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CANDIDA UTILIS- A RARE CAUSE OF NEONATAL SEPSIS.

Medical Microbiology

Dr. Prasanna Gonti* Post graduation Gandhi Medical college, Hyderabad, Telangana, India. Currently Senior resident ESIC Medical college, Hyderabad, Telangana, India. *Corresponding Author

Dr. V.V. Shailaja Associate professor, Gandhi Medical college, Hyderabad, Telangana, India.

ABSTRACT

Candida spp are one among the important causes of neonatal sepsis, causing significant morbidity and mortality. Off late non-albicans Candida (NAC) are showing an increasing trend and Candida utilis is reported as a rare cause. We present two cases of C. utilis candidemia in new-borns, in the age group 0–3months, delivered and hospitalized in the same hospital, within a 6-month period in 2018. Prematurity, low birth weight, very low birth weight (<1500 g) were the risk factors. Our case reports and review highlights the importance of speciation and role of rare Non albicans candida species in cases of neonatal sepsis which is of clinical and epidemiological importance.

KEYWORDS

Candida utilis, neonatal, sepsis

INTRODUCTION:

Candida spp are one among the important causes of sepsis in critically ill patients, causing significant morbidity and mortality. Candida blood stream infection varies in its incidence different parts of the world from 1.1-1.3% in Europe, 0.5- 1.6% in North and South America, to 4-7.7% in Asia [1]. The prevalence of candidemia in India is 6–18%, with candida albicans being the most common. Off late non-albicans *Candida* (NAC) are showing an increasing trend, notably *Candida parapsilosis, Candida tropicalis, Candida krusei, Candida glabrata* [2], [3], also including rare species like *Candia utilis* [4], [5] and *Candida blankii* [6]. The incidence of Candidemia in children is highest among infants especially <3 years of age, particularly in new-borns. Prematurity, low birth weight, very low birth weight (<1500 g) hospitalisation and those prophylactic antibiotics use are considered to be the risk factors [7].

Cases reports:

We present two cases of *C. utilis* candidemia in new-borns, in the age group 0–3months, delivered and hospitalized in the same hospital, within a 6-month period in 2018.

CASE 1:

A 3-day-old female having neonatal seizures with staring looks, symptomatic hypoglycaemia was admitted in NICU. She was a very Low birth weight (1600gms) baby, full term with IUGR and delivered by normal vaginal delivery in the same hospital. She was started on IV calcium gluconate and prophylactic Antibiotic therapy with Piperacillin Tazobactum and Amikacin. She had hypocalcaemia, thrombocytopenia and CRP was positive 12mg/dl on Day 1 of investigation. Blood samples were drawn for culture under aseptic precautions on Day 2. Culture was carried out using automated BacT/Alert 3D system [BioMerieux]. The automated bottle flashed positive within 12 hrs of incubation and was subcultured onto Blood agar and MacConkey agar media. Gram stain showed Gram-positive budding yeast like cells. Blood agar showed pinpoint white opaque non haemolytic colonies and MacConkey agar showed Lactose fermenting pinpoint colonies. Primary isolation and speciation were performed using the carbohydrate assimilation tests using Vitek 2 yeast identification and antifungal susceptibility testing system. The isolate was sensitive to all the tested antifungals-amphotericin B, flucytosine, fluconazole, voriconazole, caspofungin and micafungin. Strict quality control was followed during the isolation. On Day 3 Intravenous fluconazole was initiated with 8.4mg of antifungal once a day. After 3 days of antifungal therapy the baby improved clinically, and on Day 5 of therapy her blood cultures came negative. She had no fresh episodes of seizures and was accepting feeds.

Case 2:

A 16-day-old female infant with fever, dull activity, poor acceptance of feed. She was a delivered by Emergency LSCS, at 37 weeks of GA, due to maternal pre-eclampsia, non-severe polyhydramnios. Low birth baby (2.1kg) born through consanguinity. Bood work up revealed CRP positive 24mg/dl. On day 3 of admission into NICU, the baby became irritable, developed opisthotonus posturing and , deviated angle of the mouth. Blood work up showed CRP positive 24mg/dl. Blood samples were drawn for culture under aseptic condition. Antibiotic therapy was started prophylactically with ceftriaxone 300 mg stat dose followed by 200 mg per day. On the second day C. utilis was isolated from blood culture. Blood culture was performed by automated Bact/Alert 3D system [BioMerieux]. Gram stain showed Gram-positive budding yeast like cells. Primary isolation and speciation using Vitek 2 yeast identification revealed Candida utilis and antifungal susceptibility testing showed sensitivity to all the tested antifungals-amphotericin B, flucytosine, fluconazole, voriconazole, caspofungin and micafungin. Strict quality control was followed during the isolation. Intravenous fluconazole was initiated immediately with a stat dose followed by 8.4 mg of antifungal once a day.

