal TB. Patients with lymph node TB had relatively fewer symptoms, and some patients were found incidentally upon physical examination.

In our study, the most frequent type of abdominal TB was mixed TB (51.45%), followed by peritoneal TB (12.9%). The peritoneum was the most predominant independent site, and the gastrointestinal tract did not account for many cases, possibly because of the following reasons: (a) patients initially complaining of local abdominal symptoms visited the departments of gastroenterology and general surgery; (b) our department received complicated and generalized infection cases affecting all parts of the body because of different pathogens, as shown by the results that more than 65% of our patients had abdominal TB combined with PTB and/or EPTB; and (c) a certain proportion of our patients initially suspected of having malignancy who underwent PET/CT would have been better assessed for multisite lesions.

The diagnosis of abdominal TB remains one of the most challenging in clinical practice. Clinicians always have the misconception of an extremely low TB incidence and outdated knowledge of certain types of abdominal TB, such as tuberculous peritonitis and intestinal TB (ileocecal lesions). In fact, abdominal TB mimics various diseases, such as pancreatic tumours, lymphomas, colonic cancer, gastric cancer, appendicitis, cholecystitis, and typhoid fever (14-17). Typically, malignancy was initially suspected in our patients. Thus, the median diagnosis time of abdominal TB was 60 days, with a maximum time of more than 2 years.

As the most common presentation of abdominal TB, the most common CT findings in peritoneal TB include ascites (70–90% of cases), smooth peritoneal thickening with marked enhancement after intravenous contrast injection, and densification of fat planes in the mesenteric root (in up 70% of cases) (18-20). All peritoneal TB patients underwent CT scans that showed the above-mentioned features. However, most still yielded an undetermined diagnosis or even a misdiagnosis by radiologists, possibly due to the following reasons: (a) the lack of imaging specificity, especially in non-contract CT scans; (b) inability to combine the medical histories and laboratory test results; and (c) lack of summarized CT features in confirmed TB cases. PET/CT has a

high sensitivity for detecting peritoneal lesions because 18F-FDG PET can clearly detect harbouring lesions as high-uptake foci. It was shown that extensive involvement, a uniform distribution, string-of-beads sign, and smooth uniform thickening might be significant differential features of peritoneal TB (21). Our study also showed a superior sensitivity of PET/CT in differentiating peritoneal TB from peritoneal carcinomatosis.

There are a few tests that support the diagnosis of abdominal TB, but no single test is confirmatory except for proof of mycobacterium culture, Xpert MTB/RIF (22), and histopathology. The diagnostic algorithms differ among the different types of abdominal TB. Paracentesis is a safe, convenient, and economical diagnostic method. Routine tests, biochemical tests, and adenosine deaminase in ascites are helpful. But, the yields of the Xpert MTB/RIF assay and mycobacterium culture in ascites are poor, 4-28% and ~20%, respectively (23,24), which is similar to our results. Our previous work showed that next-generation sequencing may be a promising test for tuberculous serous effusions (25), but it is still too expensive. More sensitive tests to detect *M. tuberculosis* in ascites are urgently needed. Greater peritoneal TB confirmation can be reached with percutaneous peritoneal biopsy or surgery, and both microbiological and histopathological tests should be performed. For patients with peritoneal thickening, percutaneous peritoneal biopsy may be a better option for TB diagnosis, which can also rule out other abdominal malignancies (26).

The diagnosis of lymph node TB can be achieved with endoscopic ultrasonography-guided fine needle aspiration or percutaneous biopsy. In eight out of nine of lymph node TB was confirmed microbiologically, and six out of nine were confirmed histopathologically. The diagnosis of gastrointestinal TB can be achieved with endoscopy. With colonoscopy, the terminal ileum and ileocaecal valve are usually the most involved segments, and ulcero-nodular lesions are most common, followed by ulcerative/nodular lesions (3). Diagnostic laparotomy can be reserved as the last option for histological diagnosis. The diagnostic algorithm reported by Fikri M. Abu-Zidan et al. (4) was very similar to that performed in our clinical practice.

Some limitations exist in this study. First, this was a single-centre, retrospective study with inappropriate patient selection, and most of our patients had mixed TB.

