Trichosporon beigelii Funguria in Renal Transplant Recipients

Trichosporon beigelii funguria in renal transplant recipients is usually benign and is seldom associated with invasive or deep-seated infections.

Trichosporon beigelii is frequently found in the environment and may colonize the human flora [1]. In immunocompromised hosts, it frequently causes invasive fungal infections [2]. Gastrointestinal and urinary tract colonization usually precedes invasive infections. In renal transplant recipients, the clinical significance of positive urine cultures with T. beigelii is largely unknown.

From 1992 through 1999, 11 renal transplant recipients experienced T. beigelii funguria at our institution (Hôpital Maisonneuve-Rosemont, Université de Montréal, Quebec, Canada) (table 1). All patients were receiving immunosuppressive therapy consisting of either prednisone and/or azathioprine and/or cyclosporine. The majority of cases occurred during the early posttransplantation period (≤6 months after engraftment), and results of urine cultures were repeatedly positive for T. beigelii in all patients except for patients 4, 5, 7, and 11. Five patients had urinary tract indwelling devices, and 6 patients were treated with broad-spectrum systemic antibacterial therapy when a positive urine culture for T. beigelii funguria was obtained. Seven of the 11 patients had clinical signs of infection. Three of the 7 symptomatic patients complained of symptoms of urinary tract infection, and 4 patients experienced only fever. Two patients (patients 8 and 10) had invasive urinary tract infections caused by T. beigelii.

Patient 8 developed a vesicoureteral stenosis shortly after receiving a renal cadaveric allograft, and he had a ureteral stent installed. After receiving, for 14 days, antibiotic therapy for Pseudomonas aeruginosa infection of the site of a peritoneal dialysis catheter tunnel, repeated urine cultures yielded T. beigelii. The MICs against the isolate were as follows: for amphotericin B, 1 mg/L; for 5-fluorocytosine, 8 mg/L; for ketoconazole, 1 mg/L; and for fluconazole, 0.5 mg/L; and for fluconazole, 4 mg/L. The ureteral stent was replaced, and the patient was treated with ketoconazole. After 7 days of therapy, the urine cultures remained positive for T. beigelii, and ketoconazole therapy was switched to fluconazole therapy. On day 3 of fluconazole therapy, the results of urine cultures became negative. While receiving fluconazole, the patient underwent pyelovesicostomy with removal of the ureteral stent. The patient did not experience any fungal infection at follow-up 1 month after discontinuation of fluconazole therapy.

Patient 10 was admitted with progressive dysfunction of a renal cadaveric allograft. Results of repeated urine cultures revealed T. beigelii urinary infection, which was initially treated with itraconazole followed by daily intravesical instillations of amphotericin B. Despite the antifungal therapy, the urine cultures remained positive for T. beigelii. At the time of the renal transplantation, a fungus ball at the surgically reconstructed ureter was discovered on cystoscopy and was partially removed. Direct calcofluor examination of the material removed was positive, and culture yielded T. beigelii. The MICs against this isolate were as follows: for amphotericin B, 0.5 mg/L; for 5-
Table 1. Summary of clinical data for 11 renal transplant recipients with *Trichosporon beigelii* funguria.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>Sex</th>
<th>Time after transplantation</th>
<th>Immunosuppressive regimen</th>
<th>Urinary tract indwelling device</th>
<th>Systemic antibiotics</th>
<th>Total no. positive urine cultures (no. days positive)</th>
<th>Deep-seated or systemic fungal infection</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47</td>
<td>F</td>
<td>18 y</td>
<td>Prd, Aza</td>
<td>PCN</td>
<td>Cpfx</td>
<td>2 (11)</td>
<td>No</td>
<td>AmB</td>
</tr>
<tr>
<td>2</td>
<td>36</td>
<td>M</td>
<td>180 d</td>
<td>Prd, Aza, CyspA</td>
<td>US</td>
<td>TMP-SMZ</td>
<td>2 (5)</td>
<td>No</td>
<td>AmB</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>M</td>
<td>88 d</td>
<td>Prd, CyspA</td>
<td>PCN</td>
<td>No</td>
<td>4 (6)</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>37</td>
<td>M</td>
<td>8 d</td>
<td>Prd, Aza</td>
<td>None</td>
<td>No</td>
<td>1 (1)</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>35</td>
<td>M</td>
<td>5 d</td>
<td>Prd, Aza, CyspA</td>
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<td>No</td>
<td>1 (1)</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>F</td>
<td>18 d</td>
<td>Prd, Aza, CyspA</td>
<td>None</td>
<td>Ctri-Net</td>
<td>2 (3)</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>59</td>
<td>F</td>
<td>15 d</td>
<td>Prd, Aza, CyspA</td>
<td>None</td>
<td>Ctri</td>
<td>1 (1)</td>
<td>No</td>
<td>Flu</td>
</tr>
<tr>
<td>8</td>
<td>45</td>
<td>M</td>
<td>64 d</td>
<td>Prd, Aza, CyspA</td>
<td>US</td>
<td>Cpfx-Tm</td>
<td>7 (36)</td>
<td>USI</td>
<td>Ket, Flu and surgery</td>
</tr>
<tr>
<td>9</td>
<td>49</td>
<td>M</td>
<td>14 y</td>
<td>Prd, CyspA</td>
<td>CYS</td>
<td>Pip/Taz</td>
<td>2 (2)</td>
<td>No</td>
<td>Flu</td>
</tr>
<tr>
<td>10</td>
<td>40</td>
<td>M</td>
<td>13 d</td>
<td>Prd, Aza, CyspA</td>
<td>None</td>
<td>No</td>
<td>7 (20)</td>
<td>BFB</td>
<td>It, AmB, Flu and surgery</td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>M</td>
<td>29 d</td>
<td>Prd, Aza, CyspA</td>
<td>None</td>
<td>No</td>
<td>1 (1)</td>
<td>No</td>
<td>None</td>
</tr>
</tbody>
</table>

