Medical Mycology Case Reports 1 (2012) 24–26

Contents lists available at SciVerse ScienceDirect

Medical Mycology Case Reports

journal homepage: www.elsevier.com/locate/mmcr

Neonatal fungal sepsis by *Candida krusei*: A report of three cases and a literature review

Selma Amaral-Lopes [a,*], Andressa Moura [b]

[a] Medicine Faculty/Federal University of Bahia, Largo do Terreiro de Jesus S/N, Centro Histórico, Salvador, Bahia, Brazil
[b] Resident Physician Maternity Hospital Professor José MM Neto, Salvador, Bahia, Brazil

ARTICLE INFO

Article history:
Received 16 March 2012
Received in revised form
6 April 2012
Accepted 10 April 2012

Keywords:
Neonatal fungal sepsis
Candida krusei
Fungal infection

ABSTRACT

Candida krusei has been recognised as a potentially multidrug resistant fungal pathogen due to its intrinsic fluconazole resistance and reports of decreased susceptibility to amphotericin B. Moreover, the medical literature provides only four articles that report on four cases of fungemia caused by *C. krusei* in newborns. The objective of this study was to report on the clinical and epidemiological characteristics of three cases of fungal sepsis in the neonates caused by *C. krusei*.

1. Introduction

Longitudinal studies have detected an increase in the cases of fungal infection by non-albican *Candida* species, and admission into a Neonatal Intensive Care Unit (NICU) quadruples the risk of infection by these pathogens. *Candida krusei* has been recognised as a potentially multidrug resistant fungal pathogen due to its intrinsic fluconazole resistance and reports of decreased susceptibility to both flucytosine and amphotericin B [1]. Moreover, there are only four articles in the medical literature that report on three isolated cases and an outbreak of seven cases [2] of fungemia caused by *C. krusei* during the neonatal period. Even in major epidemiological investigations, its prevalence is very low at this stage of life. The objective of this study was to report on the clinical and epidemiological characteristics of three cases of fungal sepsis in the neonatal period caused by *C. krusei* in an NICU. The day of birth was signified as day 0 in case one and two, and 30th day of life in case three.

2. Patient one

A 31-year-old mother had five prenatal appointments with negative serology, a complete use of corticosteroids, with a vaginal delivery. However, the amniotic membrane was ruptured prematurely, three days before, with a suspected diagnosis of chorioamnionitis. The newborn was a female and was born with a gestational age of 25 weeks; she had an Apgar score of 4/7 and weighed 760 g. The newborn was intubated in the delivery room and admitted to the NICU. On the same day of birth, she was also hypothermic, hyperglycaemic and had sternal retraction. She received two doses of surfactant (200+100 mg/kg). Antibiotic therapy was initiated (ampicillin 200 mg/kg/day and gentamicin 5 mg/kg/48 h), parenteral nutrition (PN) (13 day of use) and a venous umbilical catheter was used for eight days. On day 3 a trophic diet was initiated. An abdominal distention evolved with palpable and visible rings, which improved after rectal stimulation. On day 5 she showed residues of gastric bile, whereby the diet was suspended and the antibiotic scheme modified due to leucometric worsening. On day 6, prophylactic fluconazole (3 mg/kg/twice a week) was introduced and the diet was reintroduced. She also showed a positive blood culture for *C. krusei*. On day 7, a surgical dissection of the right was undertaken and lasted for 11 day. The newborn was extubated on day 9 and stably maintained in nasal intermittent positive pressure ventilation (NIPPV). Therapeutic fluconazole (12 mg/kg/day) was started on day 12, but the medication was modified to liposomal amphotericin B (5 mg/kg/day) on day 17 because clinical and leucometric worsening associated with the presence of opacity in the optic nerve was detected to the fundoscopy. Parallel to this condition, intraventricular haemorrhage with intracranial hypertension was diagnosed and ventricle derivation was indicated.

3. Patient two

A twenty-three-year-old mother had two prenatal appointments, exhibited negative serology, was a smoker, had an amniotic membrane rupture for two days, and had a double caesarean

* Corresponding author.
E-mail address: selminhalopes@gmail.com (S. Amaral-Lopes).