Second, anti-TB therapy and the therapy duration and efficacy evaluation were not mentioned because our hospital is a non-TB-designated hospital, and most of our patients were transferred to local TB-designated hospitals.

In conclusion, abdominal TB has various forms and nonspecific clinical symptoms. A high level of suspicion is still required to make a TB diagnosis due to clinical and radiologic features. The diagnosis of abdominal TB should be reached by a combination of clinical, laboratory, radiographic, microbiological, and pathological findings. Invasive procedures, including percutaneous biopsy, endoscopy, and even surgery, are encouraged to increase the microbiological and pathological confirmation rates.

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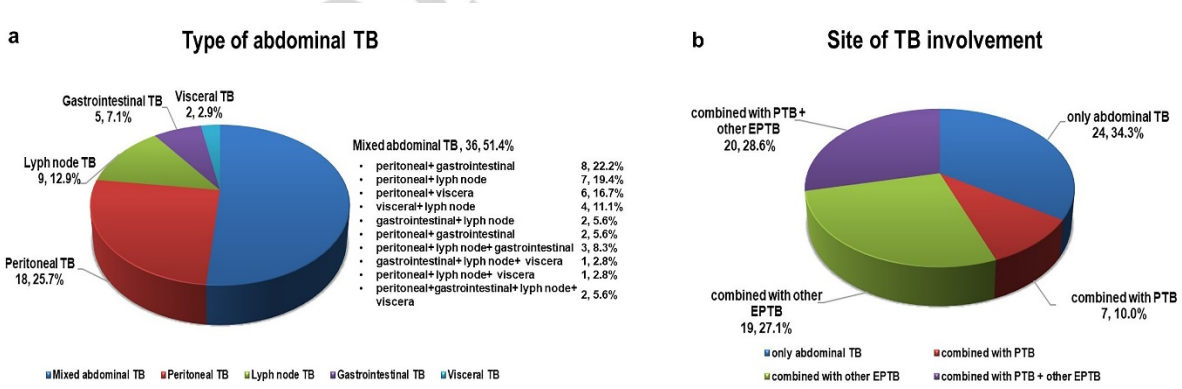

Fig 1 Type of abdominal TB and site of involvement.

Abbreviations: TB tuberculosis, PTB pulmonary tuberculosis, EPTB extrapulmonary tuberculosis

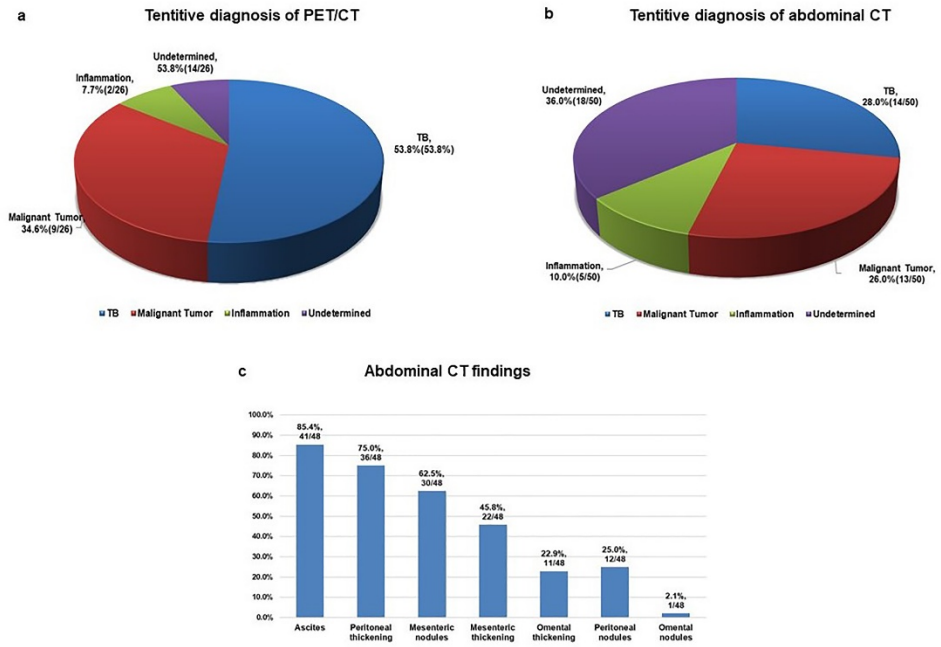

Fig 2 Imaging features of peritoneal tuberculosis.

