Peritoneal Tuberculosis: Advances and Controversies
[Version 1, Awaiting Peer Review]

Fahmi Yousef Khan*

Department of medicine, Hamad General Hospital, Qatar

*Corresponding author: Fahmi Yousef Khan, Department of Medicine, Hamad General Hospital, P.O. Box: 3050, Doha, Qatar, Tel:+974 44321276, +974 55275989; Fax:+974 44321276; Email: fakhanqal@gmail.com

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Abstract

Peritoneal tuberculosis remains a public health problem especially in the developing countries, even in the developed countries, where the disease had been mostly controlled; it poses a new challenge for health care facilities as a result of increased immigration from high prevalence area, the use of more potent immunosuppressive therapy and the acquired immunodeficiency syndrome epidemic. The diagnosis of peritoneal tuberculosis is often challenging and cannot be made or excluded on the basis of clinical findings, which are quite protean and nonspecific. Blood biochemistry, complete blood count and radiographic studies are of limited diagnostic value. Acid-fast smear of ascitic fluid has a low yield and cultures require weeks to give results and are positive in 2-50% of diagnosed cases. Polymerase chain reaction analysis for rapid detection of bacillus tubercles in ascitic fluid has low yield, and the role of other biomarkers such as adenosine deaminase and gamma interferon is less well described and currently being evaluated as diagnostic tools. Laparoscopy with directed biopsy provides a rapid and correct diagnosis in 76-100% of cases and should be performed early in suspected cases. Six-month therapy with the 4-drug regimen is effective in most of the patients, while the role of adjunctive corticosteroid therapy remains controversial.

Keywords
Tuberculous Peritonitis; Ascites; Laparoscopy; Peritoneal Biopsy
Introduction

Tuberculosis (TB) remains a major worldwide problem with significant morbidity and mortality. It ranks as the tenth leading cause of death worldwide [1]. TB is primarily a disease of the lungs, but it can affect almost any organ in the body. Extrapulmonary TB refers to TB involving organs other than the lungs (e.g., pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, or meninges) [2]. Peritoneal tuberculosis is a variant of abdominal tuberculosis; it poses a public health problem in endemic regions of the world. The aim of this review is to describe the epidemiology, pathogenesis, clinical features of the peritoneal TB and to review recent development in the methods of diagnosis and treatment.

Epidemiology

Tuberculosis (TB) is a worldwide disease. In 2015, there were an estimated 10.4 million new TB cases worldwide, of which 5.9 million (56%) were men and 3.5 million (34%) were women. Children accounted for 1.0 million (10%) and people living with HIV accounted for 1.2 million (11%) of all new TB cases. Moreover, there were an estimated 480 000 new cases of multidrug-resistant TB [1]. Tuberculosis has strong associations with socio-economic factors like poverty, malnutrition, deprivation, overcrowding, illiteracy and limited access to health care facilities, having a high prevalence in developing countries [3]. In developed countries, where the disease had been mostly controlled; TB poses a new challenge for health care facilities. Increased immigration from high prevalence area, the use of more potent immunosuppressive therapy and the acquired immunodeficiency syndrome epidemic has contributed to the resurgence of the disease in areas where it had been considered under control [3-5]. Several risk factors for peritoneal TB have been identified. Liver cirrhosis (esp. alcoholic), chronic renal failure, chronic ambulatory peritoneal dialysis, underlying malignancy, treatment with anti-tumor necrosis factor (TNF) agents, intravesical treatment with Bacillus Calmette-Guérin, diabetes mellitus, immunosuppression with prolonged steroid therapy or chemotherapeutic agents and HIV infection [6-11].

Globally, there is continuous fall in the number of TB deaths, however, there were an estimated 1.4 million TB deaths in 2015, and an additional 0.4 million deaths resulting from TB disease among people living with HIV [1].

Peritoneal TB accounts for about 0.1-0.7% of all cases of tuberculosis representing 4-10% of extra-pulmonary TB and 25-60% of abdominal TB cases [12-14]. Although peritoneal TB can develop at any age, peritoneal TB is seen more commonly between 25 and 55 years of age. The gender difference among patients with peritoneal TB varies from study to study and from country to another. Generally, in developing countries [15-19] the disease is observed predominantly in females, while in industrialized and some rich countries there is male predominance which may be attributed to the presence of male immigrants in the workforce [14,20-23].

Pathogenesis

The postulated mechanisms by which peritoneum can be involved are: [24,25].

1. Reactivation of latent tuberculous foci in the peritoneum, acquired by hematogenous spread from a primary lung focus.
2. Hematogenous spread from active pulmonary, miliary tuberculosis or silent bacteremia during the primary phase of tuberculosis.
3. Direct spread from infected organs like intestine, fallopian tubes and rupture of a tuberculous intra-abdominal lymph node.
4. Through lymph channels from infected abdominal lymph nodes. Abdominal lymph nodal and peritoneal tuberculosis may occur without gastrointestinal involvement.

