Endoscopic Ultrasound (EUS) Guided Fine Needle Aspiration: A New Modality to Diagnose Peritoneal Tuberculosis in Presence of Decompensated Cirrhosis—A Case Series and Review of Literature

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Background: The gold-standard for diagnosis is growth of *Mycobacterium tuberculosis* on ascitic fluid or peritoneal culture. Due to the non-specific signs and symptoms of disease, its early diagnosis is difficult, especially in patients with decompensated cirrhosis. The reported sensitivity of ascitic fluid is low and to obtain tissue for peritoneal biopsy in patients with cirrhosis is difficult. Endoscopic ultrasound (EUS) guided fine needle aspiration (FNA) is a good alternative to obtain peritoneal tissue for establishing the diagnosis of peritoneal TB. **Objective:** To assess the role of EUS-FNA in the diagnosis of peritoneal tuberculosis in patients with decompensated cirrhosis. **Methods:** Consecutive patients with peritoneal thickening, ascites and decompensated cirrhosis underwent EUS-FNA from the thickened omentum. Presence of granuloma or demonstration of acid fast bacilli was diagnostic of peritoneal tuberculosis. **Results:** A total of 5 patients with CLD underwent EUS-FNA from omentum. FNA cytology revealed granuloma with multinucleated cells in all patients (100%) and AFB stain was positive in 2 of them (40%). **Conclusion:** We hereby report the use of EUS guided fine needle aspiration (FNA) of peritoneum as a newer, safe and unexplored technique for diagnosis of peritoneal TB. (J CLIN EXP HEPATOL 2018;8:205–209)

Peritoneal tuberculosis (TB), a form of abdominal TB, accounts for 1–2% of all cases of tuberculosis.¹ Due to the non-specific signs and symptoms of disease, its early diagnosis is difficult, especially in patients with decompensated cirrhosis. The gold-standard for diagnosis is growth of *Mycobacterium tuberculosis* on ascitic fluid or peritoneal culture.² The reported sensitivity of ascitic fluid is low and to obtain tissue for peritoneal biopsy in patients with cirrhosis is difficult. The utility of culture is questionable when considering the delay of four to six weeks before a result is obtained.³ Laproscopic examination and histopathology is highly sensitive and specific, however, it is invasive and has its own complications, morbidity and small but significant mortality. Thus, there is an urgent need to explore newer diagnostic

modalities especially those that can provide peritoneal tissue by less invasive means. Endoscopic ultrasound (EUS) guided fine needle aspiration (FNA) is a good alternative to obtain peritoneal tissue for establishing the diagnosis of peritoneal TB. The role of EUS FNA in preoperative detection of peritoneal carcinomatosis is rapidly evolving.⁴ However, its value in establishing diagnosis of peritoneal TB has been scarcely reported in literature. We hereby report the use of EUS guided fine needle aspiration (FNA) of peritoneum as a newer, safe and unexplored technique for diagnosis of peritoneal TB.

CASE SERIES

A total of 5 patients with chronic liver disease and clinical suspicion of peritoneal tuberculosis were evaluated over a period of 18 months (August 2015–February 2017). Abdominal distension was most common presenting symptom, followed by fever with median duration of symptoms being 1 month. Mean age was 51.2 ± 11.3 year with 4 male patients. All the patients had Mantoux positive after 72 h of test. They were non-reactive for anti HIV (1/2) ELISA. CXR was within normal limits in all the patients. There was no superficial or mediastinal/periportal lymphadenopathy in these patients except one (Sr no. 4) in whom FNA from subcarinal lymph node was reactive. CECT abdomen revealed features of CLD and portal

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Abbreviations: CAPD: continuous ambulatory peritoneal dialysis; EUS: endoscopic ultrasound; FNA: fine needle aspiration

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hypertension along with thickened omentum. There was no obvious focus of primary tuberculosis. Three patients had alcohol as the cause of CLD whereas 2 were NAFLD related. Median CTP score and MELD was 8 and 10.4 respectively. Malignant cytology was negative in ascitic fluid. Fluid was low SAAG except in one. Median ADA levels was 50 IU/mL. FNA cytology revealed granuloma with multinucleated cells in all patients and AFB stain was positive in 2 of them (40%) (Figures 1 and 2). TB PCR was sent for only one patient (Sr No 4) and was positive. All of them had remarkable clinical improvement after standard ant tuberculosis treatment (Table 1).

