LATE ONSET *CANDIDA KRUSEI* SEPTICAEMIA IN A NEONATE WHICH RESPONDED TO FLUCONAZOLE MONOTHERAPY: A CASE REPORT

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ABSTRACT

Systemic candida infections in the neonatal population are commonly seen especially in low birth weight, preterm neonates admitted to the Neonatal Intensive Care Unit. Albicans spp is the most commonly isolated but in more recent times, fluconazole resistant spp such as *Candida krusei* have been reported to cause healthcare associated infections.

This is a case of a 12-day old, term, low birth weight (2.45 kg), male neonate delivered to a 32-year-old P_2^{+0} (2A) through elective caesarian section (CS) at term. He was well till the 12th day of life when he developed respiratory distress and sub-optimal oxygen saturation requiring supplemental oxygen. Chest x-ray showed prominent vascular markings with no active focal lung lesion and he was managed for suspected Aspiration Pneumonitis until a blood culture on the 10th day of admission yielded *Candida krusei*. He had a monotherapy of intravenous fluconazole, made progressive clinical improvement and was discharged on oral fluconazole to complete a 6 weeks course on outpatient basis.

Keywords: Candida Krusei, Neonate, Fluconazole

INTRODUCTION

Neonatal candida infections and outbreaks of infections are common in newborn units especially neonatal intensive care units and in the preterm, low birth weight patients.[1,4] Candida infections mimic symptoms of sepsis and often routine blood culture do not report/culture fungal organisms and therefore diagnosis require a high index of suspicion. Firstline treatment is usually with fluconazole which is readily available and which many units also use as fungal prophylaxis for susceptible patients. In recent times however there have been increasing reports of rarer species such as *Candida krusei*, well known for being fluconazole resistant.[2,3] Despite this known potential for resistance, studies have shown the susceptibility of some strains of *Candida krusei* to fluconazole.

We report a rare case of *Candida krusei* septicaemia in a low-birth-weight neonate which was successfully treated with fluconazole monotherapy.

CASE PROFILE

A 12-day old, term male neonate delivered to a 32-year-old P_2+0 (2 alive) woman through elective caesarean section on account of a previous caesarean section scar and maternal request at 38^{+5} weeks gestational age. He presented on account of difficulty with breathing and low-grade fever of a day duration. He had been feeding well, and there was no history suggestive of aspiration. There was no cough nor bluish discolouration of his lips and mucosa.

Mother registered for antenatal care at a tertiary healthcare centre. There was no history of hypertension or diabetes mellitus before or during the pregnancy. There was no known maternal risk factor for sepsis. His birth weight was 2.45kg and he cried well at delivery. He was commenced on breastfeeding shortly after delivery and had been on exclusive breastfeeding till presentation. He had received Bacille Calmette Guerin (BCG), Hepatitis B vaccine (HBV) and Oral polio vaccine (OPV). He was brought to our facility without any prior interventions or medications.

On examination at presentation, he was acutely ill, not pale, not cyanosed, anicteric and had no peripheral oedema. He was in severe respiratory distress (with nasal flaring, subcostal, intercostal recession), tachypnoiec with respiratory rate of 66cycles per minute, heart rate was 140beats per minute. His weight at admission was 2.7kg.

MANAGEMENT COURSE/RESULT

He was commenced on supplemental oxygen and was initially given intravenous Ampicillin/Sulbactam and Amikacin, parenteral Metronidazole was added due to consideration for possible aspiration. Temperature

Table 1: Result of investigations

Investigations	Day 1	Day 3	Day 6	Day 7	Day 14	Day 17
Haematocrit	50%	43%	34%	43%		42%
Micro ESR	3.3mm/hr	2mm/hr				
HIV screening	Negative					
Blood Glucose	72mg/dl					
#CRP	0.1mg/dl	0.2mg/dl		151.5mg/dl	5.2mg/dl	1.7mg/dl
Blood culture without Fungal study	Sterile after 5 days of incubation			*Yielded *Klebsiella Pneumoniae* on Day 10		
Blood culture with Fungal study					Yielded *Candida krusei* on Day 13	
G6PD Assay	Normal					

#=*C-Reactive Protein*

**=Note: Sensitive to Gentamycin, Levofloxacin, Ceftriaxone, Ceftazidime and Resistant to Amoxycillin Clavulanic acid*

was normal after admission and serial C-Reactive Protein remained normal. Tachypnoea however persisted with respiratory rate ranging between 80 - 120 cycles per minute, so antibiotics was changed to intravenous Cefotaxime and Gentamicin after 72 hours of initial antibiotics. Haematocrit reduced to 34%, so he was transfused, post transfusion PCV was 43%.

On the sixth day of admission, tachypnoea was still persistent, fever of 38.1°C was recorded and both CRP and WBC had risen significantly (see Table I). A diagnosis of healthcare associated infection was made and repeat blood culture yielded *Klebsiella pneumoniae* sensitive to Levofloxacin, Ceftazidime and Gentamicin on the 10th day of admission. Antibiotics were changed to Levofloxacin and Clindamycin with resolution of fever and normalization of CRP, however initial tachypnoea persisted.

A blood sample for fungal studies was taken on the 9th day of admission and the result was retrieved on the 13th day of admission which yielded *Candida krusei*. He was subsequently commenced on intravenous fluconazole and respiratory distress gradually resolved.

