Peritoneal tuberculosis in patients receiving continuous ambulatory peritoneal dialysis

Simon J. Quantrill¹, Mark A. Woodhead¹, Christine E. Bell¹, Alastair J. Hutchison² and Ram Gokal²

¹Department of Respiratory Medicine, ²Department of Renal Medicine, Manchester Royal Infirmary, Manchester, UK

Abstract

Background. Patients with chronic renal failure have an increased risk of tuberculosis (TB). This occurs with much higher frequency within the first 12 months of initiating dialysis and is usually extrapulmonary in nature. Patients most at risk are those from susceptible ethnic groups, especially the Indian subcontinent. Peritoneal TB, otherwise relatively uncommon, has emerged as an important form of TB in patients undergoing continuous ambulatory peritoneal dialysis (CAPD).

Methods. All cases of peritoneal TB occurring at our institution in patients undergoing CAPD over a 13 year period were identified and analysed.

Results. Eight cases were identified, of which seven were non-Caucasian. These patients’ characteristics and outcomes are presented. All were undergoing CAPD and most developed TB within 12 months of initiating dialysis. All presented with fever, but symptoms and signs were indistinguishable from bacterial peritonitis. Six were culture-positive, mainly from peritoneal dialysis fluid, but only two cases proved smear-positive. All were treated with standard anti-tuberculous chemotherapy. Three went on to permanent haemodialysis as a result of peritonitis and three have died, one of these as a result of TB.

Conclusions. Peritoneal TB, whilst otherwise relatively uncommon, is an important manifestation of TB in CAPD patients and usually develops soon after commencing dialysis. The reasons for this are unknown and require further research.

Keywords: chronic renal failure; CAPD; ethnic groups; patient characteristics; peritoneal tuberculosis

Introduction

Patients with chronic renal failure have an increased incidence of tuberculosis (TB) compared to those with normal renal function, which may be due to a decrease in cellular immunity [1–5]. Patients from susceptible ethnic groups are most at risk [6]. Previous studies have found TB to be predominantly extrapulmonary in dialysis patients and to occur soon after initiation of renal replacement therapy [2,3,6–9]. Peritoneal TB, which is seldom seen in patients with normal renal function, is a particular problem in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) [10]. The Manchester Royal Infirmary (MRI) has a large renal unit with dialysis and transplant facilities and a catchment population which includes a high proportion of non-Caucasians, especially from the Indian subcontinent.

The aim of this study was to identify and describe the clinical characteristics and outcomes of such patients seen at one hospital.

Subjects and methods

We examined the case records of patients with peritoneal TB undergoing CAPD, over a 13-year period between 1986 and 1999. Cases were identified by three methods: medical outpatient coding, microbiology records, and the respiratory unit TB database. All patients were treated at the same institution (MRI) for both renal failure and TB.