Procedure-EUS Guided FNA

In all the cases, informed consent was obtained prior to the procedure. Midazolam and pentazocine was used for sedation. Blood pressure, pulse rate and oxygen saturation was monitored throughout the procedure. A linear array echoendoscope (GFUCT180; Olympus Medical, Tokyo, Japan) was used for endosonography. EUS probe was

localized to stomach and surrounding omentum was surveyed. Thickened omentum was identified. Trans gastric FNA via the anterior wall of stomach, was obtained with the help of a 22G needle (Boston Scientific, Natick, MA, USA). Four passes of two suspected deposits, with 20 to and fro movements during each pass without negative pressure, were used to aspirate the tissue (Figures 3 and 4). Slides were both alcohol fixed and air dried. Cytology evaluation was done by cytopathologist at pathology unit.

DISCUSSION

With the resurgence of tuberculosis, particularly extrapulmonary disease, there is increasing burden of peritoneal tuberculosis all over the world. The geographical distribution of peritoneal tuberculosis is not available in the literature, however, India has the world's largest tuberculosis cases which is around 26% of the world TB cases, followed by China and South Africa.⁵

Endoscopic ultrasound showing thickened omentum with ascites

Figure 1 Endoscopic ultrasound showing thickened omentum with ascites.

Endoscopic ultrasound guided fine needle aspiration

Figure 2 Endoscopic ultrasound guided fine needle aspiration.

Table 1 Details of the Patients.

Pt	Age/ sex	SAAG	Ascites cell count/ lymphocytes %	Malignant cytology	ADA IU/mL	Fibroscan	Cause of cirrhosis/ CTP/MELD/ scores	Cytopathology	AFB	Improvement after ATT	Presenting complaints
#1	62/M	Low	3240 85%	Negative	42	75	NASH DM CTP-8 MELD-7.6	Granuloma	Negative	Yes	Abdominal distention Pedal edema
#2	60/F	Low	950 90%	Negative	50	70	Nash CTP-9 MELD-10.4	Granuloma	Positive	Yes	Abdominal distention Pedal edema Fever
#3	39/M	High	302 70%	Negative	54	55.1	Alcohol CTP-10 MELD-13.2	Granuloma	Negative	Yes	Fever Abdominal distention
#4	39/M	High	1150 82%	LN FNA-Reactive	40	48.2	Alcohol CTP-8 MELD-10.2	Granuloma	Positive	Yes	Fever
#5	56/M	Low	1213/80%	Negative	55	40.6	Alcohol CTP-8 MELD-11.2	Granuloma	Negative	Yes	Fever Dull aching pain abdomen

Figure 3 May Grunwald Giemsa stained smear shows ill defined granuloma with epithelioid cells.

Peritoneal TB occurs most commonly following reactivation of latent tuberculous foci in the peritoneum. The most common features of tuberculous peritonitis are ascites (93%), abdominal pain (73%), and fever (58%).⁶ Various risk factors have been implicated (in descending order of frequency) like cirrhosis, continuous ambulatory peritoneal dialysis (CAPD), diabetes mellitus, underlying malignancy, use of systemic corticosteroids, and acquired immunodeficiency syndrome (AIDS).³ Peritoneal tuberculosis occurs in 3 forms: (i) wet type with ascites; (ii) encysted (loculated) type with a localized abdominal swelling; and (iii) fibrotic type with abdominal masses composed of mesenteric and omental thickening, with matted bowel loops felt as lump(s) in the abdomen.⁷ A combination of these types is also common. Usually the disease has insidious onset and variable course. Peritoneal TB is diagnosed in 6.6% of the ascites cases.⁸

