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ISOLATION OF RARE SPECIES OF CANDIDA FROM SEPTIC NEONATES IN A TERTIARY CARE HOSPITAL OF WESTERN MAHARASHTRA – CASE SERIES

Medical Microbiology

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ABSTRACT

Candidemia caused by non-albicans Candida species is rising in the last few decades. The increasing use of prophylactic antifungal agents e.g. Fluconazole to prevent Candida infections has led to the emergence of resistant strains. Candida utilis has been recently identified causing neonatal septicemia. The hands of HCW serve as potential reservoirs for nosocomial transmission of Candida spp. Organisms transferred to the hub or lumen of the catheter may form a biofilm within the lumen of the catheter and subsequently spread into the circulation. We report a case series of neonatal sepsis caused by C. utilis. In all the three cases high end antifungals were given as per culture and sensitivity report. Two babies responded well to treatment and later on discharged while one baby succumbed to the infection. The three cases remained sporadic likely to the efficient infection control measures applied in the NICU. Hence strict infection control measures to prevent an outbreak of infections is also important. Our study highlighted the importance of speciation and choice of antifungal therapy for successful clinical management of such cases.

KEYWORDS

Non-albicans Candida, Candida utilis septicemia, antifungal susceptibility, infection control

INTRODUCTION

Candida bloodstream infection (BSI) is an important cause of neonatal sepsis and mortality. Common risk factors for Candida BSI include prematurity and very low birth weight (VLBW), central vascular catheterization, parenteral nutrition, use of broad-spectrum antibiotics, invasive ventilation, and prolonged NICU stay[1].

Although *C. albicans* has been the most frequently isolated species, infections caused by the non- albicans *Candida* have been diagnosed with increasing frequency in recent years, notably *C. Tropicalis*, *C. Glabrata*, and *C. Parapsilosis*[2].

The increasing use of prophylactic antifungal agents e.g.fluconazole to prevent *Candida* infections has led to the emergence of resistant species[3]. The increased isolation rates of non-albicans *Candida* species and change in antifungal susceptibility patterns have gained importance for monitoring the emergence of resistance and selecting the most appropriate antifungal agents for therapy[2]. The incidence and mortality due to candidemia are influenced by several factors including the population at risk, distribution of *Candida* species, and prevalence of antifungal resistance[4].

Candida utilis is a rare cause of sepsis in a neonate. *Candida utilis* septicemia has been reported in immunocompromised patients, neonates, and following the surgical intervention[5]. In the case of emerging pathogens, systematic monitoring of the trends of incidence, species identification, and antifungal susceptibility profile is needed[6].

MATERIALS AND METHODS

We studied in detail three cases of *Candida utilis* isolated from the blood culture of septic neonates admitted to the NICU for three months.

This was a retrospective case study carried out in the Neonatal intensive care unit (NICU) at a tertiary care hospital. The approval for the study was taken from the Institutional ethical committee.

We reviewed the clinical history and treatment details of all patients with *Candia utilis* isolated from blood cultures from the NICU.

Blood from septic neonates was inoculated into blood culture bottles. Approximately 1 to 2 ml of blood was collected under aseptic precautions and inoculated into BD BACTEC Aerobic/F culture bottles after thorough cleaning of the rubber septum of vials with 70 % ethyl alcohol.[7]

Then bottles are incubated at 37 degree C in the BACTEC instrument for 5 days. [7]

The blood culture bottles that flagged positive in the automation system, Gram staining was done. [7]

If Gram staining of blood from positive bottles showed Gram-positive budding yeast-like cells, subculture was done.

A routine medium for isolation of fungus in culture is SDA supplemented with antibiotics to prevent bacterial growth.[8]

CHROMagar is a chromogenic, differential culture medium, that is used to facilitate the isolation and presumptive identification of clinically important yeast species. [9]

Observation of colony morphology and distinctive patterns of colour are used to separate yeast species.[9] [Figure 1]

Identification of yeasts using conventional methods is time-consuming and labor invasive and therefore commercial automated systems have been developed for the identification of yeasts.[10]

VITEK -2 system is considered a reliable technique for antifungal susceptibility of yeast species and has the advantage of being more rapid and easier than CLSI broth Microdilution methods. .[11]

VITEK® 2 COMPACT (Biomerieux) automation system was used for confirmation of identification and susceptibility.

Antifungal susceptibility was done for Fluconazole, Voriconazole, Caspofungin, Micafungin, and Amphotericin B.

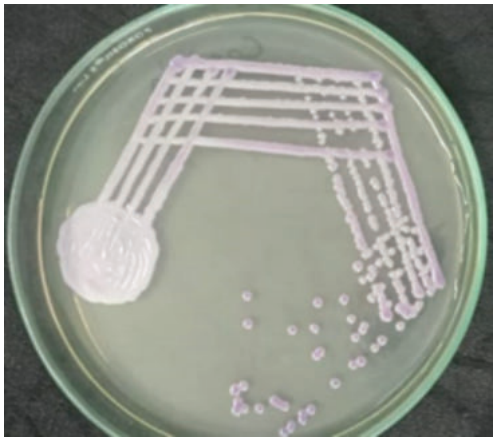

Figure 1. *Candida utilis* on HiCrome™ Candida Differential Agar

CASE 1:
43 days old Male, referred from another hospital around day 30 of life with the history of preterm delivery at 28 weeks gestation, a product of twin pregnancy.

