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Tuberculous peritonitis: an analysis of case series of 49 consecutive patients

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ABSTRACT

Objectives: The incidence of tuberculous peritonitis has been reported between 0.1% and 0.7% among all tuberculosis types. This study, it was aimed to evaluate the cases with tuberculous peritonitis, which has an important place in the differential diagnosis of patients with ascites, clinically, biochemically, microbiologically, and histopathologically.

Methods: Forty-nine patients with a definite clinical, radiological, and histopathological diagnosis of tuberculous peritonitis, which formed the basis of our study, were analyzed retrospectively.

Results: The mean age of patients with tuberculous peritonitis was found to be 39.45±19.02 years. Purified-protein derivative (PPD) was positive in 23 (72%) of 32 patients with tuberculous peritonitis whose PPD results were recorded, in 9 (28%) PPD results were evaluated as anergic or negative. QuantiFERON-TB Gold In-Tube (QFT-GIT) test was sent in 10 of the patients, the result was positive in 9 (90%) patients and negative in 1 (10%) patient. There were 32 patients in whom tuberculosis polymerase chain reaction (PCR) was studied from ascitic fluid, 7 (22%) of the patients were PCR positive and 25 (78%) negative. Mycobacterium tuberculosis culture positivity was found in 18 (69%) of 26 patients who were biopsied. In total, 29 (59%) of the patients had M. tuberculosis culture positivity.

Conclusions: Tuberculous peritonitis constitutes a public health problem in endemic regions of the world and tuberculous peritonitis should be considered in patients presenting with ascites. Despite all diagnostic difficulties, necessary tests, especially peritoneal biopsy, should be performed for early diagnosis, and it should not be forgotten that early initiation of treatment is very important in terms of morbidity and mortality of the disease.

Keywords: Tuberculous peritonitis, diagnostic difficulties, ascites

The differential diagnosis of ascites accumulating between peritoneal leaves remains a problem in many cases, despite the advanced testing possibilities we have. Tuberculous peritonitis (TBP) is an extrapulmonary manifestation of tuberculosis (TB) that involves Mycobacterium seeding of the peritoneum. It is estimated that the prevalence of TBP has decreased and now comprises 4%-10% of all extrapulmonary cases of TB worldwide. The disease occurs equally in both sexes, with most cases between the ages of 21 and 45. Poor hygienic conditions, overpopulation, and consumption of unpasteurized milk pose a risk for the development of TBP. TBP often occurs with the reactivation of dormant TB foci in the

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peritoneum caused by hematogenous spread from the primary lung focus. TBP can also occur by the hematogenous spread in the presence of active pulmonary TB or miliary TB. More rarely, TB mycobacteria enter the peritoneal cavity through contiguous TB or TB salpingitis. The diagnosis of TBP is made by clinical, immunological, microbiological, and, most importantly, histopathological methods. While the frequency of TB is gradually decreasing, there has been an increase in the number of individuals infected with TB as a result of the immunosuppressive Human Immunodeficiency Virus (HIV) infection, the increase in malignancies, and the effect of socioeconomic conditions [1-4].

This study, it was aimed to evaluate the cases with TBP, which has an important place in the differential diagnosis of patients with ascites, clinically, biochemically, microbiologically, and histopathologically. In addition, in our study, we aimed to show that serum CA-125 level may be a predictive factor in the differential diagnosis of ovarian carcinoma and TBP.

METHODS

The patients were grouped according to their clinical, serological, radiological, and histopathological analyzes and were grouped under four main headings according to their incidence (Table 1). While approximately half of the cases were decompensated liver cirrhosis, most of the remaining cases were peritonitis carcinomatosis. 49 patients with a definite clinical, microbiological, and histopathological diagnosis of TBP, which formed the basis of our study, were analyzed retrospectively, age, gender, comorbid diseases, peritoneal fluid analysis (Lactate dehydrogenase (LDH), albumin, glucose, Adenosine deaminase (ADA), Polymerase Chain Reaction (PCR)), histopathological diagnosis, Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum CA-125 level and serum albumin values of the patients were recorded, purified protein derivative (PPD), QuantiFERON-TB Gold In-Tube (QFT-GIT) test, posteroanterior (PA) chest radiographs, computed tomography (CT) reports were evaluated.