Results

Fourteen cases of TB occurring in CAPD patients including eight (57%) patients with peritoneal TB were identified over the study period. The clinical characteristics of these eight patients are illustrated in Table 1. Only one of the eight patients was Caucasian (patient 8), with six of the eight originating from the Indian subcontinent. Diabetes was present in three patients,
<table>
<thead>
<tr>
<th>Patient no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>59</td>
<td>58</td>
<td>58</td>
<td>63</td>
<td>34</td>
<td>36</td>
<td>57</td>
<td>73</td>
</tr>
<tr>
<td>Sex</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>F</td>
<td>F</td>
<td>M</td>
<td>M</td>
<td>Oriental</td>
</tr>
<tr>
<td>Ethnic group</td>
<td>ISC</td>
<td>ISC</td>
<td>ISC</td>
<td>ISC</td>
<td>ISC</td>
<td>ISC</td>
<td>ISC</td>
<td>Caucasian</td>
</tr>
<tr>
<td>Years in UK</td>
<td>2</td>
<td>25</td>
<td>13</td>
<td>22</td>
<td>34 (Born in UK)</td>
<td>14</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Extraperitoneal disease</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Pleura</td>
<td>Unknown</td>
<td>None</td>
<td>Chronic pyelonephritis</td>
</tr>
<tr>
<td>Underlying renal disease</td>
<td>Diabetes</td>
<td>Chronic pyelonephritis</td>
<td>Diabetes</td>
<td>Diabetes</td>
<td>Post-partum acute cortical necrosis</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Duration of CAPD (months)</td>
<td>12</td>
<td>12</td>
<td>16</td>
<td>12</td>
<td>63</td>
<td>6</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Fever, cloudy bags</td>
<td>Fever, cloudy bags</td>
<td>Fever, abdominal pain</td>
<td>Fever, diarrhoea, depression, abdominal pain</td>
<td>Bilateral pleural effusions, nodules</td>
<td>Unilateral pleural effusion</td>
<td>Fever, chest pain, abdominal pain</td>
<td>Fever, weight loss, anorexia, diarrhoea</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Normal</td>
<td>Cardiomegaly</td>
<td>Normal</td>
<td>Normal</td>
<td>Bilateral pleural effusions, nodules</td>
<td>Unilateral pleural effusion</td>
<td>Normal</td>
<td>Bilateral pleural effusions</td>
</tr>
<tr>
<td>Smear-positive</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes (peritoneal biopsy)</td>
<td>No</td>
<td>Yes (PD fluid)</td>
<td>No</td>
<td>Yes (PD fluid)</td>
</tr>
<tr>
<td>Culture-positive</td>
<td>Yes (PD fluid)</td>
<td>Yes (PD fluid)</td>
<td>Yes (PD fluid)</td>
<td>Yes (PD fluid)</td>
<td>Yes (PD fluid)</td>
<td>Yes (PD fluid)</td>
<td>Yes (PD fluid)</td>
<td>Yes (PD fluid)</td>
</tr>
<tr>
<td>Histology (peritoneal biopsy)</td>
<td>No specimen</td>
<td>No specimen</td>
<td>No specimen</td>
<td>Granulomata</td>
<td>No specimen</td>
<td>No granulomata seen</td>
<td>Granulomata</td>
<td>Granulomata</td>
</tr>
<tr>
<td>Transferred to haemodialysis</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Outcome</td>
<td>Good</td>
<td>Died</td>
<td>Good</td>
<td>Died</td>
<td>Good</td>
<td>Good</td>
<td>Died</td>
<td>Good</td>
</tr>
</tbody>
</table>

ISC, Indian subcontinent.
and one (patient 7) was taking maintenance prednisolone following a failed previous renal transplant. Patient 8 had previous occupational exposure to bovine TB as a public health inspector of meat carcasses. In five cases TB developed within 12 months or less after the initiation of dialysis.

Clinical presentation was indistinguishable from non-mycobacterial CAPD peritonitis (Table 1). All patients presented with fever as one of their symptoms. Chest X-rays did not show specific features of TB although pleural effusions were present in two cases. Peritoneal fluid was smear-positive for acid-fast bacilli in only one case but culture-positive in six of the eight. A peritoneal biopsy specimen was sent for histology in four cases, of which three demonstrated granulomata and one proved both smear- and culture-positive.

Treatment was given with a combination of isoniazid (200–300 mg/day), rifampicin (450–600 mg/day), and pyrazinamide (1.5–2 g/day), plus pyridoxine (10 mg/day) for a total of 6–12 months. Pyrazinamide was stopped after 0.5–6 months. Patient 1 suffered a number of side-effects 2 weeks into anti-tuberculous therapy, including confusion, drowsiness, and twitching, which disappeared when treatment was stopped. These symptoms did not reappear when treatment was restarted, but diarrhoea and vomiting then occurred, necessitating a switch to intravenous anti-tuberculous therapy until the symptoms abated after 2 weeks. Patient 4 developed a drug-fever, thought to be due to isoniazid.

Five of the eight patients were successfully treated and cured and one other (patient 6) is approaching the end of treatment. Three (patients 2, 3 and 8) were switched to haemodialysis as a result of their peritoneal TB: in patient 2, TB in itself was deemed an indication for catheter removal (although we subsequently changed this policy), patient 3 suffered progressive loss of ultrafiltration, and patient 8 had persistent peritonitis with cloudy bags and abdominal pain. Patients 2 and 4 have since died of causes unrelated to TB. Patient 7 died from acute small-bowel obstruction secondary to adhesions which were attributed to TB.

