Aspergillus fumigatus Epidural Abscess in a Renal Transplant Recipient

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An epidural abscess caused by Aspergillus fumigatus occurred in a recipient of a cadaveric, renal allograft. The patient had persistent back pain and peripheral neuropathy that involved the lower extremities. Signs of spinal cord compression evolved, and the diagnosis was made using histologic examination and culture of a sputum specimen. Therapy, consisting of progressive surgical debridement and intravenous amphotericin B and oral flucytosine, was unsuccessful in eradicating the organism. At postmortem examination, Aspergillus was identified at the abscess site. Our knowledge, aspergillosis presenting as an epidural abscess in the immunosuppressed, renal transplant recipient has not previously been reported and should be considered in the differential diagnosis of back pain and peripheral neuropathy in such a patient.

REPORT OF A CASE

In June 1975, a 49-year-old man with chronic renal failure received a cadaveric kidney from a HLA identical donor. Epidural anesthesia and a standard protocol for immunosuppressive therapy were used. The protocol consisted of azathoprine, 200 mg prior to transplantation, followed by a daily maintenance dose of 2 to 3 mg/kg, and methylprednisolone, 30 mg/kg given intravenously 30 minutes prior to transplantation, followed by a regimen of 4 mg/kg/day orally. Methylprednisolone dosage was reduced every four days until a dosage of 1 mg/kg/day was attained.

The posttransplantation course was complicated by acute cellular rejection, which was treated with intravenous methylprednisolone, hemodialysis, pneumonia, and intermittent leukopenia. These problems resolved, and the patient's renal function improved. He was discharged on the 52nd postoperative day with a serum creatinine value of 1.6 mg/100 ml and creatinine clearance of 45 ml/min. His medications included 100 mg/day of azathioprine and 60 mg/day of methylprednisolone.

During the next three months, the patient experienced two more episodes of acute cellular rejection; each was treated with high-dose intravenous methylprednisolone.

Five months after transplantation, the patient developed severe, left flank pain that was not related to trauma or associated with fever. Progressive, generalized weakness, fatigue, decreased appetite, and weight loss were also noted. The patient was rehospitalized.

Results of physical examination revealed an afibrile, cachectic man. His blood pressure was 140/80 mm Hg, pulse rate was 80 beats per minute, and respirations were 16/min. Examination of the lungs revealed scattered rhonchi. The heart and abdomen were unremarkable. The vertebral processes were not tender to percussion. Generalized muscle wasting, with atrophy of the orbicularis oculi, neck extensor, hip flexor, and hip extensor muscle groups, was evident. In addition, weakness of the orbicularis oculi, neck extensor, hip flexor, and hip extensor muscle groups was noted.

Results of sensory examination revealed decreased proprioception and vibratory sensation in the lower extremities. Cerebellar function was normal. Muscle-stretch reflexes were absent at the ankles but otherwise were normal and symmetrical. Extensor toe signs were not elicited.

Results of laboratory examination included a peripheral WBC count of 3,000/cu mm with 90% neutrophils, a serum creatinine value of 2.8 mg/100 ml, and a creatinine clearance of 24 ml/min. Lumbar puncture revealed clear fluid with a glucose level of 50 mg/100 ml (with a simultaneous serum glucose level of 151 mg/100 ml), a protein level of 414 mg/100 ml, and no cells. No evidence of bacteria, fungi, or acid-fast organisms were found on stain or culture. The remainder of the laboratory data was unremarkable. Roentgenograms of the chest and lumbar-sacral spine, including views of the pedicles, were normal. Tomograms of the spine were not done. An electromyogram demonstrated findings compatible with a peripheral neuropathy.

Azathioprine was discontinued and methylprednisolone was decreased to physiologic levels. The patient's condition remained stable until the fifth hospital day, when his temperature rose to 38.8 C. Urinary incontinence developed. Perfusion tenderness was noted over the tenth thoracic vertebra. A myelogram demonstrated a mass compressing the spinal cord at the level of the ninth and tenth thoracic vertebrae. Laminectomy revealed an epidural abscess extending from the eighth to the tenth thoracic vertebrae and compressing the underlying spinal cord. Involvement of the vertebral bone was not noted. A hematoxylin-eosin stain of the abscess...
revealed branching, septate organisms that resembled Aspergillus. Subsequently, A. fumigatus was identified by culture. The spinal cord was decompressed, and a regimen of amphotericin B was started. A dosage of 50 mg every other day was rapidly achieved. The minimum inhibitory concentration (MIC) was 6 \( \mu g/ml \). Flucytosine, administered at doses that were adjusted for renal impairment, was also given but was discontinued after ten days because of notable leukopenia. The MIC of flucytosine was greater than 250 \( \mu g/ml \).

