**Aspergillus fumigatus Infection of a Biloma**

**Sir**—We describe a patient with an unusual biliary tract infection caused by *Aspergillus fumigatus* localized in a biloma that was a complication of orthotopic liver transplantation. A 44-year-old male with cirrhosis secondary to alcoholism and hepatitis C underwent orthotopic liver transplantation. He was given immunosuppressive therapy with OKT3, azathioprine, cyclosporine, and steroids. Culture of a specimen obtained from the biliary T tube drainage on day 17 after transplantation yielded *Aspergillus* species. Therapy with itraconazole (200 mg po q.d.) was started. The patient was discharged from the hospital in good condition on day 41 after transplantation.

The patient was readmitted to the hospital on day 54 after transplantation with abdominal discomfort, fever (temperature to 39°C), and chills and rigors of 5 days’ duration. On physical examination he was not in acute distress. Icterus and pallor were noted. The abdomen was distended, and there was tenderness and fullness in the right upper and lower quadrants; however, Murphy’s sign and peritoneal signs were not evident. The surgical incision site and the T tube site were clean. Laboratory tests performed on admission revealed the following values: hematocrit, 19%; WBC count, 5.5 × 10⁹/L (84% polymorphonuclear leukocytes, no band forms); total bilirubin, 34 μmol/L; alkaline phosphatase, 388 IU/L (normal range, 35–117 IU/L); alanine aminotransferase, 57 IU/L (normal range, 5–25 IU/L); and aspartate aminotransferase, 61 IU/L (normal range, 5–35 IU/L). The platelet count, coagulation parameters, and levels of amylase were normal; the level of serum creatinine was at the patient’s baseline. A chest roentgenogram did not reveal any abnormalities.

An abdominal CT scan showed a collection of bile (20 × 13 × 13 cm) abutting the right lobe of the liver (figure 1). Under CT guidance, 700 mL of biliious fluid was drained; the catheter was left in place for further drainage. Gram staining of the fluid showed few neutrophils and no organisms. Culture of the original specimen and three subsequently drained specimens yielded *A. fumigatus*. Cultures of fluid drained from the original T tube also yielded *Aspergillus* species. Endoscopic retrograde cholangiopancreatography was subsequently performed, and this procedure revealed a bile leak with stricture of the common bile duct and proximal dilatation. A stent was placed for decompression. The abdominal pain decreased, but the patient continued to have high fevers while he was receiving therapy with ampicillin/sulbactam, amphotericin B (0.7 mg/kg·d), and empirical ganciclovir.

On day 59 after transplantation, exploratory laparotomy was performed; this procedure revealed a large cavity that was being filled with bile from a tear in the distal common bile duct, probably at the exit site of the original T tube. There was no gross vascular or hepatic invasion. The collection was drained, and choledochojunostomy was performed. Culture of fluid on swabs sampled from the collection intraoperatively also yielded *A. fumigatus*. Two Jackson-Pratt drains were placed, and drainage over several days yielded *Aspergillus* species. Therapy with ampicillin/sulbactam was discontinued. The patient continued to feel better but did not defervesce for another 10 days. A repeated abdominal CT scan showed resolution of the biloma. A cholangiogram showed no further leak. As the patient’s renal function worsened (peak creatinine level, 240 μmol/L), amphotericin B therapy (total dose, 2 g) was given on alternate days; this therapy was followed by oral itraconazole (100 mg q.d.). The patient has done well for more than a year. The *A. fumigatus* isolate was susceptible to both itraconazole (MIC, 0.035 μg/mL at 48 and 72 hours; minimum lethal concentration, 0.035 μg/mL at 48 hours and 0.3 μg/mL at 72 hours) and amphotericin B (MIC, 0.29 μg/mL at 48 and 72 hours; minimum lethal concentration, 0.29 μg/mL at 48 hours and 0.58 μg/mL at 72 hours).

Aspergillus infections of the hepatobiliary system are rare. In a series of 98 patients with aspergillosis, 12 patients had hepatomegaly [1]. Two cases of Budd-Chiari syndrome secondary to infection with *Aspergillus* species [2] and a few cases of hepatosplenic aspergillosis have been documented [3]. Localized wound infections [4] and peritoneal involvement (in patients with widely disseminated disease) [5] have been noted in liver transplant recipients.