For the study, approval of the ethics committee for clinical research of Erzurum Ataturk University Faculty of Medicine Ethics Committee was obtained 2019/1-51.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS v20) program was used to analyze the data. Categorical variables were presented as numbers and percentages, and numerical variables were presented as mean and standard deviation. The suitability of the numerical variables to the normal distribution was checked using the Kolmogorov-Smirnov Test, z values calculated for skewness and kurtosis, and graphing methods. Mann Whitney U was used for comparisons of non-normally distributed numerical variables between two groups, Kruskal Wallis was used for comparisons between more than two groups, Mann Whitney U with Bonferroni correction was used for posthoc analyses, and χ^2, χ^2 Trend tests were used for comparison of categorical variables. The statistical significance level was accepted as $P<0.05$ in all analyses.

RESULTS

The mean age of the patients in our study was 55.6 ± 16.7 years. Of the 618 patients with ascites evaluated, 290 (46.9%) were male and 328 (53.1%) were female. Of the patients, 305 (49.4%) had liver cirrhosis, 126 (20.4%) malignancy, 49 (7.9%) TBP, 32 (5.2%) non-cirrhotic portal hypertension, 32 heart failure (5.2%), 28 (4.5%) mixed (existence of liver cirrhosis and other diagnoses that may cause ascites), 14 (2.3%) nephrotic syndrome, 13 (There were 2.1% pancreatic ascites, 11 (1.8%) undiagnosed, 8 (1.3%) patients with ascites due to other causes (Table 1).

The mean age of patients with TBP was found to be 39.45±19.02 years. Eight (16.3%) of TBP patients

Table 1. Etiological Distribution of the Patients

Diagnosis	n	%
Liver Cirrhosis	305	49.4
Peritonitis carcinomatosa	126	20.4
Tuberculosis Peritonitis	49	7.9
Other	138	22.3

Table 2. Age, gender, and comorbidity distribution of patients with tuberculous peritonitis

Age ranges	n	%
< 20	8	16,3
21-40	20	40,8
41-60	13	26,5
> 60	8	16,3
Gender		
Female	41	84
Male	8	16
Comorbid diseases		
Diabetes mellitus	7	14,3
ESRD*	5	10,2
Steroid use	4	8,2
Cirrhosis	4	8,2
Renal Tx **	1	2
Previous tuberculous	3	6,1
Coexistence of Lung TB	1	2

ESRD = End Stage Renal Failure, **Renal Tx = Renal Transplantation

were male and 41 (83.7%) were female. Patients were grouped according to age ranges.8 (16.3%) patients were <20 years old, 20 (40.8%) patients were 21-40 years old, 13 (26.5%) patients were 41-60 years old, and 8 (16.3%) patients were >60 years old. There were comorbid diseases in 22 (45%) patients with TBP and pulmonary TB in 1 (2%) (Table 2).

PPD was positive in 23 (72%) of 32 patients with TBP whose PPD results were recorded, in 9 (28%) PPD results were evaluated as anergic or negative. QFT-GIT test was sent in 10 of the patients, the result was positive in 9 (90%) patients and negative in 1 (10%) patient. There were 32 patients in whom TB PCR was studied from ascitic fluid, 7 (22%) of the patients were PCR positive and 25 (78%) negative. Mycobacterium tuberculosis culture positivity was found in 18 (69%) of 26 patients who were biopsied. In total, 29 (59%) of the patients had M. tuberculosis culture positivity.