Abbreviations: TB tuberculosis, CT computed tomography, PET/CT positron emission tomography-computed tomography

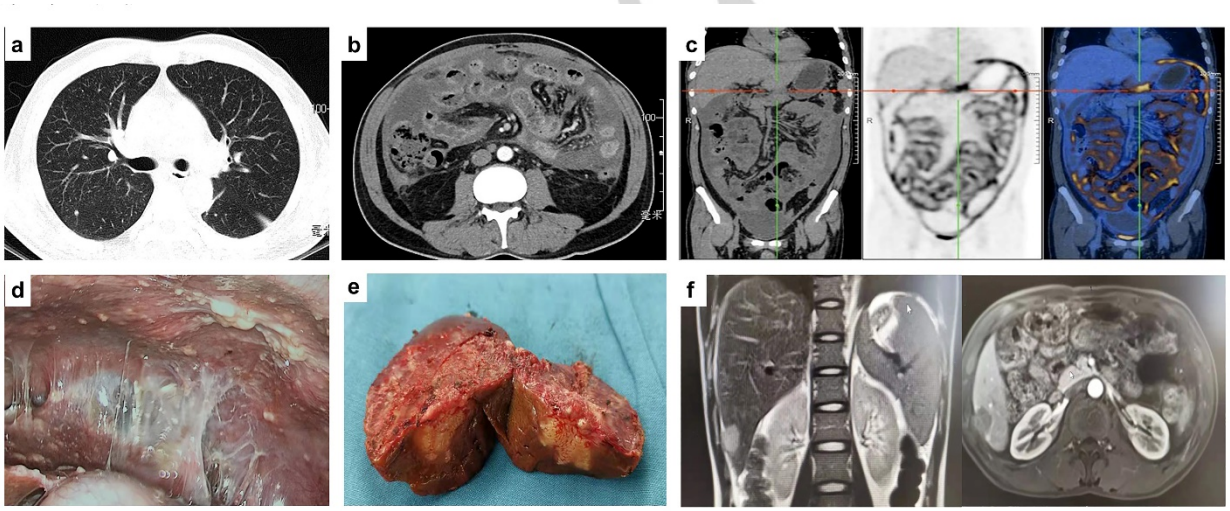

Fig 3 Images of abdominal tuberculosis.

(a-c): A 54-year-old male with miliary TB. (a) Chest CT revealed diffuse micronodules. (b) Abdominal CT revealed extensive thickening of the peritoneum and omentum with enhancement, partial thickening of the small intestinal wall. (c) PET/CT showed a thickened or nodular liver and spleen capsule, peritoneum, omentum and mesentery with an elevated SUVmax of 13.0. (d-f): 20-year-old female with dry peritoneal TB and hepatic TB. (d) Diffuse miliary nodules observed in the omentum

and peritoneum. (e) A solid grey mass under the capsule with a poor boundary. (f) Abdominal MRI revealed a hypointense lesion in the T1-weighted images in the right lower lobe of the liver. (Abbreviations: CT computed tomography, PET/CT positron emission tomography-computed tomography, MRI magnetic resonance imaging)

Table1 Demographics and clinical characteristics of 70 patients with abdominal TB

Characteristic	No (%)
Male sex	60.0%
Age(ys)	43.1±16.2 (18-76)
Underling diseases	
No underling diseases	87.1%
Rheumatic diseases	4.3%
Hepatitis or cirrhosis	2.9%
Hematological Disease	1.4%
Malignancy	1.4%
Solid organ transplantation	1.4%
ESRD	1.4%
History of TB	
No	94.3%
Yes	
PTB	4.3%
Ocular TB	1.4%
CRP (mg/L)	23.8 (6.8-54.6)
ESR (mm/H)	40 (23-71)
T-SPOT panel A	31 (21-43)
T-SPOT panel B	31 (15-55)
Leukopenia	20.0%
Lymphocytopenia	52.9%
CD^4T lymphocyte <400 cells/μl	51.6%
Serum albumin decreased (<30g/L)	30.0%
Serum prealbumin decreased (<250g/L)	88.6%
BMI decreased (<18kg/m^2)	21.4%

Diagnose time (d)	60 (30-120)

