A Fatal Outbreak of *Trichosporon asahii S*epsis in a Neonatal Intensive Care Unit

VIPIN M VASHISHTHA, AMOL MITTAL AND *AMIT GARG

*From the Department of Pediatrics, Mangla Hospital and Research Center, Shakti Chowk, Bijnor, and *Department of Microbiology, LLRM Medical College, Meerut; Uttar Pradesh, India.*

Correspondence to:
Dr Vipin M Vashishtha,
Director and Consultant Pediatrician,
Mangla Hospital and Research Center,
Shakti Chowk, Bijnor 246 701, India.
vipinipsita@gmail.com
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We describe an outbreak of *Trichosporon asahii* in 8 newborn infants with sepsis. Six out of these 8 infants died. The organism was identified on specific culture and morphologic characteristics. The organism was sensitive to amphotericin-B but resistant to fluconazole. Laminar flow unit was suspected to be the source of the outbreak.

Key words: *India*, *Neonate, Outbreak, Sepsis, Trichosporon asahii*.

Trichosporon asahii 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 immuno-compromised hosts [1]. 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 etiologic agent. Barring a few isolated case-reports, there is no information on the prevalence of disseminated trichosporonosis in India. We report a fatal outbreak of *T. asahii* sepsis in eight newborns in our neonatal intensive care unit (NICU).

CASE REPORT

Eight newborn infants admitted between 17th to 28th August, 2011 in our NICU were found to be infected with *T. asahii* (***Table* I**).

The first case was already on broad-spectrum antibiotics for last 12 days prior to admission. The blood culture grew non-albicans *candida species* (unidentified) after 24 hours of aerobic incubation at 30º. Institution of conventional IV amphotericin-B along with supportive therapy led to clinical improvement. The baby was later discharged at day 10 of treatment with follow-up advice of continuing amphotericin-B therapy for full 21 days. The *Candida* species on culture were later identified as colonies of *T. asahii.*

Initial cultures of the second case were sterile. Baby improved following partial exchange transfusion with normal saline along with empiric antimicrobials, but later developed feeding intolerance, abdominal distension, hematemesis and refractory shock. Amphotericin B added empirically failed to improve general condition and ultimately the baby died. The repeat blood culture grew colonies of *T. asahii*.

The third case had early onset sepsis. Initial blood culture grew *E. coli* which was sensitive to common beta-lactams. A dose of surfactant, assisted ventilation and appropriate antibiotics resulted in significant improvement. Later, the infant developed features of sepsis along with massive pulmonary hemorrhage and succumbed to his illness despite starting IV amphotericin B. The repeat blood culture again grew *T. asahii*.

The fourth case developed fulminant sepsis after 48 hours of admission caused by extended-spectrum beta-lactamase producing *Klebsiella pneumoniae*. A course of meropenem and supportive therapy including ventilatory support resulted in improvement. Enteral feeds were started and the baby was weaned off from the ventilator. However, at 11th day of life, the baby again showed worsening of clinical and laboratory parameters. Repeat culture revealed growth of *Trichosporon spp.* Liposomal Amphotericin B was added in the regimen but the baby did not respond, and ultimately died at the age of 21 days.

The next infant had features of early onset sepsis but cultures were negative. The baby improved after a 7-day course of empiric antibiotics. Four days later, the baby was readmitted in the NICU for the treatment of jaundice and later developed necrotizing enterocolitis (NEC), cholestasis and signs of sepsis. The repeat blood culture

TABLE I CLINICAL CHARACTERISTICS OF NEONATES WITH T. ASAHII SEPSIS

Case No.	*NICU Stay (d)*	*Mode of delivery*	*Birth weight (grams)*	*Diagnosis (at admission)*	*Mechanical ventilation*	*Outcome*
1*.	10 d	Vaginal	2400	Term-SGA with PNA with Sepsis	No	Improved
2.	9 d	Vaginal	1200	Preterm (35 week) SGA with Polycythemia with Sepsis	No	Died
3.	5 d	LSCS	1250	Preterm (32 week) SGA with PNA with PPROM with RDS	Yes	Died
4$.	21 d	Vaginal	1080	Preterm (29 week) SGA Breech presentation with PNA with PPROM	Yes	Died
5$.	20 d	LSCS	1720	Preterm (34 week) SGA with BOH with PPROM	No	Improved
6$.	6 d	LSCS	1235	Preterm (28 week) AGA with PNA with twin pregnancy with PPROM with anemia	Yes	Died
7.	7 d	Vaginal	1550	Preterm (31 weeks) SGA with RDS (HMD)	Yes	Died
8.	7 d	LSCS	2890	Term AGA with MSAF with PNA	No	Died