NOTE. AmB, amphotericin B; Aza, azathioprine; BFB, bladder fungal ball; Ctri, ceftriaxone; Cpfx, ciprofloxacin; CyspA, cyclosporin A; CYS, percutaneous cystotomy; Flu, fluconazole; Itr, itraconazole; Ket, ketoconazole; Net, netilmicin; PCN, percutaneous nephrostomy; Pip, piperacillin; Prd, prednisone; Taz, tazobactam; Tm, tobramycin; TMP-SMZ, trimethoprim-sulfamethoxazole; US, ureteral stent; USI, ureteral stent infection.

fluorocytosine, 0.06 mg/L; for ketoconazole, 0.25 mg/L; for itraconazole, 0.016 mg/L; and for fluconazole, 2 mg/L. Renal function progressively deteriorated, and the kidney graft was eventually removed. Acute signs of rejection were present on histopathologic examination, but no sign of fungal infection was observed. Results of fungal cultures of the removed kidney remained negative. After surgery, the patient received fluconazole treatment for 7 days, and the results of urine cultures remained negative, with no signs of urinary or systemic fungal infection at follow-up 1 month after discontinuation of fluconazole therapy.

Haupt et al. reported that 3.7% of immunosuppressed patients had urinary colonization with *T. beigelii* and that two-thirds of them developed invasive infections [3]. Among renal transplant recipients, only 3 cases of disseminated invasive infections caused by *T. beigelii*, including 1 case of urinary tract infection with subsequent fungemia, have been reported to date in the literature on the subject [4–6]. As supported both by such literature and by our present series, *T. beigelii* funguria in renal transplant recipients is usually benign and is seldom associated with invasive or deep-seated infections. Funguria that occurs after renal transplantation, even in the absence of systemic manifestations, is frequently thought by clinicians to mandate therapy, because upper urinary tract infection is probable, usually at the site of ureteric anastomosis. Five patients in our series received no antifungal therapy for their *T. beigelii* funguria. Despite the fact that 4 of these 5 patients were in their immediate posttransplantation period (<30 days after transplantation), none experienced complicating ascending fungal urinary or systemic fungal infection.

Controversies surround the use of antifungal therapy for invasive infections caused by *T. beigelii*. Anaissie and colleagues showed that, compared with amphotericin B, azoles have better in vitro activities against *T. beigelii* [7, 8]. Walsh and colleagues reported that, compared with fluconazole, itraconazole and ketoconazole have lower MICs against isolates of *T. beigelii* [2]. Despite having similar in vitro observations, ketoconazole and itraconazole initially failed to eradicate the *T. beigelii* isolates from the urinary tracts of patients 8 and 10 in our series, probably as a result of poor renal excretion of ketoconazole and itraconazole. Urinary tract instrumentation and the use of broad-spectrum antibiotics are important risk factors for persistent *T. beigelii* funguria.

