CASE REPORT

TJG
The Turkish Journal of Gastroenterology

Diagnosis of tuberculous peritonitis using endoscopic ultrasound-guided fine-needle aspiration biopsy of the peritoneum

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Background/aims: *Tuberculous peritonitis is prevalent in developing countries and its diagnosis is still challenging due to the lack of specific clinical characteristics and the difficulty in obtaining tissue from the peritoneum without laparoscopy. Endoscopic ultrasound - guided fine needle aspiration is emerging as the most effective and safe method for obtaining tissue from the structures surrounding the gut lumen. Our study aimed to elucidate the efficacy of endoscopic ultrasound-fine needle aspiration of the peritoneum in the diagnosis of tuberculous peritonitis.* ***Materials and Methods:*** *Three patients (2 male and 1 female; aged 38, 25, and 65 years, respectively) suspected of having tuberculous peritonitis were recruited into the study. Clinical evaluation including computed tomography imaging and analysis of ascitic fluid were performed. Endoscopic ultrasound-fine needle aspiration biopsy of the peritoneum was performed trans-gastrically with a 19-gauge ProCore needle in all patients. At least two different areas of the peritoneum suspected to be involved were sampled and paraffin-embedded cell blocks were prepared for each biopsy specimen.* ***Results:*** *Biopsy specimens were positive for Mycobacterium tuberculosis by polimerase chain reaction in 2 patients and positive for multinucleated giant cells in all patients. Treatment for tuberculosis resulted in the resolution of symptoms and ascites. No procedure-related complications occured.* ***Conclusions:*** *Endoscopic ultrasound-fine needle aspiration is an efficacious and safe method to obtain tissue from the peritoneum to use in the diagnosis of tuberculous peritonitis.*

Key words: Endosonography, fine needle aspiration biopsy, tuberculous peritonitis

Endosonografik yöntemle peritonun ince iğne aspirasyon biyopsisinin tüberküloz peritonit tanısındaki yeri

Amaç: *Tüberküloz peritonit gelişmekte olan ülkelerde sık görülür. Spesifik klinik bulguların olmaması ve laparoskopi kullanmaksızın periton hücre örneklemesinde zorluklar bulunması tanı konusunda klinisyenin zorluk yaşamasına sebep olur. Endoskopik ultrasonografi eşliğinde ince iğne aspirasyonu, barsak lümeni etrafındaki yapıların örneklenmesinde en iyi sonuç alıcı ve en güvenli tanı metodu olarak gündeme gelmektedir. Çalışmamızda, tüberküloz peritonit tanısında peritona yönelik endoskopik ultrasonografi-ince iğne aspirasyonu işleminin etkinliğini araştırmayı hedefledik.* ***Gereç ve Yöntem:*** *Tüberküloz peritonit şüphesi olan 3 hasta (2 erkek, 1 kadın; yaşlar sırasıyla 38, 25 ve 65 idi) çalışmaya alındı. Hastalarda klinik değerlendirme kapsamında yapılan bilgisayarlı tomografik görüntüleme ve asit sıvısı analizleri tanısal değildi. Tüm hastalardan, transgastrik yoldan 19-gauge ProCore iğne ile peritona yönelik endoskopik ultrasonografi-ince iğne aspirasyonu işlemi yapıldı. Periton örneklemesi için en az iki şüpheli infiltre bölgeden örnek alındı. Tüm hastalar için hücre blokları hazırlandı.* ***Bulgular:*** *İki hastadan alınan periton biyopsi örnekleri Mycobacterium tuberculosis polimeraz zincir reaksiyonu incelemesi için pozitifti. Tüm hastaların periton biyopsi örneklerinde multinükleer dev hücreler görüldü. Tüberküloz tedavisi ile tüm hastalarda semptomlar iyileşti ve asit kayboldu. İşleme yönelik herhangi bir komplikasyon yaşanmadı.* ***Sonuç:*** *Endoskopik ultrasonografi-ince iğne aspirasyon yöntemi, tüberküloz peritonit tanısında periton örneklemesi için etkili ve güvenli bir tanısal metod olarak kullanılabilir.*

Anahtar kelimeler: Endosonografi, ince iğne aspirasyon biyopsisi, tüberküloz peritonit

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Manuscript received: 16.05.2012 **Accepted:** 05.06.2012

Turk J Gastroenterol 2013; 24 (1): 65-69
doi: 10.4318/tjg.2013.0543

INTRODUCTION

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. The major histopathological feature of tuberculosis is tuberculous granuloma. Within the granulomas, macrophages differentiate into epithelioid cells (differentiated macrophages) and/or fuse to form multinucleated giant cells, also called Langhans giant cells (1). 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 (2).

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 (3).

