Absidia corymbifera Infections in Neonates

Sanjiv B. Amin, Rita M. Ryan, Leon A. Metlay, and Wendy J. Watson

We report the first two documented cases of neonatal zygomycosis caused by *Absidia corymbifera*. A premature infant developed disseminated disease from a cutaneous site with pulmonary, gastrointestinal, and cerebral involvement. The infant died despite amphotericin B therapy and surgical debridement. The second case occurred in a full-term infant with congenital heart disease and fungal pneumonitis. Zygomycosis was not suspected because of underlying cardiac disease and a complicated postoperative course, and this infant also died. *Absidia* joins a growing list of opportunistic fungal pathogens of the compromised neonate.

Case Reports

Case 1

A 1,500-g female infant was born precipitously in the emergency department at 31 weeks’ gestation. During the first few hours of life, she was mechanically ventilated and given a dopamine infusion because of hypotension. Therapy with ampicillin and gentamicin was started empirically. Physical examination revealed that the infant had ambiguous genitalia. By 24 hours of life, blood cultures yielded nontypeable *Haemophilus influenzae*. Ampicillin and gentamicin therapy was discontinued, and the infant was treated with cefotaxime.

On day 4 of life, hydrocortisone therapy (25 mg/[m²·d]; twice the maintenance dosage) for congenital adrenal hyperplasia was started. The patient’s condition appeared to be stable, and the umbilical arterial catheter was removed on day 11 of life. On the same day, a small sharply demarcated necrotic lesion in the periumbilical area was noted. Blood specimens for culture were obtained, and nafcillin therapy was started. On day 14 of life, because of the increasing size of the periumbilical eschar, the lesion was debrided, and tissue biopsy specimens of the lesion were cultured for bacteria and fungi. Gram staining of the necrotic material revealed hyphae, and amphotericin B therapy (0.5 mg/[kg·d]) was started. The patient’s condition worsened over the next week; she developed a right lower lobe infiltrate and an ileus.

On day 21 of life the dosage of hydrocortisone therapy was increased to 50 mg/[m²·d], and fludrocortisone treatment was started because of persistent hypotension and hyponatremia. On day 23 of life, a gastrocutaneous fistula in the periumbilical area was noted. The following day, the necrotic abdominal wall was excised, and an ileostomy was created. The patient’s condition continued to deteriorate with persistent hypotension, generalized edema, and renal failure. She died on day 28 of life. Multiple blood cultures were negative, while all biopsy specimen cultures yielded *A. corymbifera*; identification of the organism was performed by the New York State Department of Health Mycology Laboratory (Albany, New York).

Autopsy revealed necrosis and hyphae in the abdomen near the gastric fistula involving sections of the transverse colon (figure 1), ileum, and jejunum. Microscopic examination of the affected bowel demonstrated that the fungal elements were confined to the serosal surfaces (figure 2). Hyphae were also seen in a large hemorrhagic abscess in the right lower lung and multiple cerebral abscesses.

Case 2

A full-term male infant was delivered by elective cesarean section because of breech presentation. Routine antenatal ultrasonography had demonstrated tricuspid atresia. After delivery, echocardiography revealed tricuspid atresia with a hypoplastic right ventricle. On day 2 of life, a modified right Blalock-Taussig shunt was created. Postoperatively, the patient required inotropic support and remained intubated. He developed a right pneumothorax, and over the next 4 days, placement of several chest tubes was required.

On day 8 of life, the Blalock-Taussig shunt was surgically revised. In the immediate postoperative period, the patient de-
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The paper describes the first cases of neonatal zygomycosis with culture-proven A. corymbifera infection. The diverse clinical manifestations of zygomycosis can usually be categorized as rhinocerebral [8, 9], pulmonary [9], disseminated [2, 9], gastrointestinal [1, 2, 9], and cutaneous [5]. Absidia infection also has been described in patients with ocular [6], renal [3], and musculoskeletal [10] disease. Regardless of anatomic site, characteristics include invasion of vessel walls with subsequent infarction and necrosis. Diagnosis of infection often requires biopsy, as the organisms are tissue-bound and seldom grow in blood cultures [4].