Pathology

Peritoneal TB occurs in three forms: (1) wet type with ascites, (2) encysted (loculated) type with a localized abdominal swelling; and (3) fibrotic type with abdominal masses composed of mesenteric and omental thickening, with matted bowel loops felt as lumps in the abdomen. Considerable overlap of these types can be observed [25].

Grossly, the peritoneum is studded with multiple yellow-white tubercles (<5 mm) scattered over the visceral and parietal peritoneum [23-25]. In addition, the peritoneal lining along with the omentum and mesentery is thickened and adhesions develop with abdominal organs. Microscopically, the tubercles composed of numerous, large, confluent granulomas of variable size, composed of epithelioid cells, with a peripheral zone of lymphocytes and Langhan’s giant cells with central caseous necrosis and surrounding fibrosis are seen [26].

Causative Agent

Mycobacterium tuberculosis causes most of the cases; however, Mycobacterium bovis has been identified in few reports. [5,21,23].

Clinical Features

The clinical manifestations of peritoneal TB are quite protean, nonspecific and mimic many diseases and pathological conditions; therefore, it is necessary to maintain a high index of clinical suspicion in order to avoid the morbidity and mortality associated with delayed diagnosis. Generally, the onset is quite insidious, with symptoms usually persisting for weeks to months before the patients sought medical help, and a diagnosis of peritoneal TB was made [14,19-23]. Abdominal pain and swelling are the common presenting symptoms in many studies [14-23]. Other symptoms include fever, night sweats and weight loss. Ascites, abdominal tenderness and hepatomegaly may be noted on physical examination [14-23].
Diagnosis

The diagnosis of peritoneal TB is often challenging and cannot be made or excluded on the basis of clinical findings. Herewith, we review all available diagnostic modalities for peritoneal TB.

Purified Protein Derivative (PPD) Tuberculin Skin Test

A positive tuberculin skin test has been reported in 24-100% of the cases; this test is diagnostically insignificant, as negative skin test may be seen in many patients with histologically confirmed peritoneal TB [14].

Ascitic Fluid Analysis

Biochemistry and Cytology

The typical analysis of ascitic fluid from patients with peritoneal TB demonstrates high protein concentration (>3gm/dl) with serum to ascites albumen gradient of < 1.1 gm/dl and predominant lymphocytic pleocytosis. [14] Predominance of neutrophils, however, may be observed in patients undergoing peritoneal dialysis [11,14,27,28].

Microbiology

Identification of Acid-fast bacilli in the ascitic fluid through both smear and culture methods remains a useful mean to diagnose peritoneal TB. However, acid-fast smear of ascitic fluid has a low yield with a reported sensitivity of 0-6%, [29] while the frequency of a positive culture for M. tuberculosis was 2-50% [14-22]. Techniques to improve the diagnostic yield of TB culture in the peritoneal fluid were attempted. Singh et al. assumed that one liter of ascitic fluid can provide up to 83% of positive results [24]. This technique is impractical as this large amount of fluid needs special centrifuge machines. Interestingly, conventional mycobacterial culture takes up to 4-6 weeks to achieve results, even with liquid culture methods the process requires at least 12 days. This delay may increase morbidity and therefore, other diagnostic tools for early diagnosis of tuberculosis are needed.

Carbohydrate Antigen 125 (CA-125)

Previous reports have noted that CA-125 is not crucial in differentiating malignancy and tuberculosis since ascitic CA-125 levels also increase in other diseases with peritoneal involvement [30].

Polymerase Chain Reaction (PCR) Techniques

The performance of conventional PCR was disappointing. Recently, modified PCR techniques (The GeneXpert MTB/RIF assay, real time PCR and nested PCR) have been used by many authors for early detection of Mycobacterium in ascitic fluid; however, their role is not firmly established as the obtained results are non-conclusive [31-33].

Biomarkers

Other rapid and non-invasive tests for the diagnosis of peritoneal tuberculosis had been attempted. Measurement of adenosine deaminase (ADA) and gamma interferon (IFN-γ), in the supernatant of fluid specimens has been used to diagnose peritoneal tuberculosis. However, literature review showed that despite being helpful in peritoneal TB diagnosis, neither of these modalities is proved to be reliable for replacing the peritoneal biopsy [14,33-37].

The Enzyme-Linked Immuno Spot (ELISPOT) Assay

A number of studies have now reported that the ELISPOT assay may be a useful tool to diagnose peritoneal TB in smear-negative ascites by measuring gamma producing T-cell responses to early secreted antigenic targets of mycobacterium tuberculosis [38-40]. Although the preliminary results are promising, it is too early to make a final conclusion on their role in diagnosis of peritoneal TB, as more studies are needed.

