Short communication

Aspergillus Peritonitis in Chronic Peritoneal Dialysis Patients: Review of the Literature and Report of Two Cases

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Abstract

Although gram positive bacteriae are the most common causative microorganisms of chronic peritoneal dialysis (CPD) peritonitis, fungi are responsible for 1-15% of all cases. On the other hand, fungal peritonitis episodes may potentially cause serious consequences such as resistance to treatment, extended hospital stay and also a higher probability of death. Fungal peritonitis due to Aspergillus spp is relatively uncommon, but its mortality rate and severity is known to be even higher. It was our aim to conduct a review of the medical literature regarding the treatment and clinical outcome of Aspergillus related CPD peritonitis and to present two cases. One of the patients died due to Aspergillus flavus and the other was with fungal colonization in titanium adapter proven by positive fungal culture for the presence of Aspergillus niger.

Key words: peritoneal dialysis, fungal peritonitis, Aspergillus, Aspergillus flavus, Aspergillus niger

Introduction

Peritonitis is one of the most important complications of chronic peritoneal dialysis treatment and is reported to be responsible for 40-47% of technical failure with mortality rates as high as 1-6% and frequent hospitalizations seen in that treatment modality [1,2]. Although gram-positive bacteriae are the most common cause of CPD peritonitis, fungi are responsible for 1-15% of all cases [3,4]. On the other hand, fungal peritonitis episodes may potentially cause serious consequences including resistance to treatment, extended hospital stay and also a higher probability of death [5]. Fungal peritonitis due to Aspergillus spp is relatively uncommon, but its mortality rate and severity is known to be even higher [6]. It was our aim to conduct a review of the medical literature regarding the treatment and clinical outcome of Aspergillus related CPD peritonitis and to present two cases. One of the patients died due to Aspergillus flavus and the other was with fungal colonization in titanium adapter proven by positive fungal culture for the presence of Aspergillus niger.

Cases

Our first patient was a 49-year-old man with end-stage renal disease secondary to type I diabetes mellitus and has been included into our continuous peritoneal ambulatory dialysis (CAPD) program since 2008. He had undergone an inguinal hernia surgery at the 18th month after commencing CAPD treatment. In 2012, he was admitted to the Emergency Department with abdominal pain, nausea and cloudy dialysate. His blood pressure was 130/80 mmHg, pulse 82 beat/minute and body temperature 37.2°C. The physical examination revealed disseminated abdominal tenderness and he was positive for signs and symptoms of peritoneal irritation. No signs of infection around the exit site and catheter tunnel was observed. Laboratory test results of our patient were as follows: peripheral blood white blood cell (WBC) count: 18,450/mm3 (N=4.800-10.800), hemoglobin 9.5 gr/dl (12-16 gr/dl), erythrocyte sedimentation rate 120 mm/hour, C-reactive protein 46.1 mg/dl (0-0.5 mg/dl) and creatinine 12.6 mg/dl (0.7-1.2 mg/dl). His peritoneal effluent WBC count was found to be 3020 /mm3 with a differential of neutrophils: 570/mm 3, lymphocytes: 280/mm3, monocytes: 2080/mm3. Based on his clinical picture and laboratory criteria, he was diagnosed as having CPD-related peritonitis. Because of drainage problems in his peritoneal dialysis catheter, after initial samples for cultures and peritoneal effluent cell counts were taken, peritoneal dialysis catheter was removed and hemodialysis was initiated. Direct microscopic investigation of peritoneal fluid with gram staining showed no microorganisms. Peritonitis treatment was initiated with cephazidime intravenous 1 gr 2x1 and ampicillin/ sul-
bactam 1 gr 4x1 empirically. But despite treatment, his abdominal pain and clinical condition have not improved. Cultures for aerobic and anaerobic bacteria and tuberculosis were negative. But eventually, Aspergillus flavus was isolated from his peritoneal fluid samples and also from his removed catheter tip cultures. Therefore, intravenous administration of liposomal amphotericin B 200 mg/day was initiated at the fourth day of his hospitalization. This treatment was continued for 26 days. At days 0, 7, 14, 21 and 26, his C-reactive protein (CRP) levels were 24.8 mg/dl, 18.4 mg/dl, 17.7 mg/dl, 26 days. At days 0, 7, 14, 21 and 26, his C-reactive protein of his hospitalization. This treatment was continued for tericin B 200 mg/day was initiated at the fourth day fore, intravenous administration of liposomal ampho-
and also from his removed catheter tip cultures. There-
fluavus 

immune system [8], possibly non-biocompatible high

Although fungi may be found in the regular flora of human skin and mucosa, long-term antibiotic usage [7], use of immunosuppressive drugs and diseases suppressing immune system [8], possibly non-biocompatible high glucose containing dialysis solutions [9] and mechanical and/or chemical irritations caused by peritoneal catheters may be among the causes of fungal peritonitis. Transvaginal entrance of fungi into the peritoneal cavity may also occur. Intestinal perforations caused by diverticulitis have also been reported to cause fungal peritonitis.

