Cutaneous aspergillosis with fatal dissemination in a renal transplant recipient

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Aspergillosis is an extremely serious complication in immunosuppressed patients, particularly renal allograft recipients, who are treated with drugs that significantly alter immunologic responses and are therefore more prone to bacterial, viral and fungal infections. We report an unusual case of fatal aspergillosis infection in a renal allograft recipient. The primary site of colonization and subsequent invasion was a wound that became purulent following reconstruction of an arteriovenous fistula site. At autopsy systemic spread from the primary site was confirmed.

Case report
Clinical course

The nephrotic syndrome developed in a 30-year-old man in 1967, and a renal biopsy revealed advanced chronic glomerulonephritis. Prednisone therapy was given from 1968 until 1976 without improvement in either proteinuria or renal function. Dialysis was eventually required, but his general status remained poor for a person of his age with uremia.

After 10 months of dialysis the patient was admitted to hospital to receive a cadaveric renal allograft. Dialysis was necessary following the operation and for the next 30 days because of acute tubular necrosis associated later with acute cellular rejection (Fig. 1). Immunosuppressive therapy was begun with the oral administration of azathioprine and prednisone. Cyclophosphamide and methyprednisolone were infused intravenously on five occasions, and antilymphocyte globulin (Pressimmune; Hoehst Canada Inc., pharmaceutical division, Montreal), 2 g/d, was given intravenously for 5 days.

A moderate reduction in the leukocyte count (to between 1.9 and 4.5 × 10^9/l) appeared 17 days after transplantation and lasted 20 days. At the same time, the site of a recently evacuated hematoma surrounding an arteriovenous fistula on the left wrist showed marked purulent inflammation. On the 22nd day after transplantation Aspergillus fumigatus was grown in pure culture from a biopsy specimen of this site, which by then was covered with necrotic tissue (Fig. 2). Light microscopy of a specimen of the lesion revealed superficial dermal hyphae.

Topical treatment was attempted with Dakin’s (sodium hypochlorite) solution, but the left forearm showed progressive cellulitis. Repeated cultures of pus and blood failed to grow bacteria, but cloxacillin was administered as a prophylactic measure. As well, two doses of gentamicin were given. Amphotericin B ointment was applied and the surrounding edema gradually resolved. However, cellulitis appeared distally on the back of the hand, necessitating repeated surgical drainage. Multiple cultures of copious pus from these areas grew only A. fumigatus. In the meantime the fistula site had become clean and dry, with healthy granulation tissue. Improvement coincided with the discontinuing of

FIG. 1—Patient’s course after renal allograft transplantation.

FIG. 2—Sutured fistula site covered with dark-green necrotic tissue on left wrist on 22nd day after transplantation. Microscopic examination of biopsy specimen confirmed mycotic infection of skin.
the immnosuppressive drugs except for prednisone, which was given in 30-mg doses on alternate days.

On the 55th day after transplantation a high fever accompanied by an elevated leukocyte count (26 × 10^9/l) developed. Three days later the prednisone therapy was stopped because a roentgenogram of the hand revealed diffuse carpal osteopenia and proximal metacarpal involvement suggestive of osteomyelitis. Grossly, however, the hand and fistula site seemed to have healed properly. Chest roentgenograms taken at regular intervals during the entire course of the disease were always normal.

Then, on the 60th day after transplantation the patient had a left-sided seizure and complained of right visual field loss and severe headache. Computerized axial tomography of the brain showed a left occipitotemporal hematoma and a right parietal cortical abscess with a thick capsule (Fig. 3).

The patient became increasingly confused and had more seizures. Because craniotomy to rule out a bacterial abscess was judged to be too risky, therapy with dexamethasone, chloramphenicol, penicillin and anticonvulsants was started. As an ancillary measure hemodialysis was instituted although the allograft had maintained stable but poor function (the creatinine clearance was 10 to 15 ml/min). After 10 days of therapy the patient showed marked clinical improvement, but on the 78th day after transplantation he had a generalized seizure and died.

