TUBERCULOUS PERITONITIS IN DIFFERENT DIALYSIS PATIENTS IN SOUTHERN TAIWAN

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Abstract. Eleven cases of tuberculous peritonitis (TBP) in hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) patients at the Kaohsiung Veterans General Hospital in Kaohsiung, Taiwan between 1991 and 2000 were studied retrospectively (six cases in the HD group and five cases in the CAPD group) The diagnosis of TBP was established by either positive ascite tuberculosis (TB) culture or biopsy-proven chronic granulomatous inflammation. Fever and abdominal pain were the most common symptoms, while leukocytosis and unexplained hypercalcemia were the most common laboratory findings. Ascite analysis showed a lymphocyte predominance in all HD patients, but in only 40% of the CAPD patients. The mean duration of a diagnosis by ascite TB cultures was six weeks, while a diagnosis confirmed by laparascopic biopsy took one week. All four fatal cases were diagnosed by TB cultures. Based on our review of all possible abstracts found in a Medline search from 1966 to 2002 using the keywords tuberculosis, peritonitis, uremia, and dialysis, this may be the first study of TBP in different dialysis patients.

INTRODUCTION
There has been an increasing trend in the incidence of tuberculosis (TB) worldwide. One of every three people in the world is infected with the tubercle bacillus and at risk of developing this disease. Patients receiving dialysis therapy are at increased risk of developing TB compared with those with normal renal function, which may be due to a decrease in cellular immunity. However, tuberculous peritonitis (TBP) in patients receiving dialysis therapy has been rarely reported. Furthermore, almost all previous studies showed that TBP was present only in continuous ambulatory peritoneal dialysis (CAPD) patients. We are not aware of any previous study that reported the presence of TBP in different dialysis patients. The aim of this study was to determine if any different clinical features of TBP in both hemodialysis (HD) and CAPD patients at a single dialysis center in Taiwan.

PATIENTS AND METHODS
We examined the case records of patients with TBP undergoing either HD or CAPD at the Kaohsiung Veterans General Hospital in Kaohsiung, Taiwan over a period of 10 years between 1991 and 2000. There were 1,261 dialysis patients during this time period (1,159 HD patients and 102 CAPD patients), and we identified 55 cases of TB of all types. Among them, 11 cases of TBP were found. A definitive diagnosis was established by the presence of either caseous necrosis, granuloma, acid-fast bacilli (AFB), or a positive TB culture. We analyzed concomitant renal diseases, clinical presentations, and laboratory findings, mainly those with biochemical data and imaging studies such as ultrasonography and computerized tomography. All treatment regimens, responses of the patients, side effects, compliance, treatment results, and prognosis were recorded. This study was reviewed and approved by the medical records review committee of Kaohsiung Veterans General Hospital.

RESULTS
From 1991 to 2000, 11 cases (seven males and four females) of TBP underwent either HD or CAPD in our hospital. Di-verse renal diseases were found in these cases (Table 1). However, none was predominant. The predisposing factors for TBP included diabetes mellitus (two cases) and recent use of immunosuppressive drugs (two cases). There were six cases of TBP in the HD group (all males) and five cases in the CAPD group (M:F ratio = 1:4). The calculated crude rates of TBP were 0.52% (6 of 1,159) in the HD group and 4.9% (5 of 102) in the CAPD group.

Fever, abdominal pain, and anorexia were the most common symptoms (Table 2), while an elevated erythrocyte sedimentation rate (ESR), leukocytosis, and unexplained hypercalcemia were the most common laboratory finding in our TBP patients (Table 3). A purified protein derivative skin test with five tuberculin units was performed in only two patients in the HD group and one tested positive. The duration of diagnosis before symptoms of TBP was longer in those in the CAPD group (mean = 27.4 months) than in those in the HD group (mean = 13.3 months).

An analysis of ascites showed lymphocyte predominance in all HD patients, but in only 40% of the CAPD patients. There were two cases associated with extraperitoneal TB (Table 4), one with pulmonary and spleen TB and one with pulmonary and joint TB. Concurrent bacterial peritonitis was observed in two patients. Duration of diagnosis before symptoms or signs of TBP was longer in the CAPD group (mean = 27.4 months)

Table 1: Characteristics of 11 patients with tuberculous peritonitis*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HD (n = 6)</th>
<th>CAPD (n = 5)</th>
<th>Total (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>65.7 ± 18.1</td>
<td>50 ± 16.5</td>
<td>53.1 ± 16.8</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>6:0</td>
<td>1:4</td>
<td>7:4</td>
</tr>
<tr>
<td>Underlying cause of uremia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM nephropathy</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>SLE</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Crescentic GN</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CIN</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Unknown cause</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

* HD = hemodialysis; CAPD = continuous ambulatory peritoneal dialysis; DM = diabetes mellitus; SLE = systemic lupus erythematosis; GN = glomerulonephritis; CIN = chronic interstitial nephritis.
than in the HD group (mean = 13.3 months). Analysis of ascites showed lymphocytosis (lymphocytes comprising more than 70% of the white blood cells) in all HD patients, but in only 40% (2 of 5) of the CAPD patients. The diagnosis of TBP (Table 5) was made by culture of ascites in six patients, laparotomy biopsy in one patient, and laparoscopic biopsy in four patients. An AFB smear of ascites was positive in only one patient.