Discussion

Fungal peritonitis episodes in CPD patients present as severe clinical form of peritonitis with high mortality rate of 20-30% [10]. Candida spp are known to be the most common cause of fungal peritonitis. But much less frequently, PD peritonitis may be caused by Aspergillus spp such as Aspergillus thermomutatus [11], Aspergillus niger [12,13], Aspergillus flavus [14], Aspergillus fumigatus [8], Aspergillus terreus [15,16], Aspergillus oryzae [5], Aspergillus sydowii [17]. In 2002, Matsumoto, et al. reviewed 20 Aspergillus spp peritonitis cases that have been published between 1968-2002. In our literature review covering the period from 2002 to 2013, we were able to find the records of 13 published cases of aspergillus peritonitis, including our two cases presented here (Table 1) [18-21]. Combined outcome results of two series reveal that, out of 33 cases presented since 1968, 11(33%) died and 13(39%) had to be transferred to hemodialysis. Only 8 patients (24%), including two patients with no signs and symptoms of overt peritonitis with culture proven Aspergillus colonization in the cathe-
ters, (Reference 19 and our second case presented in this report), were able to continue chronic peritoneal dialysis treatment suggesting a high risk clinical profile. Presence of severe abdominal pain, fever, delay in withdrawal of catheter, intensive antibiotic usage longer than three months and technical difficulties are reported to be related with mortality in fungal peri-
tonitis [3,4]. On the other hand, as we have reported in our patient, Aspergillus spp, also seen in peritonitis episodes caused by other fungi, have a tendency to form adhesive fibrin plugs causing drainage problems and total obstruction of peritoneal catheter [10]. Interestingly, in one case, Aspergillus niger peritonitis was reported to be associated with eosinophilia, which is a clinical sign of pulmonary aspergillosis [22]. In our patient, both initial peripheral blood cell and dialysate eosinophil counts were within normal limits (0.9% and 0.4%, respectively). If we analyze the fatal outcome in one of our patients, regarding the risk factors given above, the patient was neither on any immunosuppressive drugs nor there were any laboratory or clinical signs of hematologic or oncologic problems which may potentially affect his immune system besides known type I diabetes. Clinically, only abdominal pain was observed as one of the stated morta-
ty of the general
therapeutic measures, our patient died the 26th day of the admission. *Aspergillus*-related peritonitis episodes can be treated with amphotericin B alone or in combination with azol derivatives such as ketocanozol, fluconazole or itracanazole. Because of serious side effects such as fever, chills, rigor, nausea and hypotension intravenous use of conventional amphotericin B is often limited. Therefore, lipophilic form of amphotericin B is recommended and it is reported to be equally effective [11]. On the other hand, intraperitoneal use of amphotericin B may induce a chemical peritonitis with severe abdominal pain and it is not recommended. Intravenous use of amphotericin B may not be sufficiently effective because of drug’s high protein binding capacity and limited transfer to the peritoneal area [23]. *Aspergillus terreus* has been reported to be resistant to amphotericin B both in vivo and in vitro [24].

**Conclusions**

In conclusion, despite the use of recommended therapeutic measures, *Aspergillus* induced fungal peritonitis in CPD patients may still be fatal. There is a need for development of more efficient therapeutic approaches including the type, dose and route of antifungal therapy.

**Conflict of interest statement.** None declared.

**Reference**


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**TABLE 1. Summary of reported CPD-related peritonitis cases caused by *Aspergillus spp* 2003-2013**

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Gender</th>
<th>Species</th>
<th>Catheter removal</th>
<th>Antimicrobials</th>
<th>Outcome</th>
<th>Reference</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td><em>Aspergillus terreus</em></td>
<td>Yes</td>
<td>Amphotericin B</td>
<td>Death</td>
<td>17</td>
<td>2003</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td><em>Aspergillus fumigatus</em></td>
<td>No</td>
<td>Amphotericin B, oral itracanazole</td>
<td>Death</td>
<td>15</td>
<td>2004</td>
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<td>3</td>
<td>F</td>
<td><em>Aspergillus terreus</em></td>
<td>Yes</td>
<td>Amphotericin B, itracanazole</td>
<td>Death</td>
<td>16</td>
<td>2004</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td><em>Aspergillus fumigatus</em></td>
<td>Yes</td>
<td>Amphotericine B</td>
<td>HD</td>
<td>6</td>
<td>2005</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td><em>Aspergillus sydowii</em></td>
<td>Yes</td>
<td>No treatment</td>
<td>HD</td>
<td>17</td>
<td>2005</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td><em>Aspergillus fumigatus</em></td>
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<td>Amphotericin B</td>
<td>HD</td>
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<td>2006</td>
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<tr>
<td>7</td>
<td>F</td>
<td><em>Aspergillus terreus</em></td>
<td>Yes</td>
<td>Itracanazole (Catheter colonization)</td>
<td>PD</td>
<td>19</td>
<td>2006</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td><em>Aspergillus terreus</em></td>
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<td>Voricanazole</td>
<td>Death</td>
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<tr>
<td>9</td>
<td>M</td>
<td><em>Aspergillus oryzae</em></td>
<td>Yes</td>
<td>Amphotericin B, caspofungin, itracanazole</td>
<td>HD</td>
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<td>2007</td>
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<td>F</td>
<td><em>Aspergillus nidulans</em></td>
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<td>Amphotericin B, voricanazole</td>
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<td>21</td>
<td>2011</td>
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<tr>
<td>11</td>
<td>M</td>
<td><em>Aspergillus flavus</em></td>
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<td>Voricanazole</td>
<td>HD</td>
<td>14</td>
<td>2013</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td><em>Aspergillus flavus</em></td>
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<td>Amphotericin B</td>
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<td>Case I</td>
<td>2013</td>
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<tr>
<td>13</td>
<td>M</td>
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<td>No treatment (Catheter colonization)</td>
<td>PD</td>
<td>Case II</td>
<td>2013</td>
</tr>
</tbody>
</table>