Postoperatively, the neurologic deficit did not improve. Marked diarrhea developed; weight loss and debility continued. Massive gastrointestinal hemorrhage from multiple esophageal and gastric erosions resulted in the patient's death on the 55th hospital day. A total of 1,092 mg of amphotericin B had been given.

Results of postmortem examination revealed a thickening of the dura mater, which was 4 cm in length at the area of the ninth and tenth thoracic vertebrae, and which extended into the subarachnoid space. Microscopical examination revealed a granulomatous process that consisted of necrotic tissue and numerous branching, septate hyphae, which were identified morphologically as Aspergillus. Cultures of this area were not performed. The vertebral bone and underlying neural tissue showed evidence of fungal invasion and necrosis. The remainder of the postmortem examination failed to reveal Aspergillus, although chronic pneumonitis, necrotizing ulcerations of the esophagus and stomach, and chronic allograft rejection were found.

**COMMENT**

Central nervous system involvement may occur in patients with aspergillosis; however, reports of patients with epidural abscesses are extremely uncommon. \(^1\) \(^2\) These patients have had grossly normal immunologic defense mechanisms, although one was being treated with corticosteroids. \(^3\) To our knowledge, this is the first report of an epidural abscess occurring as the initial manifestation of aspergillosis in an immunosuppressed, renal transplant recipient.

Several factors associated with increased risk of developing fungal infections have been previously identified. As this course progressed, our patient was exposed to three of these factors: (1) treatment with immunosuppressive agents, \(^4\) \(^5\) \(^6\) (2) broad-spectrum antibiotic therapy, \(^7\) \(^8\) (3) acute transplant rejection and treatment with repeated courses of high-dose intravenous corticosteroids. \(^9\)

An unusual aspect of this case is the lack of an identifiable portal of entry for the organism. Primary pulmonary or gastrointestinal focus with subsequent local or hematogenous spread is the most frequent route of dissemination. \(^1\) \(^2\) \(^3\) Infection of the paranasal sinuses, mastoid air cells, external auditory canal, eye, and skin may also result in disseminated disease. \(^1\) \(^2\) \(^3\) \(^4\) \(^5\) \(^6\)

Although antemortem and postmortem examination failed to reveal infection of these areas, it is possible that a small primary focus had been present. Iatrogenic implantation, with development of a cervical epidural abscess, after repeated intralumbar injections of penicillin has been reported. \(^6\) Our patient received epidural anesthesia during transplantation and may have been infected at that time. It is also remotely possible that the organism may have been introduced during a dialytic procedure or through an indwelling intravenous catheter.

This case demonstrates several of the difficulties involved in confirming the diagnosis of aspergillosis in the immunosuppressed host. Cultures of blood, sputum, and the gastrointestinal tract are rarely positive. \(^1\) \(^2\) \(^3\) \(^4\) \(^5\) \(^6\) \(^7\) \(^8\) \(^9\) \(^10\) Aspergillus is infrequently isolated, and laboratory contamination by airborne spores is well recognized. \(^1\) \(^2\) \(^3\) \(^4\) \(^5\) \(^6\) \(^7\) \(^8\) \(^9\) \(^10\) As demonstrated in this case, routine analysis of CSF is usually not diagnostic. Smears and cultures are rarely positive, even if meningitis is present. \(^1\) \(^2\) \(^3\) \(^4\) \(^5\) \(^6\) \(^7\) \(^8\) \(^9\) \(^10\) Results of serologic testing for circulating antibodies in immunosuppressed patients with widespread aspergillosis vary. \(^1\) \(^2\) \(^3\) \(^4\) \(^5\) \(^6\) \(^7\) \(^8\) \(^9\) \(^10\) The most reliable method of diagnosis remains biopsy with histologic examination and culture. Therapy in the present case consisted of discontinuation of immunosuppressive medications, surgical debridement, intravenous amphotericin B, and a short course of flucytosine. Amphotericin B is useful in treating systemic aspergillosis in immunosuppressed renal transplant recipients. \(^3\) In vitro synergy with flucytosine has been demonstrated. \(^1\) \(^2\) It is possible that if amphotericin B was given for a longer period, either alone or in combination with flucytosine, therapy might have been more successful.

In conclusion, this case describes an occurrence of aspergillosis in the immunosuppressed renal transplant recipient such as has not been previously reported. Epidural abscesses caused by Aspergillus should be considered in the differential diagnosis of back pain and peripheral neuropathy in such patients. This may be extended to include the entire diverse group of immunosuppressed patients.

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**Nonproprietary Names and Trademarks of Drugs**

Amphotericin B—Fungizone.

Azathioprine—Imuran.

Flucytosine—Ancobon.

**References**


