Disseminated Trichosporon spp infection in preterm newborns: a case report

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Abstract

Objective: To report the first case of disseminated Trichosporon spp infection in a newborn infant in Brazil, discussing a few aspects concerning management and treatment. A new spectrum of pathogens associated with severe infections in neonatal ICU has arisen, afflicting mainly newborn infants weighing less than 1,000 g at birth. Infection with Trichosporon asahii is rare and often fatal in this group of patients.

Description: A case of Trichosporon spp fatal infection in a newborn weighing 815 g at birth is reported. Literature search in the main databases returned only nine articles, reporting 14 cases of infection with this fungus in preterm newborns.

Conclusions: The rate of invasive fungal infection is around 6% in this group of patients, Trichosporon infection being a likely occurrence. Mortality rate in these cases is extremely high, but early treatment with triazole antifungals improves prognosis significantly.


Introduction

Prematurity is one of the most relevant problems in modern perinatology, accounting for high mortality and morbidity rates among newborn infants without congenital anomalies. Preterm birth occurs in approximately 11% of pregnancies and accounts for 70% of neonatal deaths and 50% of neonatal neurological sequelae, including cerebral palsy.1

Sepsis and its complications emerge as the major cause of mortality among these little patients. Susceptibility to infection results from problems related to various components of body defense systems and to an unbalanced acquisition of the endogenous microbiota.1

Fungal infection is associated with high mortality rates, ranging between 10 and 28%, among newborn infants weighing less than 1,000 g at birth. The most common fungal pathogens are C. albicans, C. parapsilosis, C. tropicalis, C. lusitaniae, and C. glabrata.1

Trichosporon asahii (formerly known as Trichosporon beigelli or cutaneum) is an uncommon cause of fungal sepsis among very low birth weight newborn infants.2-10 In general, it causes superficial dermatologic infections in immunocompetent individuals (white piedra and onychomycosis), being a rare cause of disseminated disease among immunocompromised patients.11 Neonatal cases are exceptionally rare and almost always fatal. We report a case of invasive Trichosporon spp infection in a preterm newborn infant to warn neonatologists of the likely occurrence of this infection in very low birth weight preterm newborns.
infants with severe sepsis, discussing considerations on the management of this infection.

Case report

We report the case of a 29-week gestation male newborn infant, born at the Obstetric Center in the University Hospital of Universidade Luterana do Brasil (ULBRA), Canoas, southern Brazil. Cesarean section was performed due to vaginal bleeding and history of amniotic fluid leakage one week before delivery. The newborn infant was depressed at birth (Apgar score 6/7), weighing 815 g. The infant was then intubated and ventilated in the delivery room, with subsequent recovery. In the neonatal ICU, the newborn showed increasing respiratory dysfunction, receiving mechanical ventilation and the instillation of pulmonary surfactant (100 mg/kg), with great response. After the cultures were collected, ampicillin and gentamicin were prescribed. Umbilical arterial and peripheral venous catheters were inserted, and total parenteral nutrition was prescribed. Favorable clinical evolution was observed until the fifth day of life, when the patient showed, suddenly, significant abdominal distension and respiratory failure due to necrotizing enterocolitis, which progressed to perforation. The arterial catheter was removed, and antibiotics were replaced with vancomycin, amikacin and metronidazole. Due to clinical instability, a peritoneal drain was inserted for relief until the newborn, after 48 hours, could be submitted to exploratory laparotomy, when an enterectomy (excision of 20 cm of the intestine) and an ileostomy were performed. The patient responded well to treatment during the following week, progressing to weaning. However, 16 days after birth, the infant showed new worsening of clinical and laboratory conditions (anemia, leukocytosis, metabolic acidosis), new cultures were then collected and a new antibiotic regimen was introduced (vancomycin and meropenem). At this occasion, yeast growth was observed in two blood cultures after 2 days of incubation, leading to prescription of amphotericin B and removal of the deep catheters. A clear worsening of clinical and laboratory conditions was observed within 24 hours, and an increase in the ventilatory parameters was necessary. In addition, the patient showed hyperglycemia, anemia and thrombocytopenia, requiring several transfusions of platelets and erythrocyte concentrates. A new blood culture revealed yeast growth (unidentified) after 48 hours, fluconazole being then added to the management regimen. However, the newborn developed important abdominal distension and refractory shock, requiring very high parameters for mechanical ventilation, vasoactive drugs, volume expansions, and transfusion of blood-derived products. The patient progressed to cardiac arrest, was unresponsive to resuscitation procedures, and died after 38 days of life. An autopsy was performed, and postmortem blood culture identified Trichosporon spp.

Yeast identification was conducted in the microbiology sector at the Microanalysis Laboratory of ULBRA University Hospital. The sample for blood culture was inoculated into a BacT/ALERT® blood culture bottle and incubated until evidence of positive culture. After the cultures were positive, a Gram-stained slide was prepared and the sample was grown on an agar-blood plate. Bacterioscopic examination revealed yeast-like structures, and, based on that, the sample was grown on fungus-specific culture media (Sabouraud and Mycosel). After the media were incubated for 48 hours, macro and microscopic examination of the colonies obtained was performed. Identification was based on the presence of septate hyphae that disarticulate to form arthroconidia, with budding capacity evident under microscope, and waxy (and brain-like under microscope) colonies, characteristic of the genus Trichosporon spp.