Autopsy findings

Autopsy showed osteomyelitis of the left hand, with hyphal elements in areas of bone resorption. The valves of the heart were normal, but hyphal invasion was found in the myocardium, in the papillary muscles and in thrombi of two main coronary vessels. The lungs were free of infection. Hyphae were also found in the spleen, the grafted kidney and two focal areas of the colon. Multiple punctate lesions were visible on the surface of both cerebral hemispheres and the cerebellum. With sectioning, similar lesions were found throughout the brain substance; Grocott's stain showed that many of them contained branched, partially septic hyphae. The brain stem was normal. The left parietal cortex was hemorrhagic, necrotic and amputated. The right hemisphere contained a lesion 2.5 × 1.0 cm with a discrete border; a blood vessel near the cortical margin was eroded and contained abundant fungal elements. Death was attributed to extensive destructive brain infection.

Discussion

Disseminated aspergillosis in immunocompromised hosts has been extensively reviewed. It is a rare but dreaded complication of immunosuppressive therapy in renal transplant recipients. Aspergillus skin infection as a primary lesion is extremely uncommon, and to our knowledge this case is the first one reported in a renal transplant recipient. At least 10 cases of primary skin infection due to Aspergillus are reported in the medical literature; the five responsible species were *A. fumigatus*, *A. niger*, *A. flavus*, *A. glaucus* and *A. terreus*. Six of the infections developed in patients with severe hematologic disorders, such as leukemia and aplastic anemia; the course was usually fulminating, death frequently occurring from systemic spread within a few days. Four other cases in otherwise healthy individuals were easily managed with incision, topical nystatin therapy, copper sulfate therapy or no treatment at all.

Initially our patient's infection appeared to be localized and improving. However, it disseminated, as is seen in patients with leukopenia from hematologic disorders. Parenteral amphotericin B therapy was withheld for the following reasons: (a) the infection was thought to be responding well to local therapy; (b) in the absence of pulmonary involvement, dissemination only became apparent terminally; (c) the results of therapy for disseminated aspergillosis with intravenously administered amphotericin B have been poor; and (d) survival of the allograft was deemed essential to this patient because his response to dialysis in the past had been poor.

Uremic patients are immnosuppressed, and when they receive a renal transplant the therapy for rejection episodes, even without leukopenia, places them at high risk for infection. The susceptibility to opportunistic infection may be enhanced by the use of antilymphocyte globulin and perhaps by prophylactic topical antibiotic therapy, as recommended by some authors (cephalothoin powder was applied in this case during the hemotoma evacuation on the 17th day after transplantation).

Aspergillus usually enters the body as airborne spores that are inhaled. Systemic spread nearly always starts from a pulmonary focus. Primary skin invasion is unusual and typically starts at a needle puncture site or a wound.

![FIG. 3—Left occipitotemporal hematoma (black arrow) and encapsulated right parietal cortical abscess (white arrow) that proved to be myotic at autopsy, demonstrated by computerized axial tomography.](image-url)
dressing site. The lesion in our patient represented colonization and infection of an open wound in an immunocompromised host. Systemic spread only became evident more than a month after invasion of the skin.

Conclusion

Cutaneous infection with *Aspergillus* may occur in transplant recipients; when it is found, extensive dissection with débridement and parenteral amphotericin B therapy are warranted. Our case was interesting in that dissemination occurred from a skin lesion and the lungs were spared.

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References


Cas de leuconychie modifié à la suite d'une intervention chirurgicale et revue des leuconychies

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Le propos de cet article est de rapporter un cas de leuconychie totale acquise, disparue temporairement à la main gauche à la suite d'un traumatisme et d'une greffe cutanée pratiquée à ce niveau. Nous proposons une hypothèse neurovasculaire susceptible d'expliquer la disparition de la coloration unguéale blanche.

Histoire de cas

Un homme de 19 ans se présente à l'urgence de notre hôpital après un accident au cours duquel sa main gauche a été écrasée dans une presse d'imprimerie. Il présente alors une plaie bénigne au niveau de la paume de la main gauche et un lambeau cutané attaché aux tissus sous-jacents par ses portions digitales et latérales. Outre sa plaie traumatique on est également frappé par une leuconychie totale des ongles des deux mains et des deux pieds; cette leuconychie aurait débuté 4 ans auparavant. L'examen révèle aussi des taches blanches au niveau des incisives qui seraient ap-