2211-7539/$ - see front matter © 2012 International Society for Human and Animal Mycology. Published by Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.mmcr.2012.04.002

delivery. The firstborn twin was a male with a gestational age of 31 weeks and weighed 1680 g. Treatment for presumed neonatal sepsis with ampicilina (200 mg/kg/day) and gentamicina (4 mg/kg/day) was started. On day 4 he had bilious regurgitations, and there was evidence of pneumoperitoneum on the x-ray of the abdomen. He underwent an urgent surgery to resection the distal ileum, on day 6, and the echocardiogram showed echogenic formation on the ventricular outflow tract. On day 17, there were signs of a positive blood culture of *C. krusei* and a positive blood culture for *Candida tropicalis*. Liposomal amphotericin B (5 mg/kg/day) was used for five days and fluconazole (12 mg/kg/day) was used for 19 day. An ileostomy was undertaken to reconstruct the transit on day 59. A wide spectrum of antibiotic therapy was used for 64 day, PN was used for 30 day, and central venous access was used for 53 day.

4. Patient three

A twenty-one year-old mother had two prenatal appointments, negative serology, and had a caesarean delivery with serious gestational hypertension (GH). She underwent corticotherapy. A female was born with a gestational age of 29 weeks and weighed 938 g. She had an Apgar score of 9/10. The newborn was intubated in the birthing ward and received one dose of surfactant. She was extubated after 24 hours and a nasal continuous positive airway pressure (CPAP) was maintained for three days. Thereafter she made good progress and for 4 weeks she fed normally and gained weigth. On the 30th day after birth, she developed an abdominal distention with enterorrhagia, hyperactivity, hyperglycaemia and free fluid in the abdominal cavity evident in the abdominal ultrasound. An appendectomy was undertaken with exploratory laparotomy. There was evidence of a positive blood culture of *C. krusei* on day 1, and a positive evolution in the condition after using liposomal amphotericin B (5 mg/kg/day) for 23 day was observed. PN was used for 30 day, central venous access was used for 22 day, and wide spectrum antibiotic therapy was used for 14 day.

5. Discussion

The literature has accumulated approximately 10 cases of *C. krusei* in the neonatal period (the findings are summarised in Table 1). Important data in these cases include the findings that the amniotic membrane rupture occurs between 48 and 72 h before the birth, allied with precocious gastrointestinal symptoms (abdominal distension, and bilious regurgitation) and that there is an association with other risk factors for fungal sepsis, including prematurity and prolonged use of PN. In our NICU, between April 2008 and June 2011, we had 173 cases of fungal infection, 67 through *Candida albicans* and 106 non-albicans (61.27%). Cases one and two, though initially precocious, had favourable outcomes that were likely related to the earliness of the start of the treatment. The second case responded favourably to fluconazole, possibly because *C. krusei* was not the infecting pathogen. In this study, despite the third case showing later fungal infection, the three newborns showed precocious gastrointestinal symptoms.

Even in major studies about epidemiological surveillance, there has not been any identification of *C. krusei* infection during the neonatal period. Horn et al. (2009) [3] evaluated the outcome of 2019 cases of candidemia, where he discovered 51 cases of *C. krusei* but none in the neonatal period. In the study by Fridkin et al. (2006) [4], the incidence of infection with candida between 1995 and 2004 was evaluated, and only three cases of *C. krusei* were found. Tiraboshi et al. (2010) [5] reported one case of

Table 1
Clinical data for reports of *C. krusei* fungemia.

References	Weight/sex	GA/age	Underlying condition	Previous antifungals	Risk factors	Presentation	GastS	Culture's origin	Therapy	Outcome/evolution
Wanjari et al., 2008 [6]	1900 g/M	28 w/2 d	Prematurity, Congenital tuberculosis	No	No	Fever	Gastric colonisation	Gastric blood	FluC AmB	Live
Patted et al., 2009 [7]	*/M	34 w/60 d	Prematurity, SDR Surfactant	*	TPN BSA	Loss of consciousness Pancytopenia Endocarditis	NEC	Right ventricular mass	*	Death
Natale et al., 2009 [8]	1160 g/M	26 w/17 d	Prematurity	FluC prophylaxis	BSA PICC	Thrombocytopenia, fever, apnoea, hypoactivity	*	Peripheral blood culture	LAmB CaspF	Live

