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Disseminated *Trichosporon Spp* Infection in Preterm Newborn: A Case Report at Tertiary Care Hospital in North India

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ABSTRACT

To report the case of disseminated Trichosporon spp infection in a newborn infant in tertiary care hospital, 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 preterm infants weighing less than 1,000 g at birth. Infection with Trichosporon asahii is rare and often fatal in this group of patients. 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.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.

KEYWORDS : Newborn infant, premature infant, low birth weight, sepsis

Introduction:

Trichosporon asahii, basidiomycetous yeast-like anamorphic organisms, widely distributed in nature and found predominantly in tropical and temperate areas; is an uncommon cause of fungal sepsis among newborn infants, but it is now emerging as an important life-threatening opportunistic systemic pathogen, especially in immunocompromised hosts[1, 2]. Trichosporonosis is usually an insidious disease and its diagnosis is likely to be missed, particularly in developing countries, because of lack of awareness and lack of acquaintance with the salient diagnostic feature of the etiological agent. Barring a few isolated case-reports, there is no information on the prevalence of disseminated trichosporonosis in India.

Case report:

Blood from a preterm (35weeks) new born with hyperbilirubinemia and sepsis, who was already on broad-spectrum antibiotics for last 16 days prior to admission at Sir Sundar Lal Hospital, IMS, BHU, Varanasi was received in Dept of Microbiology, IMS, BHU, Varanasi. Caesarean section was performed due to vaginal bleeding and history of amniotic fluid leakage one week before delivery. The new born 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 new born 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. Favourable 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, leucocytosis with left deviation, metabolic acidosis), new cultures were then collected and a new antibiotic regimen was introduced (vancomycin and meropenem). At this occasion, the blood culture grew yeast cells suspected of *candida species* (unidentified) after 24 hours of aerobic incubation at 37º C on Sabauraud's Dextrose Agar. The *Candida* species on culture were later identified as colonies of *T. asahii* based on fndings that it was urease positive and there was presence of arthroconidia after culture on cornmeal agar plate (Dalmau culture plate) and incubated at 22º C for 48 hours and then observed under microscopy. Antibiotic susceptibility was determined by the Clinical Laboratory Standards Institute (CLSI) disk diffusion testing (document M44-A). Commercially available paper discs for amphotericin-B (100 U/disc), fluconazole (25 mg/disc) and voriconazole (1 mg/disc) were used. The interpretive breakpoints (zone diameters) were defined as sensitive (≥ 15 mm for amphotericin-B, ≥ 19 mm for fluconazole and ≥ 17 mm for voriconazole) and resistant (≤ 10 mm for amphotericin-B, ≤ 14 mm for fluconazole and ≤ 13 mm for voriconazole). Yeast was sensitive to amphotericin B and voriconazole but resistant to fluconazole. Urine sample of the same patient also yielded *Trichosporon asahii* which was also confirmed by presence of arthroconidia after culture on cornmeal agar plate (Dalmau culture plate) and incubated at 22º C for 48 hours and then observed under microscopy and sugar assimilation test. Institution of conventional IV amphotericin-B along with supportive therapy led to clinical improvement in the patient.

Discussion:

Trichosporon asahii is opportunistic yeast described as an emerging pathogen in disseminated nosocomial infections in NICUs[3-8]. 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.[9] 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 defence systems and to an unbalanced acquisition of the endogenous microbiota. 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 cause of invasive fungal infection in preterm, extremely-low birth weight (ELBW) neonates is Candida species (*C. albicans*, *C. parapsilosis*, *C. tropicalis*, *C. lusitaniae*, and *C. glabrata*.[9]). Over the past two decades, several studies have reported opportunistic and nosocomial sepsis by other uncommon fungal spp. such as, *Malassezia, Trichosporon, Rhodotorula* and *Hansenula* in immunocompromised patients and rarely in newborns[10]. *Trichosporon asahii* (formerly known as *Trichosporon beigelii* or *cutaneum*) is an uncommon cause of fungal sepsis among very low birth weight newborn infants.[3-7] 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. Early recognition of these unusual pathogens are important because most of these infections have unpredictable antifungal susceptibility and they carry a poor prognosis.

We report a case of invasive *Trichosporon spp* infection in a preterm new born infant to warn neonatologists of the likely occurrence of this infection in very low birth weight preterm infants with severe sepsis, discussing considerations on the management of this infection. The organisms were found to be sensitive to amphotericin B and voriconazole but resistant to fluconazole.

Clinical manifestations of infection with this microorganism are non-specific and infections often results in poor prognosis[3,7,8] . This is probably the first report of an invasive outbreak in a neonatal unit in India. August is the month of the year which has very high humidity and high rates of neonatal admissions. Due to high work load, a breach in asepsis protocol might have occurred. Most strains of *T. asahii* may be confused with *Candida spp*. on initial culture examinations. Therefore, delays in appropriate treatment may occur. Several studies have demonstrated low in vitro sensitivity of *T. asahii* to commonly used antifungal agents[2,4,12] . The fungus is known for varied susceptibility to amphotericin B and laboratory studies have shown that it is relatively resistant to this agent[2,12] . On the other hand, many authors have described good results of early administration of amphotericin B[3,5]. In our case also, the isolates was sensitive to amphotericin B and voriconazole, but resistant to fluconazole. However, a favourable clinical response was observed in case despite using amphotericin B quite early on the first suspicion of nosocomial sepsis in most neonates. The in vivo resistance of the drug can be explained due to formation of a biofilm by *Trichosporon spp*[13], which may explain persistence of the infection in spite of in vitro sensitivity of the drug. Since there are no pathognomonic clinical features, the diagnosis of disseminated trichosporonosis depends primarily upon clinical suspicion, to be followed by intensive mycological investigations. Infection with this agent should be taken into consideration when dealing with low birth weight preterm infants, particularly those with nosocomial sepsis having cocktail of broad spectrum antibiotics for a prolonged period but still with unfavourable clinical progress.

Conclusion:

The diagnosis of *Trichosporon asahii* is likely to be missed particularly in developing countries, because of a general lack of awareness and lack of acquaintance with its salient diagnostic features. All budding yeast cells are not due to *Candida species* and there lie the importance of culture and different diagnostic test for Trichosporonosis.

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