Abdominal Sonography

Abdominal sonography is the most commonly used first-line imaging modality for evaluating patients with suspected peritoneal TB as it can easily assess the peritoneum [41]. The most common findings include multiple thin septae, visible debris of different densities within the fluid. Other findings include peritoneal thickening and nodularity [41-43]. As illustrated in many reports, these findings lack specificity and are not useful for differentiating peritoneal TB from other diseases such as peritoneal carcinomatosis [14,41]. However, abdomen sonography can be used to guide abdomen tapping and peritoneal biopsy.

Abdominal Computed Tomography (CT)

Abdominal CT assists in the identification of peritoneal diseases. Common CT Abnormalities that are seen in most patients with peritoneal TB include peritoneal thickening, free and loculated ascites. Other findings include mesenteric or omental thickening, mesenteric or omental strand and mesenteric or omental nodes[44-48]. Although these findings are nonspecific, in our experience and in view of available data, these findings may suggest peritoneal TB and their absence may at least argue against it.

A Positron Emission Tomography (PET)/CT Scan

Recent data show that PET/CT findings in the parietal peritoneum are useful for differentiating between peritoneal TB and peritoneal carcinomatosis [49]. However, further large prospective studies are needed to confirm these findings.
Peritoneal Biopsy

Peritoneal biopsy gives a better diagnostic value than ascitic fluid alone. It can be obtained by different procedures including blind percutaneous peritoneal biopsy, transabdominal sonographic or CT guided peritoneal biopsy and laparotomy or laparoscopic biopsy [50]. Laparoscopy with directed biopsy is an excellent tool for diagnosing tuberculous peritonitis. It is safer and provides better inspection, as well as it allows a shorter hospital stay, rapid postoperative recovery and quick return to social activities. Characteristic laparoscopic appearance includes free ascites, multiple yellowish-white nodules or tubercles on visceral and parietal peritoneum, peritoneal or visceral adhesion, and occasionally inflamed hemorrhagic areas on the peritoneum [50-53].

It was reported that macroscopic picture of peritoneum during laparoscopy was suggestive of tuberculosis in 85-100% of the cases and laparoscopically guided peritoneal biopsy had detected caseating granulomas in 76-100% of patients [14,50-53]. Microbiological studies of biopsy should be performed in all cases to identify nontuberculous mycobacteria (especially in patients on continuous ambulatory peritoneal dialysis), to detect drug resistance tuberculosis and to increase the diagnostic yield of the procedure, as it may be positive even in the absence of a characteristic histopathological picture [14]. Laparoscopic biopsy specimens reveal Acid-fast bacilli in 3-25% and cultures were positive for M. tuberculosis in 38-98% [14,50-53]. There is lack of data on diagnostic yield of PCR study for M. tuberculosis on peritoneal biopsy. Although laparoscopic biopsy is safe but it is not free of complications such as intestinal perforation and haemorrhage [51].

Treatment and Prognosis

The currently recommended regimen for treatment of peritoneal TB is largely similar to treatment for tuberculosis elsewhere and includes the ‘4-drug regimen’; an initial phase of 2 months followed by a continuation phase of 4 months. Treatment in the 2 month phase is usually including daily administration of rifampicin, isoniazid; pyrazinamide and ethambutol can be discontinued following by a continuation phase where isoniazid and rifampicin are again given daily for 4 months. Although the disease usually responds to this standard anti-TB drug therapy[14-23], the optimal duration of therapy is debatable. Some physicians use antituberculous therapy for 9-12 months without any scientific justification. In our experience, anti-TB drug therapy can be used for 9 months or 12 months in patient who use second line therapy due to drug resistance or drug sensitivity. Duration of therapy also can be extended because of side effect developed during treatment. Corticosteroid administration combined with anti-tuberculosis treatment has been advocated by some researchers to reduce the complications; however, there is a controversy about the benefit that can be obtained [14].

Conclusions

Available data show that there is no specific sign or symptom for the diagnosis of peritoneal tuberculosis. A high index of suspicion is always required. Peritoneal TB should be considered early as a differential diagnosis in patients who have unexplained low gradient ascites with high lymphocytes. The role of advanced diagnostic modalities such as modified PCR techniques and biomarkers remain controversial. Laparoscopically guided peritoneal biopsy remains the best diagnostic tool in our hand nowadays as it provides a rapid and correct diagnosis, therefore, it should be performed early in suspected cases. Six months of treatment with the 4-drug regimen is effective and markedly improves the outcome.

References

47. Shim SW, Shin SH, Kwon WJ, Jeong YK, Lee JH. CT Differentiation of Female Peritoneal Tuberculosis and Peritoneal Carcinomatosis From Normal-Sized Ovari-