*Uninformed; F, female; M, male; GA, Gestational age in weeks; BSA, broad-spectrum antimicrobials; Age: days of life; SDR: Respiratory Distress, TPN, parenteral nutrition; GastS, Gastrointestinal symptoms; NEC: Necrotising enterocolitis, AmB. Amphotericin B; LAmB: Liposomal amphotericin-B; FluC, fluconazole; CaspF, caspofungin; PICC, percutaneous inserted central inserted central catheter.

congenital candidiasis in a premature baby of 27 weeks of gestational age and a weight of 1020 g. Chorioamnionitis was determined to be a triggering factor. Parallel to this finding, blood cultures tested positive for *C. albicans* and *C. krusei*. The author concluded that *C. krusei* did not play a pathogenic role.

Another study, undertaken by Wanjari et al. (2008) [6], reported one case of a 28-week-old premature baby that weighed 1900 grams with a diagnosis of congenital tuberculosis. On the second day after birth, the newborn had a positive blood culture for *C. krusei*. The pathogen was sensitive to amphotericin B and resistant to fluconazole, and a good clinical response developed after the institution of adequate treatment.

Sound practices in the handling of premature newborns includes the following: hand hygiene among health professionals, the immediate removal of catheters when a fungal infection is suspected, the rational use of antibiotics, an enteral diet that is initiated as soon as possible with the purpose of diminishing the time for using parenteral nutrition, the avoidance of H2 blockers and the use of prophylactic fluconazole in premature newborns with a weight below 1000 g; these practices can diminish the incidence of fungal infection in neonatal units. Studies have shown that *C. krusei* has reduced sensitivity to fluconazole, however, prophylactic fluconazole can be effective in the prevention of neonatal candidemia (Manzoni et al., 2011) [9]. Despite studies that show that fungal sepsis is related highly to morbidity–mortality, our patients cited in this article had a good clinical response and were eventually released from the hospital. A diagnosis of candidemia should be considered in cases of gastrointestinal symptoms in neonatal patients. The cases of neonatal *C. krusei* in our NICU and the indexed medical literature were rare.

Conflict of interest

The consent of Clinical Research Directorship was obtained for publication of these cases. The authors declare that they have no competing interests.

References

[1] Pfaller MA, Diekema DJ, Gibbs DL, et al. *Candida krusei*, a multidrug-resistant opportunistic fungal pathogen: geographic and temporal trends from the ARTEMIS DISK antifungal surveillance program, 2001 to 2005. Journal of Clinical Microbiology 2008;46:515–521.
[2] Handrick W, Schonmborn C, Spencer FB, Huckel D. Infections due to *Candida krusei* in neonates. Paediatric und Padologie 1989;24:289–295 [German].
[3] Horn DL, Neofytos D. Epidemiology and outcomes of candidemia in 2019 patients: data from the prospective antifungal therapy alliance registry. Clinical Infectious Diseases 2009;48:1695–1703.
[4] Fridkin SK, Kaufman D, Edwards JR, Shetty S, Horan T. Changing incidence of *Candida* bloodstream infections among NICU patients in the United States: 1995–2004. Pediatrics 2006;117:1680–1687.
[5] Tiraboschi IC, Niveyro C, Mandarano AM, et al. Congenital candidiasis: confirmation of mother–neonate transmission using molecular analysis techniques. Medical Mycology: Official Publication of the International Society for Human and Animal Mycology 2010;48:177–181.
[6] Wanjari K, Mathur M, Baradkar VP, Kumar S. Congenital tuberculosis with candidal sepsis in a neonate. Indian Journal of Pathology and Microbiology 2008;51:289–291.
[7] Patted SV, Halkati PC, Yavagal ST, Patil R. *Candida krusei* infection presenting as a right ventricular mass in a two month old infant. Annals of Pediatric Cardiology 2009;2:170–172.
[8] Natale F, Castronovo A, Regoli D, Curtis M, Manzoni P. Successful treatment with caspofungin of refractory *Candida krusei* candidemia in a very low birth weigth preterm infant. Pediatric Infectious Disease Journal 2009;28:452.
[9] Manzoni P, Jacqz-Aigrain E, Rizzollo S, et al. Antifungal prophylaxis in neonates. Early Human Development 2011;87:59–60.