The diagnosis of TBP is often difficult due to nonspecific symptoms, inadequate microbiological diagnostic methods and non-specific findings from imaging tests (4,5). Although laparoscopy-guided peritoneal biopsy was accepted as the most sensitive and specific diagnostic tool for early identification of TBP, the invasiveness and potential complications of this test, as well as, the scarcity of gastroenterologists with experience in this procedure have prevented this tool from being widely adopted (6).

While the usage of endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) has been described in the diagnosis of TB in mediastinal and intra-abdominal lymph nodes, its role in the diagnosis of TBP has been less well studied (7). We report our experience with 3 cases to highlight the utility of minimally invasive EUS-FNA in the diagnosis of TBP.

PATIENTS AND METHODS

Patients

Case 1: A 38 year-old male patient presenting with abdominal pain and loss of appetite lasting over 3 months was admitted in April 2011. Analysis of the ascitic fluid revealed an exudative type of effusion. The laboratory and imaging results of the patient are described in Table 1. Linear EUS was used in determining the etiology of ascites. EUS revealed sheetlike and nodular peritoneal deposits visualized as hyperechoic lesions during the examination (Figure 1). EUS-FNA with 19-gauge ProCore biopsy needle was performed for all peritoneal deposits. Paraffin-embeded cell blocks were prepared for each biopsy. Histological examination of the biopsy specimens was positive for multinucleated giant cells and PCR was used to confirm *M. tuberculosis* (Figure 2). Anti-tuberculous treatment including rifampicin, isoniazid, ethambutol and pyrazinamide was used and resulted in relief from ascites and constitutional symptoms and all the symptoms resolved after 9 months of treatment.

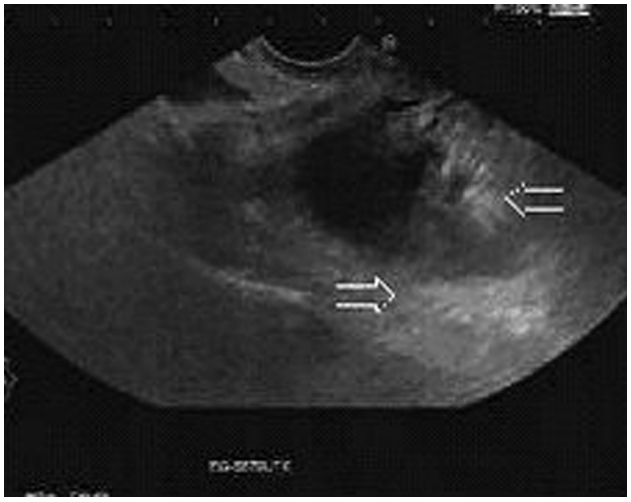

Figure 1. Linear EUS showing sheetlike (upper arrow) and nodular (lower arrow) deposits on the peritoneal surface.

Table 1. Demographic, laboratory and imaging findings of the patients

No	Age (y/Gender)	MTST	HIV	Chest X-Bay	Abd. CT	Ascites	A-ADA	A-AFBS	A-PCR	A-AFBC
1	38/M	+	-	-	Ascites and peritoneal deposits	Exudative	45	-	-	-
2	25/M	-	-	-	Ascites and peritoneal deposits	Exudative	36	-	-	-
3	65/F	-	-	-	Ascites and peritoneal deposits	Exudative	52	-	-	-

MTST: Mantoux tuberculin skin test, HIV: Human immunodeficiency virus, Abd. CT: Abdominal Computed Tomography, A-ADA: Ascites-adenosine deaminase (IU/L), A-AFBS: Ascites-acid fast bacilli smear, A-PCR: Ascites-polymerase chain reaction, A-AFBC: Ascites-acid fast bacilli culture.

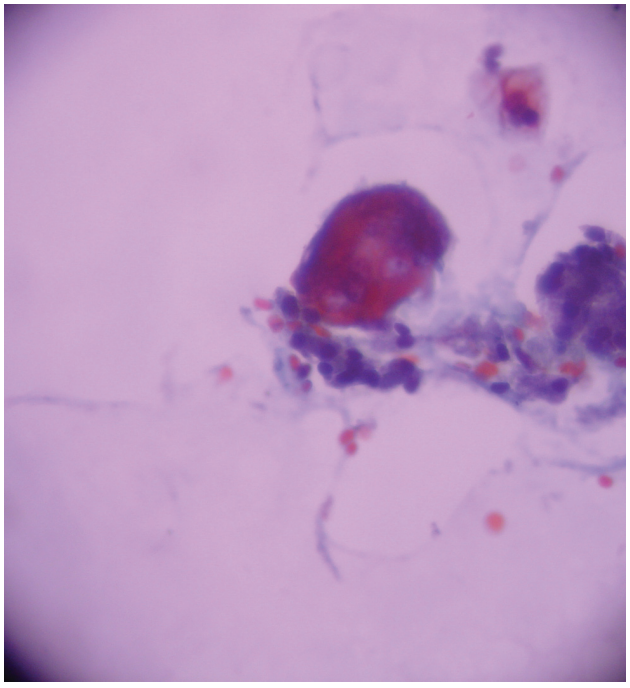

Figure 2. Microscopic examination of peritoneal biopsy specimens showing multinucleated giant cells (Hematoxylin and Eosin; 400x).