There were 15 patients diagnosed with TBP whose ADA level was studied in ascitic fluid, the ADA cutoff value was taken as 30 U/L, and the ADA level was found to be high in 15 (100%) of the patients. The mean ADA level of the patients was found to be 121.80±42.72 U/L. CRP levels were high in 47 (95.6%) patients with TBP, and CRP values were normal in 2 (4.1%) patients. ESR results from patients with TBP were studied in all patients. ESR elevation was present in 40 (81.6%) patients. ESR was normal in 9 (18.4%). The distribution of microbiological and biochemical data of patients with TBP is shown in Table 3.

The patients were diagnosed with TBP microbiologically, clinically, or histopathologically. While the microbiological diagnosis was made in 11(22,5%) of 49 patients with TB peritonitis, 12 (24,5%) were diagnosed clinically and 26 (53%) histopathologically. In 11 (%22) patients diagnosed microbiologically, M. tuberculosis was isolated in the acidic fluid. Eight (16.3%) of the patients who were diagnosed histopathologically had paracentesis findings supporting TBP and a high ADA level. With high ascites ADA level, 1 (2%) patient had a QTF-GIT test, 3 (6.1%) patients had PCR, and 7 (14.3%) had PPD positivity. Ascites ADA level was not studied in 18 (37%) patients who were diagnosed histopathologically. In these patients, PCR was positive in 2 (4.1%) patients, the QTF-GIT test was positive in 3 (6.1%) patients, and PPD was positive in 10 (20.4%) patients, together with high clinical suspicion and paracentesis findings supporting TBP and 2 (4.1%) patients had a history of previous TB. While paracentesis findings were supporting TBP in 4 (8.2%) patients, a minimally invasive peritoneal biopsy was performed on high clinical suspicion. Since most of our patients with TBP are women, we compared serum CA-125 levels, which may be useful in the differential diagnosis of ovarian malignancies, which is a common cause of ascites in women. Patients with TBP and patients with ovarian carcinoma were divided into 2 groups. There were 49 patients with TBP and 50 patients with ovarian carcinoma. The mean age of patients with TBP was found to be 39.45±19.02 years. The mean age of patients with ovarian carcinoma was 56.68±12.40 years. The mean serum CA-125 level of patients with TBP was found to be 437.78±383.66 U/mL. The mean CA-125 level of patients with ovarian carcinoma was found to be 1814.06±1767.52. When the mean CA-125 levels of the patients were compared, a significant difference was found between the groups (P<0.001). The mean

Table 3. Distribution of microbiological and biochemical data of patients with tuberculous peritonitis

Test type	Tested patients (n)	Positive patients n (%)
Pürified protein derivative	32	23 (72)
Quantiferon	10	9 (90)
Polymerase chain reaction	32	7 (22)
Adenosine deaminas	15	15 (100)
C-reactivated protein	49	47 (95.6)
Erythrocyte sedimentation rate	49	40 (81.6)

CA-125 level of patients with ovarian carcinoma was higher than patients with TBP.

Quadruple anti-TB was given to patients diagnosed with tuberculous peritonitis, and two months later, dual anti-TB treatment was continued and completed for a total of 6 months (The first two months are isoniazid (INH), rifampicin, pyrazinamide, and ethambutol, and after the second month INH and rifampicin for 4 months). It was determined that all patients tolerated the treatment well and no significant adverse events were observed except for mild transaminase elevation observed in 2 (4%) patients. As a result of the clinical and radiological evaluations made after the treatment, ascites disappeared except for 2 (4%) patients, and it was seen that these 2 (4%) patients had Multi-Drug Resistant (MDR-TB).

DISCUSSION

Diseases that can cause ascites to take place in a very wide range. In these diseases whose treatments are completely different, morbidity and mortality of the disease can be reduced by early diagnosis. Although ascites can be seen in many diseases, the most common cause is liver cirrhosis. TBP, which is a rare cause of ascites, is seen at a rate of 10%, especially in underdeveloped countries. Ascites related to TBP were detected in our study at a rate of 7,9%, which is important because it shows that TBP is a more important etiological cause in our country than in Western countries [2-4].