Our first case demonstrates the unusual feature of extension of infection from a periumbilical cutaneous catheter site, through the abdominal wall, and into the abdomen that caused a gastrocutaneous fistula. This sequence of events is supported by the presence of hyphae only on the gastrointestinal serosal surfaces (figure 2). This finding is in contrast to other case reports of gastrointestinal zygomycosis secondary to infection with Rhizopus species that demonstrate mucosal involvement, thus implicating a different portal of entry for the spores. In case 2, A. corymbifera was cultured from the chest tube site, and hyphae were identified only in the right chest wall and right lung, again suggesting extension from cutaneous inoculation (in this case the chest tube site). The infant was a full-term neonate without an identified immunodeficiency. Potential risk factors included antibiotic therapy for both patients and corticosteroid therapy in case 1.

A. corymbifera has been identified in soil and decaying vegetation and causes disease in birds and animals [11]. One study [12] demonstrated a seasonal variation in equine titers of antibody to Absidia with peak titers in the early winter months, thus suggesting significant exposure during the autumn. Both of our patients developed disease within 1 month of each other, one in October (case 1) and one in November (case 2), and both developed acute renal failure with generalized edema. On day 9 of life, he developed a right basilar pleural effusion that resolved after placement of a chest tube and drainage.

On day 10 of life, the patient had evidence of excessive pulmonary blood flow, and an attempt was made to surgically narrow the central shunt. His medications at this time included dopamine, digoxin, furosemide, and vancomycin. Multiple blood specimens for culture that were obtained throughout the hospital course were negative. On day 21 of life, the infant developed renal failure, hypotension, and coagulopathy. On day 25 of life, inotropic and ventilatory support was stopped after consultation with the family. The infant died on the same day. A culture of serosanguineous discharge from the chest tube site that was obtained shortly before death yielded A. corymbifera; identification of the organism was confirmed by the New York State Department of Health Mycology Laboratory.

Autopsy revealed multiple thrombi containing nonseptate hyphae in the small branches of the pulmonary arteries and throughout the right lung. Hyphae were also found in the bronchi with extension into alveolar spaces, findings consistent with fungal pneumonitis. Macroscopically, the chest tube site was unremarkable, while microscopic examination of the skin near the chest tube site on the right chest wall revealed nonseptate hyphae.

Discussion

Zygomycosis occurs predominantly in immunocompromised hosts [1–6]; premature infants may also be at particular risk for this disease [7]. The most common organism identified in neonatal zygomycosis is Rhizopus, which has been described in numerous case reports [1, 2, 5]. To our knowledge, this
patients were initially admitted to the intensive care nursery. However, one patient (case 2) spent only a few hours in the nursery before undergoing surgery and was subsequently cared for in the pediatric intensive care unit on a different floor. Approximately 6 weeks elapsed before the fungi were identified in both cases; in the interim, no further cases were noted, and no formal investigation was performed. Since that time, no subsequent cases of absidia zygomycosis have been identified in children or adults in our institution.

In most cases of zygomycosis, the source is not identified; however, in certain cases, environmental factors have been implicated, including ongoing construction, air-conditioning filters, elastic bandages, and wooden tongue depressors [13–15]. Because our patients had evidence of inoculation from different sites (umbilical arterial catheter in case 1 vs. chest tube placement in case 2) in different parts of the hospital, it is unlikely that a single fomite was the source, and even though construction was occurring on other floors, there was no construction in the vicinity of either intensive care unit. It appears most likely that the patients were exposed to airborne spores in a season when these spores were more prevalent, the spores were inoculated through the skin, and infection was able to progress given the debilitated state of the patients. Further identification of neonatal cases will help delineate the epidemiology and important characteristics of absidia zygomycosis.

Treatment of zygomycosis involves surgical debridement and appropriate antifungal therapy. Specific identification of the organism in cases of zygomycosis may not be routinely done. However, recent data on in vitro antifungal susceptibility showed that MICs of agents differed for the various genera of Zygomycetes [16, 17]; all members of the genera *Mucor* and *Rhizopus* were resistant to azoles (itraconazole, ketoconazole, and clotrimazole) with MICs of 25 to 100 mg/L, while isolates of the genus *Absidia* were sensitive to azoles with MICs of 0.045 to 0.19 mg/L. All three genera were susceptible to amphotericin B and resistant to flucytosine and natifine. This information has yet to be studied clinically, but it emphasizes the importance of genus identification and suggests that there may be wider options for treatment of patients with absidia zygomycosis.

Early recognition is critical for the timely institution of appropriate treatment of zygomycosis. The previously reported mortality rates associated with neonatal zygomycosis due to *Rhizopus* species are very high [1]. Our experience with absidia infection in the neonatal population suggests that clinical outcome is comparable with that of rhizopus infection. These cases highlight the invasive nature of absidia zygomycosis in infants and the importance of considering fungal disease in a severely ill neonate.

References