In conclusion, the clinical impact of *T. beigelii* funguria in renal transplant recipients seems to be no different than the impact of candiduria observed in other patient populations where ascending or systemic fungal complications are rare [9, 10]. Persistent *T. beigelii* funguria should, however, alert clinicians to possible urinary tract or systemic infection and should prompt them to investigate for disseminated invasive or deep-seated fungal infections.

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References

Conservative Management of Biliary Obstruction Due to Fasciola hepatica

We report a case of temporary biliary obstruction due to fascioliasis. This case report shows that in Central Europe, fascioliasis is one of the differential diagnoses of abdominal pain, especially if it is associated with eosinophilia. Successful medical treatment is possible even with obstruction of the bile duct.

Fascioliasis (liver fluke disease) is an infrequent infectious disease in Western Europe and the United States. If the diagnosis is established (e.g., by examination of stool or bile), medical treatment is the first choice for management. However, several reports have been published showing that biliary obstruction due to fascioliasis is almost always relieved by surgical intervention. Here we report a case of liver fluke disease with biliary obstruction that occurred in Germany, for which conservative medical treatment rather than surgery was attempted.

In October 1998, a 43-year-old woman presented to the outpatient department of our institution because of the recent onset of pain in the right upper abdominal quadrant and bouts of nausea 1–3 times a week, lasting for up to several hours each time. She did not have fever, diarrhea, or vomiting. The patient worked as a cleaning person in a hospital in Munich and had traveled during the previous 3 years only to Turkey, her homeland, where she stayed for several weeks with her family in a big city (Antalya) 2 months before her admission. None of her family members or friends had similar symptoms. She had no history of other diseases and did not take any medication.

On physical examination the patient was found to be obese but otherwise normal, and eosinophilia was the only laboratory abnormality detected. Stool examination for ova and parasites was repeatedly negative. Ultrasonographic examination of the abdomen showed some hepatic enlargement.

On 4 January 1999, she experienced severe abdominal pain, nausea, and fever and was admitted to our hospital. On admission she was in mild discomfort, but no jaundice, chills, or sweats were noted. Her temperature was 38.8°C, her pulse was 88 beats/min, and her respirations were 20 breaths/min. Her blood pressure was 170/100 mm Hg. The right upper abdominal quadrant was painful on palpation, and the liver edge descended 4 cm below the right costal margin, with a liver span of 15 cm.

Laboratory tests were performed (table 1). The levels of hemoglobin, platelets, glucose, electrolytes, creatinine, blood urea nitrogen, serum protein, lipase, amylase, and creatinine kinase were normal, as were the prothrombin and partial thromboplastin times and the urinalysis results. Microscopic examination of stool samples for ova and parasites was negative. Two blood cultures did not grow any organisms. Findings of electrocardiography, chest and abdominal radiography, and gastroscopy were normal.

Ultrasonography revealed that the common bile duct was dilated to 15 mm in its proximal portion, with a normal width in the distal portion. No gallstones were detected. A hypoechogenic structure (10 mm) was seen at the transition between the normal and the dilated portion. The patient received fluids and ceftriaxone iv because of suspected cholangitis. A CT scan performed on the second hospital day showed a dilated biliary system, 2 hypodense structures within the liver, and a hyperdense structure in the distal ductus choledochus (figure 1).

On the fourth hospital day, endoscopic retrograde cholangiopancreatographic examination demonstrated an impassable stenosis in the distal ductus choledochus. A malignant tumor was suspected and an operative approach discussed. A percutaneous transhepatic cholangio-drainage procedure was performed. Again, a concentric stenosis was found. At that time an infectious disease consultation led to the differential diagnosis of fascioliasis.

Microscopic evaluation of the bile fluid revealed eggs of Fasciola hepatica, which established the diagnosis of fascioliasis (liver fluke disease). Meanwhile, results of serological testing for F. hepatica were received and showed strongly positive antibody titers (table 1).

A second abdominal ultrasonograph revealed a hyperecho- genous structure (18 × 5 mm), possibly the adult worm, within the gallbladder. To avoid surgical intervention, medical treatment was tried. Triclabendazole (Egaten, a nonregistered compound, obtained as a kind gift from Novartis Pharma AG [Nyon, Switzerland]) was given orally once to the patient (10 mg/kg) after informed consent had been obtained on the basis of compassionate drug use.

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