*LSCS- Lower segment caesarean section; SGA-Small for gestational age; AGA-Appropriate for gestational age; PNA-Perinatal asphyxia; PPROM-Prolonged premature rupture of membranes, RDS-Respiratory distress syndrome; BOH- Bad obstetric history; MSAF- Meconium-stained amniotic fluid; $ Received Total parenteral nutrition; *Did not receive treatment with H2 –blockers.*

revealed *Trichosporon spp.* With the addition of amphotericin-B in the regimen, the infant gradually responded, blood culture became sterile at 10th day of therapy, and the baby was discharged at 20th day of life with follow up advice of completing IV amphotericin B course for total 21 days.

The sixth case was second born twin delivered to a third-gravida mother. After packed cell transfusion and supportive treatment, the infant stabilized. However, the baby later developed respiratory distress that necessitated assisted ventilation. After weaning off from the ventilator, the baby developed repeated apneic spells and repeat culture grew fungal colonies identified as *T. ashii.* Addition of IV amphotericin-B to the antimicrobial regimen failed to salvage the baby who developed massive gastrointestinal hemorrhage, perforation and shock, and died after 6 days of admission.

The next case was a premature infant who developed Hyaline membrane disease soon after birth and was treated successfully with surfactant and assisted ventilation. Later, the infant developed signs of sepsis in form of apnea, pallor and hypotension. Repeat culture grew yeast colonies, identified as as *Trichosporon spp*. The baby developed massive pulmonary hemorrhage and died at the age of 7 days despite adding IV amphotericin-B to the regimen.

The last case was a term neonate who developed meconium aspiration syndrome and was treated with high-flow oxygen, antibiotics and IV fluids. Five days later, the infant started exhibiting dullness, apnea, and later gastrointestinal bleeding. The repeat blood culture grew colonies of *Trichosporon spp*. Amphotericin B was added to the regimen. However, the baby developed features of disseminated intravascular coagulation and died at the post-natal age of 7 days.

Identification of T asahii: The blood culture was done by automated BacT/ALERT 3D 120 blood culture System. Gram stain showed elongated blastoconidia and septate pseudohyphae. Broth from the positive blood cultures bottles were sub-cultured on blood agar and Sabouraud's dextrose agar (SDA) with chromphenicol. The colonies of yeast like fungi were isolated after 24 hrs of incubation. Identification and sensitivity was done by Vitek 2 Compact. The macroscopic and microscopic morphology of *T. asahii* was compatible with the standard description of the species.

DISCUSSION

Trichosporon asahii is opportunistic yeast described as an emerging pathogen in disseminated nosocomial infections in NICUs [2-7]. Clinical manifestations of infection with this microorganism are non-specific and infections often results in poor prognosis [2,6,7]. This is probably the first report of an invasive outbreak in a neonatal unit in India. Case 1 probably represented the index case; responsible for spreading the infection in other neonates who had nosocomial sepsis during the course of their stay.

Literature search revealed reports of *T.asahii* neonatal infection in 15 preterm newborns. Of these, 11 weighed less than 1,000 g at birth and only one weighed

more than 1,500 g at birth. All deaths (seven) occurred in the extremely low birth weight group. However, in our series, the preterm infants were not extremely premature and had comparatively higher weights, and even full term neonates were affected. *Trichosporon* infections in neonates have been almost uniformly fatal. In our series also, six out of eight neonates died. Many of our patients had one or more of the risk factors often blamed for nosocomial sepsis and fungal diseases [8].

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. Surprisingly on performing microbial surveillance, we found that one surface culture from laminar flow unit yielded positive growth of *Candida spp* with morphological features similar to *T. asahii*. We stopped using laminar flow for preparing intravenous fluids and the entire unit was thoroughly fumigated with formaldehyde. Hence, it can be presumed that laminar flow unit was probably the source of this outbreak.

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 [1,3,9]. The fungus is known for varied susceptibility to amphotericin B and laboratory studies have shown that it is relatively resistant to this agent [1,9]. On the other hand, many authors have described good results of early administration of amphotericin B [2,4]. In our series also, all the isolates were sensitive to amphotericin-B, but resistant to fluconazole and flucytosine. However, a favourable clinical response was observed in only two cases 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* [10], 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.

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