Table 5 shows the methods used to diagnose TBP. A positive diagnosis of TBP was made by an ascite TB smear in only one case. The mean duration of diagnosis by ascite TB cultures was six weeks, while a diagnosis confirmed by laparoscopic biopsy took one week. All four fatal cases were diagnosed by TB cultures.

The differences in some of the variables for HD and CAPD patients are shown in Table 4. In the HD group, three patients who were not treated with anti-TB medications and for whom took 4−6 weeks (mean = 5 weeks) to obtain positive ascite TB cultures died of TBP. In the CAPD group, one patient died of disseminated TB (peritoneal, pulmonary, and spleen TB), and one later died of ovarian cancer. The interval between symptoms or signs of TBP and a laparascopic biopsy was one week in one patient who continued to receive CAPD (Table 4). Another patient who removed a CAPD catheter and was shifted to HD showed a delayed diagnosis of six weeks of TBP by ascite culture. The overall mortality rate was 45%.

DISCUSSION

Based on our review of all abstracts found in a Medline search from 1966 to 2002 using the keywords tuberculosis, peritonitis, uremia, dialysis, this may be the first description of TBP focusing on the different types of dialysis patients. Our case study is unique for several reasons. First, our cases of TBP involved both CAPD and HD groups. Most previous studies focused on patients receiving CAPD.9–16 In one recent study in the United Kingdom,16 Quantrill and others reported that no cases of peritoneal TB occurred in any of their HD patients. Other investigators have reported that TBP predominated in CAPD patients.17,18 However, our study indicated that TBP is a still a disease of high morbidity, requiring early diagnosis in HD patients. In addition, our cases included only one single race without the confounding factor of ethnicity. All our patients were followed up in a single medical center with detailed histories and medical records.
The major clinical presentation of TBP in our dialysis patients include fever, abdominal pain, anorexia, and a high ESR, which are nonspecific. The peritoneal differential cell count showing a predominance of neutrophils is more common in TBP complicating CAPD. The clinical presentation of TBP in CAPD patients, which includes fever, abdominal pain, and a cloudy peritoneal dialysis effluent, is very similar to that of bacterial or fungal peritonitis. A peritoneal differential cell count is not helpful in distinguishing these conditions since a predominance of neutrophils is more common in TBP complicating CAPD. However, ascite lymphocytosis is a common finding in TBP complicating HD. Why this occurs requires further study.

The incidence rate of hypercalcemia (63%) in our case series was higher than that of dialysis patients without active TB in Taiwan (18.2%). Previous studies have reported conflicting results regarding issues of hypercalcemia in TB patients. The discrepancies among the previous reports depend on whether serum calcium levels were adjusted with albumin levels, differences in vitamin D availability, and calcium intake in different regions. These discrepancies may be caused by higher calcium intake, either from a phosphate binder or a diysate, and an increased active form of vitamin D caused by granulomatous inflammation. However, other possibilities require further investigation. Recently, Lee and others reported an HD patient with TBP with asymptomatic hypercalcemia observed eight months before ascites became detectable. They indicated that hypercalcemia could be an early sign of TBP without other symptoms and signs.

Our study showed that an AFB smear of ascites was positive in only one patient. Therefore, an AFB smear of ascites is not sensitive in diagnosing TBP. Thus, the diagnosis of TBP in most CAPD patients requires a positive AFB culture from peritoneal fluid. However, positive cultures were observed in only 54% of those tested in our study, and these cultures take several weeks to grow, which may delay diagnosis and treatment. Our study also showed the mean duration of diagnosis by ascite TB cultures was six weeks, while diagnosis confirmed by laparoscopic biopsy took one week. Therefore, laparoscopic biopsy is necessary for diagnosing TBP as early as possible, without waiting for culture results in patients with unexplained lymphocytic peritonitis and common neutrophil-predominant peritonitis unresponsive to antibiotics.

In this study, since TBP in maintenance dialysis patients may accompany concurrent bacterial peritonitis, we cannot exclude the possibility of TBP if bacteria were isolated from ascites in dialysis patients. In view of the nonspecific finding of TBP, difficulty in making an early diagnosis, and poor outcome, we recommend that in all dialysis patients with unexplained fever and abdominal pain in endemic areas, ascites should be evaluated for TBP as soon as possible.

In conclusion, when diagnosing chronically ill HD patients with peritoneal signs and positive results for ascite lymphocytosis, TBP should be highly suspected. For CAPD patients with lymphocytic peritonitis or neutrophil-predominant peritonitis unresponsive to antibiotics, a laparoscopic biopsy should be performed to initiate timely treatment.

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