Discussion

Peritoneal TB, an otherwise relatively uncommon condition, developed in eight patients over the 13-year study period, representing over half the cases of TB in our CAPD population. Data from the North West Region Public Health Department (Dr M. Painter, personal communication, 22/12/99) showed that overall peritoneal TB accounted for only 1.4% of the total cases of TB notified in Manchester over the same time period. Other investigators have also noted this form of TB to be prominent in CAPD patients [10,11]. However, the reasons for the predominance of this site are obscure. No cases of peritoneal TB have occurred as yet in any of our haemodialysis patients.

Over the 13-year study period approximately 1000 new patients have commenced dialysis on our renal unit, of which about 12% are of Asian origin. Since 12/14 of our dialysis patients with TB were Asian this means that 12/120 (10%) Asian patients going on to dialysis developed TB. The incidence of TB in the UK is up to 30 times higher in the Asian community (114.7/100,000 (Indian), 120.1/100,000 (Pakistani) compared to 4.3/100,000 in the white population) [12], occurring mostly in immigrants whose primary infection occurred whilst resident in their country of origin. Approximately 70% of new immigrants to the UK from the Indian subcontinent aged 15–29 years old have a positive tuberculin skin test [13], and our institution has a catchment area with a large Asian (mainly Pakistani) population. It is, therefore, perhaps not surprising that most of our patients on dialysis with TB are Asian. In addition, extrapulmonary TB accounts for proportionally more cases of TB in Indian subcontinent (38%) than in Caucasian patients (21%) [12].

Patients with chronic renal failure have an increased risk of developing TB, possibly due to decreased cellular immunity [1–4,6,10]. Malnutrition may also be responsible in some cases [5]. Most studies which have reviewed TB in chronic renal failure, though, have been in patients undergoing regular haemodialysis [3,7,8]. Reactivation, which is presumably what this tuberculous peritonitis represents in these patients, most commonly occurs in the lungs. Its occurrence in the peritoneum argues strongly that local derangements in the intraperitoneal immune defence, linked to the process of CAPD, are responsible. Defects of immune function in the peritoneal cavity in CAPD include reduced phagocytosis by macrophages, reduced cytokine production, and a significant reduction in the total number of peritoneal lymphocytes [14]. These defects occur possibly as a result of the high lactate and hydrogen ion concentration of the dialysate; a dilutional effect of the relatively large volumes of dialysate used also results in a reduction in macrophage/organism interaction.

As in previous studies, we have found that TB tends to develop soon after initiating dialysis, i.e. usually within 12 months, and frequently occurs in extrapulmonary sites [2,3,6–9]. This seems to be true of both haemodialysis and CAPD, but again the reasons are unknown: correction of uraemia appears to trigger reactivation of TB (most TB in adult non-Caucasians is reactivated, not primary) [15]. The reason for the relatively early development of TB and its usual predominance for lymph nodes may be related to the improvement in lymphocyte response seen after dialysis: this occurs as a result of the removal of dialysable factor(s) responsible for the reduced cellular immune response in uraemia [16,17]. Evidence for a poor cellular immune response to TB amongst dialysis patients comes from a number of clinical studies that have shown a high frequency of anergy on skin testing [3,9,7,18–20].

In common with others, we have shown that the presentation of peritoneal TB may be non-specific and
similar to non-tuberculous bacterial peritonitis. Only two of our cases were smear-positive (one from peritoneal biopsy, one from PD fluid), although six were culture-positive. In a population with undefined renal function and peritoneal TB, only 2% of ascitic taps were found to be smear-positive although 83% were culture-positive [21]. The results of mycobacterial culture may take several weeks, so a high index of suspicion is required to make this diagnosis, especially in patients from the Indian subcontinent. Peritoneal biopsy may be helpful, but treatment must sometimes be given on clinical grounds alone. Interestingly, whilst three of our patients were transferred to haemodialysis, most (five of eight) were able to continue with CAPD—thus, removal of the dialysis catheter is not always necessary in this condition.

One solution to the problem of TB in dialysis patients may be to give anti-tuberculous chemotherapy to all high-risk patients (e.g. those from certain ethnic groups) commencing CAPD or haemodialysis. Indeed, this has already been advocated by some workers, and treatment may only need to be given for 6–12 months in total [6,10,22,23].

In conclusion, peritoneal TB, an otherwise uncommon entity, is an important manifestation of TB in patients undergoing CAPD. It should always be considered when at-risk patients on CAPD develop peritonitis unresponsive to conventional antibiotics. In such patients, peritoneal fluid should always be investigated for mycobacteria, and peritoneal biopsy considered.

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References


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