

Case Report

Fatal disseminated *Acremonium strictum* infection in a preterm newborn: a very rare cause of neonatal septicaemiaMehmet Yalaz,¹ Suleyha Hilmioglu,² Dilek Metin,² Mete Akisu,¹ Deniz Nart,³ Hasan Cetin,¹ Cengiz Ozturk,¹ Ecmel Isik³ and Nilgun Kultursay¹

Correspondence

Mete Akisu
makisu@med.ege.edu.trDivision of Neonatology, Department of Pediatrics¹, Department of Microbiology and Clinical Microbiology² and Department of Pathology³, Ege University Faculty of Medicine, Izmir, TurkeyReceived 2 December 2002
Accepted 29 April 2003

Species of the genus *Acremonium* (*Cephalosporium*) are opportunistic micro-organisms that are environmentally widespread saprophytes in soil and can, very rarely, be pathogenic in humans. Disseminated infection has been described in patients with immunodeficiency, but has previously been reported in only one neonate. A preterm infant with *Acremonium strictum* fungaemia is reported here. The patient was born at 27 weeks gestation and weighed 870 g at birth. She needed intensive respiratory management and became septic on day 11 of life. Blood and cerebrospinal fluid (CSF) cultures were positive for *A. strictum*. The patient did not respond to therapy with amphotericin B plus fluconazole and died on day 25 of life. The autopsy showed foci due to *A. strictum* in the brain, liver and heart.

Introduction

The genus *Acremonium* (*Cephalosporium*) comprises opportunistic, environmentally widespread soil saprophytes that can occasionally be pathogenic in humans. Disseminated infections have been described in patients with immunodeficiency, as well as in animals (Fincher *et al.*, 1991). In recent years, the number and diversity of infections caused by *Acremonium* species have increased and numerous species have been implicated (Guarro *et al.*, 1997). *Acremonium* species have been reported to be the cause of localized or disseminated infections in patients with predisposing conditions such as Addison's disease, neutropenia, immune suppression and intravenous drug abuse (Fincher *et al.*, 1991; Guarro *et al.*, 1997; Anadolu *et al.*, 2001). However, *Acremonium* fungaemia is extremely rare in the neonatal period. We report a case of invasive infection by *A. strictum* in a prematurely born neonate as, to our knowledge, the second case in the literature.

Case report

The patient, a female who weighed 870 g, was delivered vaginally to a para 1 healthy, 26-year-old mother. She was born following intractable contractions after 27 weeks gestation. Apgar scores were 5 and 7 at 1 and 5 min,

respectively. In the delivery room, the patient was intubated and ventilated mechanically. Thereafter, she was transferred to the neonatal intensive care unit because of prematurity and respiratory distress syndrome (RDS); the chest roentgenogram was suggestive of severe RDS. An umbilical vein catheter was inserted and synchronized intermittent positive pressure ventilation was initiated. Synthetic surfactant (Survanta; Abbott Laboratories) (100 mg kg⁻¹ dose⁻¹) was administered for RDS and the patient was given empirical antibiotic therapy with sultamicilin and amikacin. In addition, surfactant therapy was repeated on the second and sixth days, due to progressive RDS. On admission, haemoglobin was 15.3 g dl⁻¹ and the leukocyte count was 10 × 10⁹ l⁻¹, with a differential count of 62 % polymorphonuclear leukocytes, 30 % lymphocytes, 6 % monocytes and 2 % eosinophils and a platelet count of 229 × 10⁹ l⁻¹. Initial blood culture was negative on admission.

On day 6 of life, the patient (still under mechanical ventilation) began to have bradycardic episodes. Bacteriological studies did not provide any evidence of septicaemia. On the eleventh day, while still receiving sultamicilin and amikacin therapy, the infant appeared to be septicaemic with hypothermia, abdominal distension, a high C-reactive protein (CRP) level (2.9 mg dl⁻¹; N < 0.8 mg dl⁻¹) and thrombocytopenia (87 × 10⁹ l⁻¹). After blood and CSF cultures were obtained, the antibiotic regimen was changed to meropenem (40 mg kg⁻¹ day⁻¹) and amphotericin B lipid complex (ABLC) at 0.5 mg kg⁻¹ day⁻¹, escalated daily up to 1 mg kg⁻¹. Both the blood and CSF cultures were positive for *A. strictum*. The umbilical vein catheter was removed, although

Abbreviations: CSF, cerebrospinal fluid; RDS, respiratory distress syndrome.