In patients with cirrhosis with portal hypertension the diagnosis of peritoneal TB becomes even more challenging. Findings on physical examination are usually nonspecific. The classic doughy abdomen is uncommon. These nonspecific features and close resemblance to clinical manifestations of cirrhosis with portal hypertension makes it really difficult to arrive at the diagnosis. Routine laboratory studies are also nonspecific. Around 70% of patients have positive tuberculin testing with purified protein derivative (PPD), however a negative result does not exclude the disease.⁹

Laboratory evaluation of the ascitic fluid help in suspecting peritoneal TB. Most of patients have protein content of the ascitic fluid usually >3.0 g/dL and a relative lymphocytic pleocytosis. The serum-ascites albumin gradient (SAAG) is <1.1 g/dL in patients without underlying cirrhosis, however, up to 50 percent patients with chronic

Ziehl Neelsen staining shows acid fast bacilli (100X).(arrow)

Figure 4 Ziehl Neelsen staining shows acid fast bacilli (100×) (arrow).

liver disease have a SAAG ≥ 1.1 . Microscopic detection of AFB has a sensitivity of less than 10%, because of the pauci-bacillary nature of the disease.² The utility of ascitic fluid PCR assays in detecting TB peritonitis has not been well established. In cirrhotics, due to the characteristically poor humoral and T-cell mediated response, the sensitivity of ADA is substantially lower (approximately 30%).¹⁰ ADA measurement has its greatest utility in settings where tuberculous peritonitis is suspected in non-cirrhotic patients.

Ultrasound and CT imaging may reveal thickening of peritoneum, omental caking, lymphadenopathy (with hypodense center), and the presence of ascites (typically high density) with fine mobile septations. However for detecting peritoneal implants less than 1 cm, helical CT scanners have a poor sensitivity (25–50%).¹¹

The gold-standard for diagnosis is either growth of *Mycobacterium* on ascitic fluid culture or peritoneal biopsy. Reported sensitivity of ascitic fluid culture is low (approximately 35%). Usually a peritoneal biopsy performed under direct visualization is needed.¹² The sensitivity of culture of peritoneal biopsy is variably reported to be between 38 and 92%. Laproscopic examination and histopathology have high sensitivity and specificity (93 and 98%). However laproscopic biopsy is invasive procedure and has a risk of complications which are higher in cirrhotics and also increase with Child-Pugh status.¹³ Image guided peritoneal biopsy/FNAC like US guided or CT guided have been proven to be safer and cost effective. In a series of 173 patients with thickened omentum positive diagnostic results were obtained in 81% of the patients, although the specimen was considered adequate in 98% of them.¹⁴

The ability of EUS to guide a biopsy needle into lesions that are too small to be identified by CT or MRI, or too well encased by surrounding vascular structures to allow

percutaneous biopsy, secures its role in a variety of clinical settings. EUS has been traditionally used for diagnosis of tuberculosis involving lymph nodes both mediastinal as well as intraabdominal.¹⁵ There have been very few reports of EUS guided FNA for diagnosis of difficult to diagnose peritoneal tuberculosis.^{16,17} Reported complication rates following EUS-guided FNA have been variable, which are usually non fatal. In a report by Kocaman et al., 3 patients who were suspected to have tubercular peritonitis were evaluated with transgastric EUS guided biopsy.¹⁸ They found multinucleated giant cells in all biopsy specimens and positive polymerase chain reaction in 2 patients. No complications were reported post procedure. Learning curve exists for EUS-FNA, which may have bearing upon the likelihood of complications.

Thus, to conclude, EUS-guided FNA of the peritoneum is a good modality for diagnosis of peritoneal tuberculosis, especially in the setting of decompensated cirrhosis, when symptoms, signs and laboratory features of peritoneal tuberculosis are masked by presence of ascites due to liver disease. This modality should be used more often to procure peritoneal tissue for cytological confirmation of tuberculosis.

ETHICAL STATEMENTS

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from patients for being included in the study.

CONFLICTS OF INTEREST

The authors have none to declare.

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