



## Understanding tuberculous peritonitis: A difficult task to overcome

Tuberculosis (TB), one of the most common infectious diseases worldwide, is characterized by the formation of tubercles or tuberculous granulation and caseous necrosis in tissues. Lungs are the primary site of TB infection and from there the infection spreads to other organs including the kidneys, spine, genitals, and only rarely the peritoneum. With the global resurgence of tuberculous peritonitis (TBP), it has become a significant health concern not only in endemic areas, but also in the United States and Western Europe. Recently, evidence has accumulated that there has been an increased incidence of extrapulmonary TB. TBP occurs in up to 5% of patients with pulmonary TB and comprises 25-60% of cases of abdominal TB (1).

TBP is a subacute disease and has protean symptoms evolve over a period of several weeks to months. The disease can present in three different forms which are: the wet-ascitic, fibrotic-fixed and the dry-plastic form. They have overlapping symptoms except for abdominal distension which does not occur in the dry-plastic form. Ascites is the predominant finding and present in about 73% of the patients (2). Low-grade fever that often accompany a night sweat occurs in about 59% of the cases. Weight loss is seen in about 61% of cases and reversibility of this manifestation has been reported as a sign of disease recovery (3). Abdominal tenderness on palpation is common in TBP and occurs in almost 48% of the patients. Abdominal pain is one of the most common presenting sign and usually accompanied by abdominal distension. As its etiology is thought to be related to the tuberculous inflammation of the peritoneum and mesentery or to the obstruction of the bowel, the pain is widespread and non-localized (4). An enlarged liver or splenomegaly is uncommon, and presence of hepatomegaly and splenomegaly suggests a direct tuberculous involvement of the liver and presence of portal hypertension, respectively (3,5).

TBP should be considered in all patients presenting

with unexplained lymphocytic ascites with a serum-ascites albumin gradient of  $<1.1$  g/dL. The gold-standard for diagnosis is culture growth of *Mycobacterium* on ascitic fluid or a peritoneal biopsy. Peritoneal biopsy under direct visualization is the cornerstone for obtaining enough tissue for diagnosis. Adenosine deaminase activity (ADA) of ascitic fluid with a cut-off value of 39 IU/L is a good parameter for detecting TBP. Although the yield of ascitic fluid PCR assays in diagnosing TBP has not been well established, one review of 11 cases of abdominal tuberculosis revealed a positive PCR for *M.Tuberculosis* of the ascitic fluid in all cases. Tuberculin testing with purified protein derivative (PPD) is positive in approximately 70 percent of patients with tuberculosis of gastrointestinal tract and peritoneum (6).

The classic treatment of TBP for adult patients with previously untreated TB includes a 2-month initial phase of INH, RIF, PZA and EMB given on a daily basis and 4-month continuation phase where INH and RIF are again given on a daily basis. The rapid resolution of symptoms is the characteristic treatment response just after starting treatment in TBP patients. Fever usually resolves within one week of commencing anti-tuberculous treatment. More than 90 percent of patients have improvement in abdominal ascites within weeks of initiating treatment (6).

TBP with ambiguous patient symptoms and diagnostic difficulties still poses a great challenge in clinical practice. In this month's issue of Turkish Journal of Gastroenterology, Dulger and colleagues report on analysis of cases with tuberculous peritonitis (7). This was a real-world, single-center, retrospective review of 21 patients with TBP. The authors reported that fifteen patients had consumed unpasteurized milk products at least 3 times a week. Products from unpasteurized cow's milk have been associated with certain infectious diseases and carry the risk of transmitting *M.bovis*, a pathogen that primarily infects cattle. The source of

infection in this TBP cohort seems closely related to the consumption of unpasteurized cow's milk. As the comorbid conditions associated with TBP was liver cirrhosis in one patient, chronic renal failure in 2 patients, and colon cancer in one patient, the cornerstone for development of TBP in the eastern part of Turkey is easy availability of *M.bovis* via unpasteurized milk products rather than underlying immunocompromised conditions.

As approximately 70 percent of patients have symptoms for more than four months before the diagnosis is established (6), the symptom-to-diagnosis interval in this study (2.6 months) is shorter compared to the data in the literature. The high rate of patients with ascites in this study appears to be related with early diagnosis of TBP. The presence of abdominal pain in all patients was thought to be related to the omental involvement and abdominal distension due to ascites. An interesting point germane to the findings of physical examination is the high frequency of hepatosplenomegaly. As there is no supportive data with respect to presence of hepatic involvement of tuberculosis and portal hypertension, an immunologic response to the TBP infection in the liver and spleen may be a potential scenario for this finding.

The relatively high mean ADA levels in ascitic fluid in this study is a good reflection of normal immune response of patients recruited to this study. The diagnostic yield of ADA measurement in the ascitic fluid may be higher in TBP cohort in the developing countries due to low rate of associated immunosuppressive conditions compared to the developed countries. As ascitic CA-125 can be increased in ascites due to any cause, it is not useful to measure CA-125 level in TBP patients with ascites, which may be accepted as a limitation for this study.

The treatment for TBP serves two major tasks: palliation of symptoms and confirmation of diagnosis. Detection of *Mycobacterium* was provided only in 8 patients. The remaining thirteen patients with supportive data for TBP was given anti-tuberculous treatment and the confirmation of diagnosis was assessed with treatment trial. The increasing effect of delayed

treatment on mortality, difficult microbiological diagnosis in some patients (even with laparoscopic biopsy) should prompt the physician to start the anti-tuberculous treatment as soon as possible in case of having high index of suspicion and supportive data for TBP. Dulger et al followed this basic rule about the treatment of TBP and achieved a high treatment response in their cases.

In conclusion, the study with Dulger et al. (7) shed light on clinical characteristics of TBP. The confirmation of diagnosis with treatment in substantial number of patients means that there is still a long way to go in diagnostic evaluation of patients with TBP.

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