A photograph showing *A. strictum* colonies from haemoculture is available as supplementary material in JMM Online.

blood culture from the catheter was negative. Cultures from the perineum, bronchopulmonary lavage and urine were negative for *A. strictum*. Surveillance cultures of other patients and the unit were also found to be negative. A second set of blood and CSF cultures on day 15 again revealed the same pathogen; thereupon, fluconazole was added to the regimen at 5 mg kg⁻¹ day⁻¹. Supportive immunotherapy with intravenous immunoglobulin (IVIG) was administered. A fourth dose of exogenous surfactant was given to treat the progressive bronchopneumonia on day 16 of life. On cranial ultrasonographic examination, multiple foci that were suggestive of fungal infection were detected. Abdominal ultrasonography and echocardiography did not detect any fungal foci in the kidneys or heart. On day 23, the infant manifested deterioration of respiratory function, signs of gastrointestinal tract dysfunction and shock. The infant died on day 25 from respiratory failure. The final blood cultures were positive for *A. strictum*.

Isolation and identification of *A. strictum* were performed in the Mycology Laboratory, Ege University Medical Faculty Hospital. For both blood and CSF cultures, the Bact T Alert method (Organon Technica) was used. The blood culture was positive on the third day of incubation. Passages were made on sheep blood agar plates and on the third day, white fungal colonies were observed (see Supplementary Figure A in JMM Online). Multiple passages were performed on Sabouraud's glucose agar plates at 26 °C and white tufted colonies with a pale, salmon pink-coloured base developed. Lactophenol cotton blue preparations from the colonies revealed abundant, small, cylindrical conidia that were produced from the phialidic tips of long, slender, lateral hyphae (Fig. 1). These findings identified the fungus as *A. strictum*. Molecular analysis was not performed.

On autopsy, mycotic thrombi were demonstrated in the brain, liver, lung, kidney and heart, from which *A. strictum* was again isolated (Figs 2 and 3).



Fig. 1. Micromorphology of a colony of *A. strictum* (lactophenol cotton blue preparation, $\times 40$).

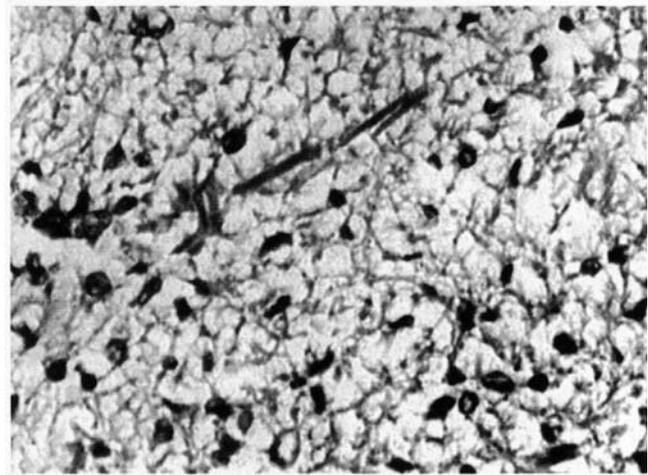


Fig. 2. Mycotic formations in brain tissue (haematoxylin–eosin stain, $\times 40$).