(Abbreviations: ESRD end-stage renal disease, TB tuberculosis, CRP C-reaction protein, ESR erythrocyte sedimentation)

Table2 Clinical features of 70 patients with abdominal TB

	All cases (n=70)	Mix abdominal TB (n=36)	Peritoneal TB (n=18)	Lymph node TB (n=9)	Gastrointestinal TB (n=5)	Visceral TB (n=2)	P
Systemic symptoms							
Fever	42.9%	44.4%	50.0%	33.3%	40.0%	0	0.800
Night sweats	30.0%	41.7%	22.2%	11.1%	20.0%	0	0.306
Weight loss	44.3%	52.8%	55.6%	0	40.0%	0	0.013[&]
Abdominal symptoms							
Ascites	58.6%	62.9%[@,#]	100.0%[*,%]	0	0	0	0.000
Abdominal distension	48.6%	55.6%[@]	72.2%[*]	0	20.0%	50.0%	0.001
Abdominal pain	30.0%	44.4%	16.7%	22.2%	40.0%	0	0.226
Change in bowel habits	17.1%	27.8%	5.6%	0	20.0%	0	0.141
Diarrhea	12.9%	19.4%	5.6%	0	20.0%	0	0.420
Intestinal obstruction	5.7%	11.1%	0	0	0	0	0.573
No symptoms	11.4%	2.8%	0	33.3%	40.0%	50.0%	0.001[&]

&: $P < 0.05$ There were differences in whole groups and no differences among separate groups, @: $P < 0.05$ mix TB vs.Lymph node TB, #:$P < 0.05$ mix TB vs. gastrointestinal TB, *: $P < 0.05$ peritoneal TB vs. Lymph node TB, %: $P < 0.05$ peritoneal TB vs. gastrointestinal TB.

Table 3 Diagnostic method of 70 patients with abdominal TB

	All cases (n=70)	Mix abdominal TB (n=36)	Peritoneal TB (n=18)	Lymph node TB (n=9)	Gastrointestinal TB (n=5)	Visceral TB (n=2)
Diagnositic method						
Microbiologic diagnosis	49 (70.0%)	21 (58.3%)	15 (83.3%)	8 (88.9%)	3 (60.0%)	2 (100.0%)
Confirmed by microbiologic diagnosis	20(40.8%)	8 (38.1%)	3 (20.0%)	6 (75.0%)	1 (33.3%)	2 (100.0%)
Microbiologic diagnosis(except ascites）	22 (38.6%)	8 (30.8%)	1 (5.6%)	8 (88.9%)	3 (60.0%)	2 (100.0%)
Confirmed by microbiologic diagnosis	14 (63.6%)	4 (50.0%)	1 (100.0%)	6 (75.0%)	1 (33.3%)	2 (100.0%)
Histological diagnosis	26 (37.1%)	8 (30.8%)	3 (16.7%)	6 (66.7%)	2 (40.0%)	2 (100.0%)
Comfirmed by histological diagnosis	18 (69.2%)	9 (69.2%)	3 (100.0%)	3 (50.0%)	1 (50.0%)	2 (100.0%)
Clinical diagnosis	45 (64.3%)	26 (72.2%)	12 (66.7%)	3 (33.3%)	4 (80.0%)	0
Invasive procedure						
Operation	7 (10.0%)	3 (8.3%)	2 (11.1%)	0	1 (20.0%)	1 (50.0%)
Confirmed by operation	6 (85.7%)	3 (100.0%)	2 (100.0%)		0	1 (100.0%)
Percutaneous biopsy	7 (10.0%)	4 (11.1%)	1 (5.6%)	1 (11.1%)	0	1 (50.0%)
Confirmed by percutaneous biopsy	7 (100.0%)	4 (100.0%)	1 (100.0%)	1 (100.0%)		1 (100.0%)
Endoscopy or colonoscopy	12 (17.1%)	6 (16.7%)	0	5 (55.6%)	1 (20.0%)	0
Confirmed by endoscopy or colonoscopy	6 (50.0%)	1 (16.7%)		4 (80.0%)	1 (100.0%)	
Paracentesis	34 (48.6%)	18 (50.0%)	16 (88.9%)			
Confirmed by paracentesis	6 (17.6%)	2 (11.1%)	4 (25.0%)			