Her renal function parameters were deranged (serum creatinine6.35 mg/dL, blood urea 152mg/dl). Ultrasonogram of abdomen revealed grade 1 bilateral renal parenchymal changes. Arterial blood gas analysis showed metabolic acidosis. Based on clinical presentation they were suspecting Barters syndrome.

Poor prognosis was explained and the patient left against medical advice (LAMA).

DISCUSSION:

Candida utilis is a rare cause of candidemia. It has a telomorphic form of *Pichia jadinii (Cyberlinderia jadini)*. It is commonly used in the food industry as a yeast additive [7]. Retrospective studies from UP identified 1 isolate [8], New Delhi < 5 isolates of *C. utilis* [2] respectively. The studies identified them as unusual isolates and also reported an increased trend of NAC infections [2]. *Candida utilis* fungaemia has mainly been reported in adult immunocompromised patients, neonates and following surgical interventions. There has been case reports of *C. utilis* causing chronic UTI, Central line catheter related infections and post-surgical infections in elderly immunocompromised patients [9], [10], [11]. Only few case reports of *C. utilis* in neonates and paediatric population have been found in the literature. The case reports are summarised in the Table 1.

Most of the previous case reports show a low mortality rate of *Candida utilis* and susceptibility to all antifungal drugs tested similar to our case report.

In all of the patients, a significant number of risk factors for the development of candidemia co-existed. Both the babies had a history of poor feeding, neonatal seizures and lethargy requiring hospital. They were new-borns, low birth weight babies and preterm, receiving prophylactic antibiotic therapy. Other authors have reported candidemia cases in neonatal patients associated with the same risk factors, pointing out prematurity and low birth weight as risk factors either for acquiring infection or for a bad outcome of infection [12] [13].

Table 1: Various case reports of Candida utilis

s. no	Author	Place	age	Underlying co morbidities/ risk factors	Clinical diagnosis	Prior antibiotic use	Treatment history	Out come
1	Alsina et al	Tennessee, USA, 1987	5 y/o male	Hemophiliac, neutropenic	acquired Immunodeficiency Syndrome, sepsis.	Trimethoprim-sulfamethoxazole	clindamycin, ampicillin, gentamicin, and amphotericin B	Succumbed to infection
2	Lukic et al	Great Britain	5 d/o male	prematurity 27 wks gestation. Very low birth weight. (890gms) Mechanical ventilation	ARDS Sepsis	3 mg gentamicin daily, 10 mg amoxicillin-clavulanic acid twice daily		improved clinically
			8 d/o F	Post surgical reparation of the ileum	intestinal atresia , sepsis.	(7 mg gentamicin twice daily and 20 mg metronidazole twice daily	Fluconazole 6 days, replaced by liposomal amphotericin B	improved clinically
			11 d/O F	Post surgical placement of a Silastic bag	Gastroschisis	7 mg gentamicin twice daily and 100 mg ampicillin three times daily)	f fluconazole was raised to 12 mg/kg caspofungin.	improved clinically
3	Shivadasan et al	Bangalore india 2016	19 d/o F		Neonatal seizures	ceftriaxone 300 mg stat dose followed by 200 mg per day	Intravenous fluconazole	succumbed to the infection
4	T. S. et al.,	Vellore, India, 2021	10 d/o	Neontal seizures	hypoxemic ischaemic encephalopathy	-	-	Left against medical avice.
			4d/o	two episodes of seizures Antenatal history: third trimester high fever, severe oligohydramnios.		-	I/V amphotericin B for 21days. Bab	Clinically recovered
			2month 20day old		late onset neonatal meningitis		Amphotericin B (IV) and flucytosine for 6weeks	recovered

CONCLUSION:

It is important to speciate all the *non albicans candida* to evaluate their role in cases of neonatal sepsis which is of clinical and epidemiological importance. A systematic monitoring of the incidence, and antifungal susceptibility of the new emerging species is essential with utmost priority to the neonatal intensive care units.

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