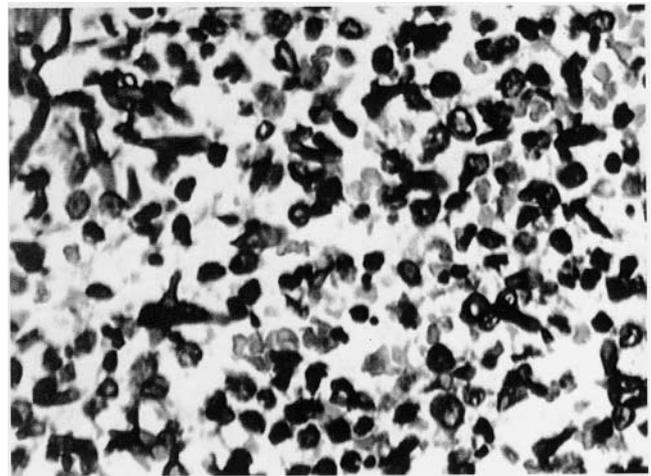


Fig. 3. Mycotic formations and thrombi in liver vein (Gomori's methenamine silver stain, $\times 40$).

Discussion

Acremonium species (previously known as *Cephalosporium* spp.) are ubiquitous soil fungi that have been found in Europe, Asia, Egypt and North and Central America (Fridkin & Jarvis, 1996). *Acremonium* is characterized by solitary, aculeate phialides or weakly branched conidiophores that arise from the vegetative filaments and bear either a wet cluster or dry chains of mostly one-celled spores (conidia). The filaments are sometimes bound together into ropes that are several cells in diameter (Fincher *et al.*, 1991; Guarro *et al.*, 1997). Such forms of *Acremonium* species are likely to be mistaken for *Candida* spp. (Schell & Perfect, 1996). In old medical literature, this micro-organism was named *Cephalosporium*; few reports have been made on the pathogenicity of *Acremonium* (*Cephalosporium*) species. In recent years, the

number and diversity of infections caused by *Acremonium* species have increased. Most infections have presented as mycetoma and ocular infections (Fincher *et al.*, 1991; Fridkin & Jarvis, 1996; Guarro *et al.*, 1997). Disseminated infections caused by *Acremonium* species have rarely been described in the literature; in a review by Guarro *et al.* (1997), there were 36 reported cases, excluding mycetoma and ocular infections. Disseminated *Acremonium* infections, including endocarditis, gastritis, fungaemia, meningitis, diffuse cerebritis and invasive pulmonary disease, have been reported in patients with predisposing conditions such as Addison's disease, neutropenia, immune suppression, burns, organ transplantation and intravenous drug abuse (Fincher *et al.*, 1991; Lau *et al.*, 1995; Fridkin & Jarvis, 1996; Schell & Perfect, 1996; Guarro *et al.*, 1997; Koç *et al.*, 1998; Anadolu *et al.*, 2001). However, in the neonatal period, only one case has been reported in English literature (Papadatos *et al.*, 1969). This patient with *Cephalosporium* meningitis, from whom *Candida albicans* was also isolated from the nose, rectum and throat, was treated with amphotericin B.

The newborn infant, especially the preterm neonate, is at increased risk for development of a considerable spectrum of opportunistic infections, due to molecular, cellular and functional deficiency of both cellular and humoral immunity (Cole, 1998). In addition, neonates with fungal sepsis have significantly longer hospitalization and higher rates of mechanical ventilation, umbilical vein catheterization, previous treatment with antibacterial agents and prior use of parenteral nutrition that includes intravenous lipid (Krcmery *et al.* 2000; Makhoul *et al.*, 2001), which may increase susceptibility. Predisposing factors and conditions in our patient included extreme prematurity, prolonged total parenteral nutrition, previous antibiotic treatment and umbilical vein catheterization.