Increasing population migration, the use of more potent immunosuppressant therapies, an increase in the number of immunocompromised HIV-infected individuals, and an increase in the incidence of malignancies have contributed to the reemergence of TB in areas where it was previously largely controlled. TBP often complicates patients with underlying end-stage renal or hepatic disease. However, diagnosing TB disease remains challenging due to the insidious nature of the disease, the many different clinical manifestations, and the limitations of current diagnostic tests. When unexplained ascites are encountered, especially in high-risk patients, the clinician should suspect TBP. TBP should be considered in the differential diagnosis of all patients presenting with unexplained lymphocytic acid and a serum-ascites albumin gradient (SAAG) <11 g/L [4, 5]. Bacteriological performance is imperfect since the culture of ascites was positive in only 58,1% and peritoneal biopsy in 73.3% of cases. Biopsy for bacterial culture and histology is essential for diagnosis [6].

With TB culture being the diagnostic gold standard for TB, ascites fluid ARB and culture positivity rates may be low due to the low density of bacilli, which is one of the difficulties encountered in diagnosis [7, 8]. A positive ascitic fluid ADA can be highly suggestive. Numerous studies have been performed looking at the optimal cutoff for sensitivity and specificity, with most studies suggesting an ADA level of > 30 IU/L as yielding sensitivities of close to 100% and specificity generally greater than 95% for TBP [4]. In our study, PCR positivity, ADA level, and QFT-GIT test positivity were determined by the literature, and these tests can be used when necessary [9].

Currently, TBP is usually diagnosed histopathologically, as it can show malignancy-like features and

bacteriological confirmation is both difficult and time-consuming. While awaiting bacteriological confirmation, the histopathological examination may speed up the diagnostic process and facilitate the early initiation of treatment. The consensus in many studies is that peritoneal biopsy is the best procedure for the diagnosis of TBP [4, 10]. In the case of suspected TBP, the laparoscopic peritoneal biopsy is the preferred diagnostic tool and should be performed without delay [11]. With the help of imaging methods, an increasing number of peritoneal biopsies have been taken recently. This method provides a safer and less expensive alternative to diagnostic laparoscopy. Recently, it has been reported that 95% of the cases are diagnosed with a peritoneal biopsy taken in this way [12].

The incidence of TBP has increased in the presence of cirrhosis, chronic renal failure patients undergoing continuous peritoneal dialysis (CAPD), and immunosuppressive patients such as the presence of HIV infection and steroid use. Almost half of the patients in our study also have comorbid diseases [13].

One of the differential diagnoses in female patients presenting with ascites may be peritoneal infiltration of ovarian cancer. Therefore, the distinction between ovarian cancer and TBP is important. As is seen in our study, serum CA-125 levels are found to be higher in epithelial ovarian malignancies than in TBP. CA-125 levels are not expected as high as in ovarian carcinoma in patients with TBP [14, 15].

Limitations

Since our study is retrospective, it can be said that the shortcomings of our study are that some TBP cases were not recorded and that some diagnostic parameters were recorded in the cases we detected.

CONCLUSION

In conclusion, TBP constitutes a public health problem in endemic regions of the world and TBP should be considered in patients presenting with ascites. Despite all diagnostic difficulties, necessary tests, especially peritoneal biopsy, should be performed for early diagnosis, and it should not be forgotten that early initiation of treatment is very important in terms of morbidity and mortality of the disease.

Authors' Contribution

Study Conception: ES, OY, BA; Study Design: ES, OY, BA, EBY; Supervision: ES, OY, BA, EBY; Funding: ES, OY, BA, EBY; Materials: ES, BA; Data Collection and/or Processing: ES, OY; Statistical Analysis and/or Data Interpretation: ES, EBY; Literature Review: OY, BA; Manuscript Preparation: ES, BA and Critical Review: BA, EBY.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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