Case 2: A 25 year-old male patient presented with symptoms of abdominal pain, fever and weight loss lasting 3 months in July 2011. Prior to admission, an abdominal ultrasound performed at another hospital had revealed ascites. The serum-ascites albumin gradient value was 0.5 g/dL suggesting exudative ascites. The laboratory and imaging results of the patient are shown in Table 1. Tuberculous peritonitis was suspected. Linear EUS examination revealed sheetlike hyperechoic peritoneal deposits. EUS-FNA biopsy of the peritoneal deposits was performed. Cytological examination of biopsy specimens revealed multinucleated giant cells and PCR analysis was positive for M. tuberculosis. The patient was treated with four anti-tuberculous medications: rifampicin, isoniazid, ethambutol and pyrazinamide. Patient follow-up demonstrated loss of ascites and amelioration of symptoms. The patient was free of symptoms at the final follow-up in March 2012.

Case 3: A 65 year-old female patient presented to our gastroenterology unit with symptoms of abdominal pain and fever in August 2011. Transabdominal examination revealed large amounts of ascites. Paracentesis showed an exudative type of ascites and malignant cells were absent by cytology. The laboratory and imaging results of the patient are shown in Table 1. Linear EUS analysis of the peritoneum demonstrated nodular peritoneal deposits. Examination of peritoneal biopsy specimens revealed multinucleated giant cells. Tuberculous polymerase chain reaction (PCR), blood and urine cultures for *M. tuberculosis,* and serological tests for antinuclear antibody and rheumatoid factor were negative. Given the high prevalence of tuberculosis in our country and the clinical findings suggestive of TBP, the patient was empirically treated with the anti-tuberculous treatment of rifampicin, isoniazid, ethambutol, and pyrazinamide. Follow-up of the patient demonstrate the disapperance of the ascites and resolution of the fever after 3 months of treatment.

Methods

Three patients with suspected TBP were recruited into the study over 6 months between April and September 2011 for EUS-FNA biopsy of peritoneal deposits possibly induced by peritoneal tuberculosis. All patients gave their informed consent before taking part in the study. The demographic data, biochemical and radiological findings, EUS-FNA indications, procedure related complications and follow-up of the patients were recorded. Noninvasive monitoring of the patients' hemodynamics and oxygenation status was carried out during treatment.

Mantoux tuberculin skin test was considered positive if a skin induration was greater than or equal to 5 mm. To diagnose TBP, the cut-off value for adenosine deaminase (ADA) level in ascites was 35 IU/L (8).

Curvilinear echoendoscope (HI VISION Preirus, Hitachi Medical Corporation, Tokyo, Japan) was used for EUS. All procedures was performed by one expert endosonographer (HŞ). Before endoscopic intervention, all patients prophylactically received intravenous 1 g ceftriaxone. Gastric localization of EUS probe was used to biopsy the peritoneal deposits and at least four passes of two suspected deposits were used to collect biopsy specimens. A 19-gauge ProCore needle (Wilson-Cook Medical Inc., Winston-Salem, NC, USA) was used for EUS-FNA of the peritoneum at 7.5 MHz. The biopsy specimens were evaluated by the pathology unit.

RESULTS

The EUS procedure lasted an average of 15 minutes. No procedure related complications were experienced during or after EUS-FNA. EUS revealed sheetlike and/or nodular deposits on the peri-

toneal surface and ascites in all patients. The examination of peritoneal biopsy specimens collected by EUS-FNA revealed multinucleated giant cells in all patients and PCR analysis was positive for *M. tuberculosis* PCR in 2 patients.

DISCUSSION

Diagnosis of TBP is clinically difficult due to its mild symptoms and is largely dependent on the experience of the clinican. Laparoscopy with peritoneal biopsy is the gold standard in the diagnosis of TBP (3). However, laparoscopy is generally performed under general anesthesia and fewer gastroenterologists now perform this procedure. Thus, a new procedure for diagnosing TBP needs to be developed.