The baby was born out by lower segment Caesarean section (LSCS) because of per vaginal (PV) leaking and breech presentation and birth weight was 920 gms (extremely low birth weight).

The baby cried immediately after birth and had respiratory distress syndrome (RDS) at the time of birth. The baby was intubated, received surfactant at birth, and ventilated for 7 days. Given late-onset sepsis, the baby received 19 days of Meropenem and Vancomycin, along with Inj. Amphotericin B for proven *Candida utilis* septicemia, for 3 weeks in the referring hospital. 10 days after hospitalization to our NICU, the baby developed abdominal distension, feed intolerance, hypoglycemia, and other signs of sepsis.

Blood culture was sent which was flagged positive the following day; showed gram-positive budding yeast-like cells. *Candida utilis* was later isolated from blood culture.

Antifungal susceptibility was done for Fluconazole, Voriconazole and Amphotericin B, Micafungin, and Caspofungin.

The organism was sensitive to Voriconazole and Amphotericin B, Micafungin, Caspofungin.

The Baby's health deteriorated over the following few days and eventually succumbed to fulminant sepsis.

CASE 2:
14 days old male neonate was initially admitted for low birth weight (LBW), RDS, and newborn care with a history of preterm birth (35 weeks), LBW of 1.540 Kg, born out of LSCS because of twin pregnancy and precious pregnancy (IVF).

The baby cried immediately after birth but developed RDS and required surfactant administration and a short brief period of ventilatory support for the same.

IV Antibiotics Piperacillin – Tazobactam and Amikacin were given for initial 5 days.

On day 6 of life, Meropenem and Levofloxacin were added, Amikacin continued and Fluconazole was added empirically because of suspected clinical sepsis. Blood investigations were suggestive of severe thrombocytopenia with raised C- reactive protein therefore Voriconazole was started and fluconazole was stopped.

The blood culture sent was flagged positive after 3 days; showed gram-positive budding yeast-like cells. *Candida utilis* was later isolated from the blood.

Antifungal susceptibility was done for Fluconazole, Voriconazole and Amphotericin B, Micafungin and Caspofungin, and Flucytosine.

The strain was sensitive to Voriconazole, Amphotericin B, and Flucytosine.

The baby was continued on voriconazole, showed good clinical and hematological improvement; received 3 weeks of treatment with voriconazole, and was discharged home.

CASE 3:
14-day-old male neonate, one of the twins, 27- 28 weeks(preterm), 1.07 kg (very LBW), admitted for prematurity, RDS, and newborn care was born by LSCS because of PV leaking.

The baby was intubated at birth and surfactant was given.

The baby initially received treatment with Piperacillin with tazobactam /Amikacin, and fluconazole started prophylactically empirically.

On the 15th day of life, Meropenem was started and voriconazole was added for suspected late-onset sepsis.

A blood culture was sent which was flagged positive after 2 days; showed gram-positive budding yeast-like cells. Antifungal susceptibility was done for Fluconazole, Voriconazole and Amphotericin B, Micafungin and Caspofungin.

Candida utilis was sensitive to Voriconazole and Amphotericin B.

The baby continued to receive voriconazole for 3 weeks; showed clinical and hematological improvement. The baby was eventually off all respiratory support and established on full feeds gaining good weight.

In the 8th week of life, the baby redeveloped signs of clinical sepsis with septic ileus requiring ventilatory support and the blood culture showing growth of *E.coli*. The species was sensitive to Meropenem which was administered for 2 weeks. The baby improved and was discharged home in the 11th week of life.

DISCUSSION

C. utilis has long been known for its industrial applications, but it has rarely been described as an infectious agent in humans.[12]

We present three cases with *C.utilis* sepsis in the NICU over 3 months in 2021 and 2022. The common predisposing factors among these three babies were intensive care admissions, invasive procedures (including intubation, IV cannulations, and umbilical/ PICC lines), and previous use of antimicrobials. It was observed that one of the babies had acquired an infection from another hospital.

Candida BSI was defined as at least one pure growth of Candida species in blood culture [13] within 72 hours of inoculation, in presence of clinical features suggestive of sepsis such as respiratory distress/apnea, tachycardia/bradycardia, poor perfusion, feeding intolerance, temperature instability, lethargy, or seizures [14]. Culture positivity within 14 days, with the same Candida species, was considered to be the same infection episode. The repeat positive culture in the first case was possibly the same infection episode.

The predominant source of infection caused by Candida spp., from superficial mucosal and cutaneous disease to hematogenous dissemination, is the patient. Most types of Candidiasis represent an endogenous infection in which the normally commensal host flora take advantage of the opportunity to cause infection. In the cases of Candida BSI, transfer of the organism from the GI mucosa to the bloodstream require prior overgrowth of the numbers of the yeast in their commensal habitat, coupled with a breach in the integrity of the GI mucosa.[15]

Exogenous transmission of Candida may also account for a proportion of certain types of Candidiasis.[15]

The hands of HCW serve as potential reservoirs for nosocomial transmission of Candida spp. [15]

Organisms transferred to the hub or lumen of the catheter may form a biofilm within the lumen of the catheter and subsequently spread into the circulation. [15]

The three cases remained sporadic likely to the efficient infection control measures applied in the NICU.

CONCLUSION

We present what we believed to be the first case series of *Candida utilis* in Western Maharashtra and that *C. utilis* is a possible cause for neonatal sepsis.

There is a need for rapid diagnosis of these new and emerging fungi.

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