The patient’s parents provided written informed consent and the study was approved by the Research Ethics Committee of the institution for publication of the case report.

Discussion

Trichosporon asahii are opportunistic yeasts described as emerging pathogens in disseminated and nosocomial infections in neonatal ICUs, despite being rare.\(^2\) Clinical manifestations of infection with this microorganism are unspecific and with poor prognosis.\(^2\)

A different expression of cutaneous fungal infection in very low birth weight newborn infants (≤ 1,000 g) was recognized in 1991, characterized by ulcerations, erosion, and extensive crusting lesions. Different from congenital candidiasis, these lesions appeared several days after childbirth and were often associated with systemic involvement. At this occasion, this entity (invasive fungal dermatitis) was suggested to represent an alternative port of entry for the development of fungal sepsis among newborn infants.\(^12\) The first reports on invasive fungal dermatitis caused by Trichosporon spp came from the United States, in 1992.\(^8\)

A search in the main databases (MEDLINE, LILACS, and SciELO) returned only nine articles reporting neonatal infection in 14 preterm newborns. Of these, 10 weighed less than 1,000 g at birth and only one weighed more than 1,500 g at birth. All deaths (six) occurred in the extremely low birth weight group.\(^2\)-\(^10\) To date, there are no reports on this type of infection among newborn infants in the Brazilian literature.

Trichosporon spp inhabits soil, water, vegetables, mammals, and birds, as a part of the normal flora of the skin (mainly in the inguinalcrural region), nails and oral mucosa. Yeast has been isolated from the genital area of almost 14% of women, vaginal delivery being the colonization agent of newborn infants.\(^3\)-\(^12\)
In addition to its correlation with low birth weight, invasive *Trichosporon asahii* disease has been related to the use of broad-spectrum antibiotics, corticotherapy, vaginal delivery, parenteral nutrition, and prolonged catheterization.\(^2\)\(^-\)\(^4\)\(^,\)\(^12\)

In neutropenic patients, cure is strongly associated with recovery from neutropenia\(^3\) and, in patients with indwelling catheter, it is strongly associated with catheter removal.\(^7\) Mortality rate ranges from 65-75% in adults, reaching almost 100% in patients without recovery of neutrophils.

The pathogen can be identified by culture and polymerase chain reaction (PCR). Most *Trichosporon asahii* strains may be confused with *Candida spp* on initial culture examinations, leading to delayed treatment.\(^4\)\(^,\)\(^6\) Curiously, latex agglutination test for *Cryptococcus neoformans* antigen may be positive in patients infected with *Trichosporon spp*.\(^14\)

Several studies have demonstrated low *in vitro* sensitivity of *Trichosporon asahii* to commonly used antifungal agents, such as amphotericin B and triazole antifungals.\(^2\)\(^-\)\(^3\) In addition, some strains are resistant to 5-flucytosine.\(^13\)

Early administration of amphotericin B may result in favorable clinical evolution\(^4\)\(^,\)\(^5\) in this type of infection. However, in newborn patients, there may be *in vivo* resistance to this drug, which might explain the high mortality rates observed in this population.\(^7\) In a study carried out by Di Bonaventura et al.,\(^15\) the authors demonstrated that biofilm formation by *Trichosporon spp* would explain persistence of the infection in spite of *in vitro* sensitivity to antifungal agents.

New antifungal drugs, despite the promising results concerning the treatment of more aggressive and resistant fungal infections in both adults and children, are yet to be studied in newborn infants.\(^2\) For instance, we mention the case of caspofungin. This is an active drug against *Trichosporon asahii*. Combination of caspofungin and amphotericin B or a triazole antifungal may increase clinical efficacy.\(^14\)

Studies using animal models and some clinical data have demonstrated that triazole antifungals, such as fluconazole, are the drugs of choice in the case of invasive *Trichosporon asahii* infection.\(^3\) Limited data also suggest that itraconazole is the agent of choice or, at least, a first-line agent against this microorganism.\(^15\) Voriconazole, a recent triazole component, showed better performance than fluconazole, amphotericin B or caspofungin against planktonic *Trichosporon asahii* cells, corroborating previous *in vitro* studies.\(^15\)

In conclusion, infection with this agent should be taken into consideration when dealing with very low birth weight preterm infants, particularly those with unfavorable clinical evolution and signs suggestive of resistant germ sepsis.

Early identification of fungus from clinical specimens should determine an urgent communication among microbiologist, infectologist and neonatologist in order to provide additional cultures, sensitivity test, and early treatment intervention. A successful treatment also depends on removal of the deep catheters and an appropriate management of neutropenia, whenever this condition is present. The growing presence of this population in our ICUs and the probability of colonization and infection with these agents require special attention from the physician assisting on the diagnosis and treatment of septic syndromes.

References