Table I: Result of investigations

Investigations	Day 1	Day 3	Day 6	Day 7	Day 14	Day 17
FBC	WBC=9670/ul (N=29.9%, L=47.2%, M=21.1%), Platelet-387,000/ul, Haematocrit= 34.9%			WBC=17,500/ul (N=72.9%, 20.9%), Platelet=154,000/ul, Haematocrit=37.8%		
Serum Electrolyte, Urea and Creatinine	Na^+=138mmol/L K^+=4.6mmol/L Cl-=103mmol/L HCO3=22mmol/L Urea=17mg/dl Cr=0.7mg/dl Ca^+=8.5mg/dl Po4=6.9mg/dl					
#BF for MP	Not seen					
***mRDT**	Negative					
Echocardiography	Situs solitus, Levocardia, Atrial and ventricular septum intact, AV and Semilunar valves are normal, Mild pericardial effusion (6mm around the right atrial border), double concordance, no mitral or tricuspid regurgitation, tiny PDA, left sided aortic arch, no coarctation, EF=77%, FS=42%. **Impression:** Tiny PDA, otherwise structurally normal heart.					
ECG readings of patient	Sinus rhythm, Heart rate=160bpm, P-wave is normal, Axis=+100, Infantile progression pattern suggestive of LVH, upright T-wave on V1, V2, V5 & V6 suggestive of RVH					

**=Malaria Rapid Diagnostic Test, #=Blood Film for Malaria Parasite*

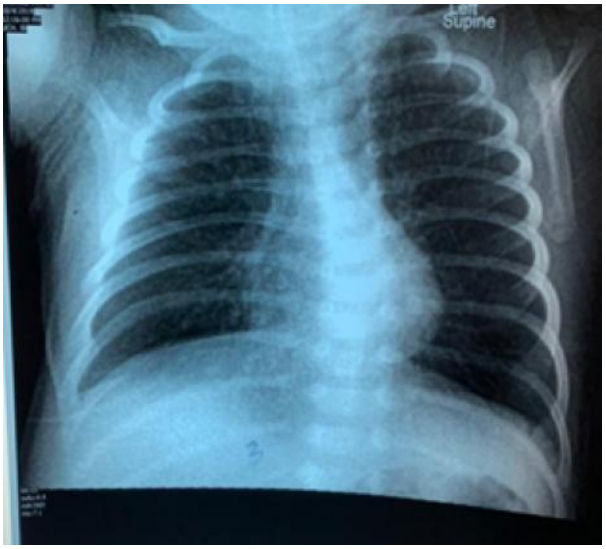

Figure 1: Plain Chest radiograph at admission. Prominent vascular markings are noted. However, no active focal lung lesion is seen. The heart and rib cage are normal.

He was weaned off oxygen on the 15th day of admission. He received 10 days of intravenous fluconazole and was discharged on oral fluconazole to complete 6 weeks. He was seen on follow up subsequently after discharge and respiratory distress had completely resolved.

DISCUSSION

The baby was a low birth weight male neonate who presented on account of difficulty with breathing and low-grade fever which persisted despite use of first line and 2nd line antibiotics. He subsequently developed features of health care associated bacterial infection which was confirmed through a blood culture that yielded *Klebsiella Pneumoniae*. The use of third line antibiotics led to a resolution of fever and drastic decrease in the C-reactive protein but the respiratory distress on account of which the baby was admitted persisted. The history of low birth weight, use of 3 lines of antibiotics with resolution of other symptoms while respiratory distress persisted despite the absence of focal lung lesion prompted the decision to carry out a fungal study which yielded *Candida krusei*. Subsequent commencement of fluconazole led to a gradual resolution of the respiratory distress.

Candida krusei has been recognized as a potentially multidrug-resistant (MDR) fungal pathogen, due to its intrinsic fluconazole resistance combined with reports of decreased susceptibility to both flucytosine and amphotericin B.[2,3]

Despite the known resistance pattern of *Candida krusei*, few studies have demonstrated sensitivity of some strains of *Candida krusei* to fluconazole. Two isolates of *Candida krusei* were classified as susceptible to fluconazole even after repeat testing, in a study to compare the in vitro activity of voriconazole with that of five other antifungal agents including amphotericin B, fluconazole, itraconazole, ketoconazole, and flucytosine carried out in Milan, Italy.[5] Similarly, a large-scale multicenter study carried out in Rome, Italy that compared six commercial systems and the national committee for clinical laboratory standards (M27-A Broth microdilution method) for fluconazole susceptibility testing of Candida species revealed that the gold standard and all but 1 of the 6 methods demonstrated greater than 80% susceptibility/dose dependent susceptibility of fluconazole to non-candida albican including *Candida krusei.*[6]

Hence, fluconazole could be effective in treatment of septicaemia due to susceptible strains of *Candida krusei* and such susceptible strains could be the aetiology of this index case which eventually responded to fluconazole therapy. In our setting, fluconazole is the readily available and safe antifungal to use as most others are unavailable, expensive or require monitoring of serum levels which is not routinely available.

In conclusion, there should be a high index of suspicion of candida infections in preterm/low birth weight neonates so as to reduce the usage of antibiotics and prevent development of multidrug resistant bacterial strains. When suspected, fungal studies should be done where available, however fluconazole should be commenced as empirical antifungal therapy immediately. Despite the known innate resistance of *Candida krusei* to fluconazole, some strains remain susceptible. There is therefore benefit in its therapeutic usage especially when such susceptible strains are identified or other alternative antifungal drugs are not readily available.

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