Localized Renal Pelvic Fungal Ball in a Patient Undergoing Bone Marrow Transplantation

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In patients with prolonged neutropenia, candidiasis is well described. It usually presents as candidemia or shortly after neutrophil recovery as hepatosplenic abscesses. 'Fungal ball' arising in renal pelvis has been described in the literature [1-3], especially in neonates [4, 5]. Its pathogenesis is not well understood. We would like to report the first case of renal pelvic fungal ball with obstructive uro-pathy in a patient undergoing autologous bone marrow transplantation. The sequence of events could also give some clues to the mechanism of this rare infection.

A 61-year-old Caucasian female was diagnosed with stage IV follicular small cleaved, follicular center cell malignant lymphoma (Lukes-Collin classification) and bone marrow involvement in 1986. She had no history of renal stones. She was treated successfully with chlorambucil and later by vincristine, cyclophosphamide and prednisone. In November 1990 her disease transformed to a higher grade, i.e. diffuse mixed small and large cell lymphoma. Chemotherapy was changed to adriamycin, etoposide, vincristine and prednisone with good initial response. However, in February 1991, the disease progressed and she received two cycles of decadron, high-dose ara-c and cisplatin (DHAP) leading to nearly complete response. Peripheral stem cells were harvested during the neutrophil recovery period after each cycle of DHAP. Bone marrow which was histologically free of tumor was harvested in May 1991. In June her disease rapidly progressed and she was given two cycles of mitoxantrone, ifosfamide, mesna and etoposide with an almost complete response. In July she received total body irradiation 12 Gy in 8 fractions over 4 days followed by high-dose etoposide 60 mg/kg given over 6 h on day 1, cyclophosphamide 100 mg/kg over 1 h on day -2 with equal dose of mesna over 24 h, and reinfusion of autologous bone marrow and peripheral stem cells on day 0. Oral norfloxacin 400 mg twice daily, acyclovir 200 mg thrice daily and fluconazole 100 mg daily were given prophylactically since admission. She developed severe nausea, mucositis and odynophagia requiring frequent morphine injection. On day 4 after stem cell reinfusion, a vaginal swab grew *Candida albicans* which was treated with topical miconazole. On the same day she spiked a temperature of 38°C. She was treated empirically with ceftazidime and vancomycin and her fever subsided 2 days later. Her urine grew α -hemolytic streptococcus and group D nonenterococcus. Blood cultures were sterile. At about the same time, she also developed urinary retention secondary to

morphine, requiring bladder catheterization. On day 10 the patient began to gain weight, developed ascites, hepatomegaly and elevated bilirubin and alkaline phosphatase; she was treated successfully for clinical veno-occlusive disease with diuretic and methylprednisolone 40 mg per day which was slowly tapered off over the following 3 weeks. On day 18 her absolute neutrophil count (ANC) reached 1,000/mm³ and all antibiotics were stopped. At that time she began complaining of left abdominal and loin pain. Serum blood urea nitrogen and creatinine slowly increased to 25 and 1.9 mg/dl, respectively on day 22. ANC slowly dropped to about 500/mm³. Despite normal body temperature, blood cultures were drawn to rule out septicemia and were all sterile. CT scan of the abdomen and pelvis showed left hydronephrosis with no extrinsic compression from retroperitoneal or pelvic mass. Cystoscopy on day 29 showed only a small patch of erythema in the left posterior bladder mucosa with normal ureteric orifices. Retrograde pyelogram showed a filling defect suggestive of calculus at the pelvic-ureteric junction (fig. 1).

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0001-5792/93/0893-0160

\$ 2.75/0

An attempt to place a left ureteric internal stent was unsuccessful. The patient started to spike a fever of 39 °C on the night after cystoscopy. Blood and urine cultures were sent and she was started empirically on aztreonam for suspected bacterial infection. Ultrasound study 2 days later showed dilated left hydronephrosis and hydroureter suggesting downward migration of the 'calculus'. A few hours later, the patient passed a 'stone' which was tan-colored and friable measuring approximately 1.5 × 1.2 × 0.8 cm and microscopically consisted predominately of pseudohyphae and yeasts (fig. 2). Blood and urine cultures sent on the night of cystoscopy both grew *C. albicans*. The patient was given amphotericin B for 3 weeks (total dose 1 g) followed by fluconazole for 2 weeks. GM-CSF was also given on day 34 (ANC 400) for 18 days which led to sustained neutrophil recovery (ANC > 1,000). The patient defervesced shortly after initiating amphotericin B, her loin and abdominal pain completely resolved and hydronephrosis and hydroureter were no longer seen on repeated ultrasound studies. Repeated blood cultures were negative. Urine culture remained positive for *Candida* until about 1 week after starting amphotericin B. The patient recuperated gradually and was discharged on day 60 after transplantation.

Fungal involvement of the kidneys were seen in postmortem examination in about 50-85% of patients who died from disseminated candidiasis [6,7]. They most commonly result from hematogenous dissemination such as infected central venous line. Renal blood flow, which accounts for about 25% of the cardiac output, leads to an early and heavy inoculation by the yeasts. On the contrary, lower urinary tract fungal infections were most commonly caused by

urinary instrumentation. Our patient developed a rare form of kidney fungal infection, i.e. fungal ball in the renal pelvis with obstructive uropathy. In this case, it is possible that the fungal infection developed retrogradely. She had vaginal candidiasis together with urinary retention which was caused by morphine toxicity. Bladder catheterization probably introduced *Candida* into the bladder and subsequently into the ureter. Hematogenous spread occurred subsequently since she became febrile with positive blood cultures only after cystoscopy. The treatment with steroid may have increased her risk for systemic candidiasis. Patients with obstructing fungal ball in the renal pelvis generally require intervention in the form of ureteral stent, nephrostomy drainage and/or percutaneous extraction of the fungal ball. This patient was unusual in that she passed the fungal ball and the obstruction resolved without drainage [2, 8-10]. It was possible that the cystoscopic and ureteric manipulation had facilitated the

Fig. 1. Retrograde pyelogram showing left proximal ureteric obstruction and left hydronephrosis by a 'calculus'.

Fig. 2. Fungal ball. HE.

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downward migration of the fungal ball. Prophylactic flu- Urinary catheterization should probably be avoided asconazole apparently did not protect our patient from Can- much as possible during recovery from bone marrowdida infection. transplantation.

In patients who develop renal 'stone'-like symptoms after bone marrow transplantation, one should suspect the development of fungal ball even if the patient is afebrile.

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