Once diagnosed, invasive *Acremonium* infection is difficult to treat and the outcome is generally poor. Optimal treatment of *Acremonium* species infections is not well-defined, due to the limited number of reported cases and conflicting results obtained in different studies (Fincher *et al.*, 1991; Lau *et al.*, 1995; Guarro *et al.*, 1997; Koç *et al.*, 1998; Anadolu *et al.*, 2001). In a review (Guarro *et al.*, 1997), the authors used a microdilution broth method to compare the *in vitro* susceptibility, minimum inhibitory concentrations and minimum fungicidal concentrations of amphotericin B, miconazole, itraconazole, 5-fluorocytosine, fluconazole and ketoconazole for several isolates of *Acremonium* species. There was general resistance to most antifungals, excluding amphotericin B and ketoconazole (Guarro *et al.*, 1997). Therefore, amphotericin B therapy, in combination with ketoconazole or another new azole or allylamine, is advo-

cated (Fincher *et al.*, 1991; Lau *et al.*, 1995; Guarro *et al.*, 1997; Koç *et al.*, 1998; Anadolu *et al.*, 2001; Nedret Koç *et al.*, 2002). Despite this treatment regimen, there are still reports of clinical failure that results in death (Fincher *et al.*, 1991; Jeffrey *et al.*, 1993; Lau *et al.*, 1995; Schell & Perfect, 1996).

Disseminated infection caused by *Acremonium* species is a serious fungal disease, especially for neonates. Early identification of the fungus from clinical specimens and determination of the species should prompt urgent communication between clinical microbiologists, infectious disease specialists and neonatologists, regarding management of the patient.

References

- Anadolu, R., Hilmioglu, S., Oskay, T., Boyvat, A., Peksari, Y. & Gürgey, E. (2001). Indolent *Acremonium strictum* infection in an immunocompetent patient. *Int J Dermatol* **40**, 451–453.
- Cole, F. S. (1998). Infections and immunologic defence mechanisms. In *Avery's Diseases of the Newborn*, 7th edn, pp. 435–540. Edited by H. W. Tausch, R. A. Ballard & J. Fletcher. Philadelphia: W. B. Saunders.
- Fincher, R. M. E., Fisher, J. F., Lovell, R. D., Newman, C. L., Espinel-Ingroff, A. & Shadomy, H. J. (1991). Infection due to the fungus *Acremonium* (*Cephalosporium*). *Medicine* **70**, 398–409.
- Fridkin, S. K. & Jarvis, W. R. (1996). Epidemiology of nosocomial fungal infections. *Clin Microbiol Rev* **9**, 499–511.
- Guarro, J., Gams, W., Pujol, I. & Gene, J. (1997). *Acremonium* species: new emerging fungal opportunists – *in vitro* antifungal susceptibilities and review. *Clin Infect Dis* **25**, 1222–1229.
- Jeffrey, W. R., Hernandez, J. E., Zarraga, A. L., Oley, G. E. & Kitchen, L. W. (1993). Disseminated infection due to *Acremonium* species in a patient with Addison's disease. *Clin Infect Dis* **16**, 170.
- Koç, A. N., Utaş, C., Oymak, O. & Sehmen, E. (1998). Peritonitis due to *Acremonium strictum* in a patient on continuous ambulatory peritoneal dialysis. *Nephron* **79**, 357–358.
- Krcmery, V., Fric, M., Pisarcikova, M. & 7 other authors (2000). Fungemia in neonates: report of 80 cases from seven University hospitals. *Pediatrics* **105**, 913–914.
- Lau, Y. L., Yuen, K. Y., Lee, C. W. & Chan, C. F. (1995). Invasive *Acremonium falciforme* infection in a patient with severe combined immunodeficiency. *Clin Infect Dis* **20**, 197–198.
- Makhoul, I. R., Kassis, I., Smolkin, T., Tamir, A. & Sujov, P. (2001). Review of 49 neonates with acquired fungal sepsis: further characterization. *Pediatrics* **107**, 61–66.
- Nedret Koç, A., Erdem, F. & Patiroglu, T. (2002). Case report. *Acremonium falciforme* fungemia in a patient with acute leukaemia. *Mycoses* **45**, 202–203.
- Papadatos, C., Pavlatou, N. & Alexiou, D. (1969). *Cephalosporium* meningitis. *Pediatrics* **44**, 749–751.
- Schell, W. A. & Perfect, J. R. (1996). Fatal, disseminated *Acremonium strictum* infection in a neutropenic host. *J Clin Microbiol* **34**, 1333–1336.