Our patient had a common bile duct leak that resulted in a biloma. Multiple cultures of specimens from the collection (including cultures of specimens taken during operative drainage) and from the biliary tree yielded *A. fumigatus*. Local infection could have contributed to duct rupture, although unnoticed dislodgment of the T tube is more likely. In a series of 393 liver transplants, biliary leakage occurred in 25, and patients who had leaks that occurred at a T tube exit site had no symptoms or minimal symptoms; no fungal infection was seen in any of the transplant recipients, and, typically, the leak was stopped by

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simple drainage or closure [6]. Our patient had significant abdominal pain and high fevers. The presence of *Aspergillus* species in the biliary tree and in the biloma was abnormal and surprising. Bacterial pathogens and *Candida* have been implicated in similar presentations [7]. The patient responded clinically to antifungal treatment. There was no evidence of invasive disease, and there were no extrabiliary sites of infection.

In our patient’s case, *Aspergillus* was probably introduced in the biliary tree at the time of transplantation or subsequently through the T tube. The classic route of entry for this fungus is inhalation of airborne spores. In transplant recipients, direct inoculation of surgical sites accounts for prothetic valve endocarditis and endophthalmitis following cataract surgery and may account for local wound infections. In a series of four liver transplant recipients whose abdominal wound cultures were positive, two had local invasive disease [4]. Thus, isolation of *Aspergillus* species from wound drainage should not be ignored. In comparison with other organ recipients, hepatic allograft recipients are at excessive risk for invasive aspergillosis [4]. It is unknown whether untreated wound infection can result in severe invasive disease or hematogenous dissemination.

There was no previous experience in the literature to guide our therapeutic decisions in the case described herein. The initial failure of itraconazole to eradicate *Aspergillus* species is notable. Itraconazole has good activity against *Aspergillus* species [8] and achieves good biliary concentrations. However, even with retrospectively favorable in vitro susceptibility results, tissue penetration and in vivo activity are unpredictable in atypical cases. In our case, the size of the biloma and the presence of a foreign body (T tube) may have compounded drug efficacy and required a combined aggressive medical and surgical therapeutic approach.

**Crohn’s Disease Complicated by Meningitis and Spinal Epidural Abscess**

Sir—We report a case of Crohn’s disease complicated by meningitis, epidural abscess, and sacral osteomyelitis.

A 33-year-old woman with a history of Crohn’s disease was transferred to our hospital for evaluation of fever, headache, and altered mental status. Crohn’s disease had been diagnosed 4 years earlier when she presented to the hospital with severe low-back and abdominal pain; at that time she also reported a recent 20-lb weight loss. She was treated intermittently with prednisone and azulfidine. Five months before transfer to our hospital her back pain had recurred, and her erythrocyte sedimentation rate had risen to 50 mm/h. This exacerbation of symptoms was somewhat diminished by increasing the dose of prednisone to 20 mg/d. Back and right-lower-quadrant pain, which was relieved by bowel movements, continued.

One week before admission to our hospital, the patient was evaluated at another hospital for severe right sacroiliac pain, fever, nausea, and vomiting. An abdominal ultrasonogram demonstrated a right ovarian cyst and a small amount of pelvic fluid. The patient responded to therapy with intravenous methylprednisolone and metronidazole, and she was discharged.

Four days later she developed a headache, and within hours she had become delirious and combative. At an outside emergency department she was found to be febrile and to have a WBC count of 31.8 × 10⁹/L. She was given one dose of imipenem and transferred to our hospital.

After administration of 2 g of ceftriaxone, a computed tomodogram of the patient’s head was obtained that showed no abnormalities. At that time a lumbar puncture was performed. Analysis of CSF revealed a WBC count of 16.1 × 10⁶/L (99% polymorphonuclear leukocytes), a protein level of 6.37 g/L, and a glucose concentration of <1.1 mmol/L. Gram staining showed sheets of polymorphonuclear cells but no bacteria. A latex agglutination test for bacterial antigens was negative.

Therapy with ceftriaxone was continued and ampicillin and nafcillin were added to the regimen. Because of concern for a parameningeal focus of infection, MRI of the spine was performed. The image showed loops of bowel adherent to the presacral fascia, a small epidural abscess with extension through the

**References**