EUS-FNA is a safe, minimally invasive, and accurate out-patient procedure for the diagnosis of many benign and malignant conditions. EUS-FNA is accepted as a valuable diagnostic tool for the evaluation of mediastinal and abdominal lymph nodes and can be used in the diagnosis of tuberculosis (9). EUS-FNA has many advantages compared to conventional diagnostic modalities in the assessment of extrapulmonary tuberculosis but requires further validation.

Diagnosing TBP is still challenging for many clinicians. Elevated lymphocyte count, decreased glucose level, elevated LDH, total protein and ADA levels (>35 IU/L) in ascites, and low serum-ascites albumin gradient (<1.1) have been used as complementary diagnostic tests for TBP. Due to the poor accuracy of these tests, a TBP diagnosis needs to be confirmed by the presence of acid-fast bacilli (Ziehl-Neelsen staining positive), positive culture for *M. tuberculosis* or PCR analysis for *M. tuberculosis* complex expression. As culturing *M. tuberculosis* is cumbersome and has a high false-negative rate, its use for TBP diagnosis not very practical. Furthermore, growing cultures takes 4-8 weeks to yield a result and reports have shown a high mortality rate for patients awaiting treatment pending the results of ascitic Mycobacteria culture (2,10). An innovative diagnostic test the for early and accurate diagnosis of TBP is needed. We recommend EUS-FNA of the peritoneum as an innovative diagnostic tool for suspected TBP, which we show to be highly accurate.

The patients in our study displayed ascites and peritoneal deposits on abdominal computed tomography (CT), which correlated with EUS findings. Helical CT scanners have a good sensitivity (85%–93%) in general, but poor sensitivity (25%–50%) for detecting peritoneal implants less than 1 cm (11). Additional indications for TBP on CT include splenomegaly, miliary microabscesses in the liver or spleen, low-attenuation lymphadenopathy, splenic or lymph node calcification, and inflammatory thickening of the terminal ileum and cecum (12). The presence of ascites helps in visualizing small peritoneal implants thus making EUS tissue sampling easier. Transgastric EUS has the disadvantage of not reaching the lower abdominal and thereby cannot detect TBP-related pathologies above the pelvic region (13). All patients in our study had no additional pathologies besides ascites and peritoneal deposits on CT and EUS. Although the ability of EUS to take biopsies in addition to visualizing peritoneal deposits is an advantage, the limitation in detecting the pathologic findings in places remote from the stomach may result in difficulty diagnosing TBP. As a result, CT as a complimentary technique to EUS may be offered for suspected TBP to close the diagnostic gap created by EUS.

In a study of 12 patients with undiagnosed ascites, Rana et al. found that EUS-FNA biopsies of peritoneal lesions from four patients with TBP contained inflammatory cells with no granulomas or acid-fast bacilli (14). However, 50% of the patients had a positive PCR result for *M. tuberculosis*. All four TBP patients in that study had mediastinal lymphadenopathy and EUS-FNA of these lymph nodes revealed granulomatous inflammation in all four patients and acid-fast bacilli in two out of the four. None of our patients had mediastinal lymphadenopathy. In our study, EUS-FNA biopsy of peritoneal deposits revealed multinucleated giant cells in all patients and a positive *M. tuberculosis* PCR result in two out of the three patients. The higher yield of peritoneal biopsies with regard to positive PCR for *M. tuberculosis* may be explained with the better tissue acquisition with 19 gauge ProCore needle in our study.

Another report by Rana et al. determined the EUS-FNA biopsy efficacy of peritoneal deposits in a patient with ascites (15). They performed EUS-guided biopsy of the peritoneum in a patient with alcohol-related cirrhosis and recurrent ascites and found a positive PCR result for *M. tuberculosis*. PCR examination and culture of ascitic fluid in this case revealed negative results for *M. tuberculosis* and thus, TBP was diagnosed based upon the positive peritoneal biopsy PCR results similar to two patients in our study.

FNA biopsy allows the pathologist to see the cells aspirated from the lesion; however, the volume of FNA samples is sufficient to evaluate the global morphology of the lesion. The disadvantage of FNA in total assessment of the lesion creates uncertainty in diagnosing tuberculosis. Therefore, the positive findings from FNA should be interpreted in conjuction with clinical and laboratory results for each patient suspected of having tuberculosis. The presence of multinucleated giant cells in patient FNA samples was an important adjunct in diagnosing tuberculosis and provided a concrete direction for anti-tuberculous therapy in our patients.

In conclusion, endosonography is a diagnostic and therapeutic tool capable of making a major impact on gastroenterology; particularly since TBP is still prevalent in developing countries. EUS-FNA appears to be an efficacious and safe method for obtaining tissue from the peritoneum to diagnose TBP.

Acknowledgments: *We thank Prof. Mohamad A. Eloubeidi for his help reviewing the manuscript.*

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