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ORIGINAL ARTICLE

Reporting an outbreak of *Candida pelliculosa* fungemia in a neonatal intensive care unit

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Background: Fungemia in preterm infants is associated with high mortality and morbidity. This study reports an outbreak of unusual fungemia in a tertiary neonatal intensive care unit (NICU).
Methods: Ten *Candida pelliculosa* bloodstream isolates were identified from six infants hospitalized in the NICU from February to March 2009. Environmental study was performed, and genetic relatedness among the 10 clinical isolates of *C pelliculosa* and six control *C pelliculosa* strains was characterized by randomly amplified polymorphic DNA assay. *In vitro*

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susceptibility of isolates to six antifungal agents was analyzed by broth microdilution method. Amphotericin B was given to infected infants and prophylactic fluconazole was prescribed to the other noninfected extremely low birth weight infants during the outbreak.
Results: Thrombocytopenia (platelet counts $<100 \times 10^9$/L) was the early laboratory finding in four infants. One of six patients died, making overall mortality 17%. Fluconazole, voriconazole, amphotericin B, and micafungin provided good antifungal activity. Cultures from the environment and hands of caregivers were all negative. Molecular studies indicated the outbreak as caused by a single strain. The outbreak was controlled by strict hand washing, cohort infected patients, confined physicians and nurses to take care of patients, prophylactic fluconazole to uninfected neonates, and proper management of human milk.
Conclusion: The study demonstrated the clinical importance of emerged non-*albicans Candida* species in NICU. For unusual pathogen isolated from immunocompromised hosts, more attention should be paid to monitor the possibility of an outbreak.

Introduction

Invasive fungal infection is the third most common cause of late-onset sepsis in very low birth weight (VLBW) infants,[1] a critical issue in neonatology over the last 20 years. *Candida* spp. account for most invasive fungal infection in VLBW infants in the neonatal intensive care unit (NICU) and are associated with high mortality rate, significant morbidity, prolonged hospital course, and neurodevelopmental impairment in later life.[1–3] Risk factors related to invasive *Candida* infection include low birth weight and gestational age, broad-spectrum antibiotics, presence of central vascular access, prolonged total parenteral nutrition, and colonization of *Candida* spp. on skin and mucosal surfaces.[2,3] *Candida albicans* and *C parapsilosis* account for most of invasive fungal infection[4,5]; recent studies in this area aim at preventing colonization by *Candida* species, using prophylactic antimicrobials in VLBW infants.[6]

Increasing numbers of reports associate nosocomial fungal infections with unusual *Candida* species. *Candida pelliculosa*, also known as *Hansenula anomala*, a yeast mainly found in plants, fruits, and oil, was first described as causative in an NICU outbreak of fungemia in 1986,[7] with sporadic events related to immunocompromised patients[8–11] and outbreaks[12–16] reported since. This study probes such an outbreak caused by this rare pathogen, *C pelliculosa*, in a tertiary NICU of China Medical University Hospital (CMUH) in Taiwan.

Methods

Hospital

CMUH is a 1700-bed tertiary-care teaching hospital located in central Taiwan. Its NICU, with a capacity of 30 beds, provides tertiary care for critical newborns; most are premature infants or those with respiratory distress.

Definitions and study design

Cases were defined as those patients with at least one blood culture positive for *C pelliculosa*. Neonates were defined as those patients aged 28 days or younger at the onset of fungemia. Preterm birth was defined as birth that occurred before 37 weeks of gestation. Medical records were reviewed regarding demographic and clinical data for assessing potential risk factors of fungus infection: e.g., younger gestational age, low birth weight, previous use of broad-spectrum antibiotics, peripherally inserted central catheter (PICC), endotracheal tube (ETT), nasal-continuous positive airway pressure (N-CPAP), usage of total parenteral nutrition (TPN). Amphotericin B was given intravenously to all infected infants, with prophylactic fluconazole given intravenously to the remaining noninfected extremely low birth weight infants during this outbreak.

Outbreak investigation

From February 4 to March 19, 2009, six preterm infants had documented *C pelliculosa* fungemia. Time span between identification of first and second patients was 24 days. Epidemiological investigation proceeded immediately on March 14, 2009, when a third case was confirmed 33 days after the first. Multiple surveillance surface cultures were performed on infected and noninfected neonates. We collected one of each culture sample from the mouth and anus of VLBW infants hospitalized from March 14 to March 31, 2009, during the outbreak. Environmental samples were obtained from patients' bedding, incubators, sinks, bottle warmers, tops of trolleys, air ducts, respiratory care equipment, Hibisol used for cleaning hands in the NICU, alcohol used for sterile performance, outer and inner surface of the refrigerator for storing breast milk, and 14 samples from breast milk fed to infants during this period. A total of 62 swabs were collected from inanimate environmental sources. Hand samples of NICU staff members (three physicians and 26 nurses) were obtained for culture.

Microbiological investigation

During the outbreak, all patients with sepsis had at least one blood culture obtained for examination. Blood samples were drawn from a peripheral vein using aseptic techniques and cultures were performed with automated Bactec 9240