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First case reports of bloodstream infection by *Candida magnoliae* in two neonates with low birth weight

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ABSTRACT

Invasive candidiasis is a serious neonatal sepsis with high morbidity and mortality despite the correct treatment. *Candida albicans* and *Candida parapsilosis* are the most common pathogens causing these events; however, a new emergent pathogen has evolved with time. Herein, we describe two cases of *Candida magnoliae* infection in neonates with a fatal outcome. This microorganism is commonly used in the food industry given its high capacity to produce erythritol and mannitol. This report is important to gain more information about this pathogen and manage it in a more effective way.

1. Introduction

The incidence of fungal infections in neonates has increased during recent decades. Prematurity, low birth weight, use of antibiotic treatments, and prolonged stays in neonatal care units favor the occurrence of sepsis due to fungal species [1]. For many years, the main causative agent of invasive candidiasis was *Candida albicans*; however, recent studies have shown a change in profile of invasive candidiasis. Rare species of emergent pathogens are appearing at a frequency of 1.2–3.2%. These species include *Candida ernobii*, *Candida pelliculosa*, *Candida lipolytica,* and *Candida norvegensis* [2–5]. Two cases have been reported in the literature on infections caused by *Candida magnoliae*: one tenosynovitis case in an immunocompetent child in the United States and the other case in a terminal oncology patient in Italy [6,7]. In the present study, we describe two low birth weight neonates with primary bloodstream infections caused by *C. magnoliae*.

2. Case reports

The first case of *C. magnoliae* infection occurred in a male neonate born on September 18, 2017, at 27 weeks of gestation in a maternity hospital. The birth was a cesarean delivery because the mother presented a serious gestational hypertension disease. The newborn had depression at birth with an Apgar score of 6/9 and weighing 0.985 g. In the birth room, the patient evolved bradycardia and was ventilated and placed in continuous positive airway pressure (CPAP). Subsequently, the child was admitted to the neonatal intensive care unit (NICU) with hypothermia (33 °C). In the unit, an umbilical catheter was introduced and the total parenteral nutrition (TPN) installed. After culture collection, ampicillin and gentamicin were prescribed. At 48 h, respiration worsened, and hence, mechanical ventilation was initiated. Additionally, a reduction in platelets and an increase in C-reactive protein (CRP) were observed. The child remained stable, and culture results from the first day of life after 48 h were negative. On day 3, the umbilical catheter was removed and a peripherally inserted central catheter (PICC) was introduced. On September 24, the child continued to present tachycardia, hyperthermia (38 °C), apnea, desaturation, bleeding through the orotracheal tube, and thrombocytopenia; new culture samples were collected, and the antibiotic treatment was changed to oxacillin and amikacin. On the same day, the child received a red blood cell transfusion (10 ml), and there was an increase in the ventilatory parameters. Two days

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later, the condition remained serious and the pulmonary auscultation presented diffuse rhonchus and an irregular respiratory pattern. In the following days, the patient remained in a serious condition, with abdominal distention, hyperthermia, hypoactivity, thrombocytopenia, and an increase in CRP level. There was infiltration of the PICC, which was changed. On October 1, because of the worsening of the condition, a new culture collection was performed, and there was a change in antibiotics, with cefepime and vancomycin being administered. On October 2, pulmonary hemorrhage and pneumothorax were observed; a chest drain was introduced and the culture collected on September 24 was received, which was positive for *C. magnoliae*. Given the culture result, amphotericin B was administered. In the following days, the patient remained in a serious condition, with hypoactivity; discolored, high volume of secretion through the tube; hyperthermia continuing for some days (reaching an axillary temperature of 40 °C); and secretion through the drain. Cultures were collected during this period, and antibiotics were changed from cefepime to meropenem. On day 21, the culture collected on day 13 was positive for *Serratia marcescens*, which was the microorganism responsible for the outbreak that the NICU was experiencing at that moment. Therefore, according to an antibiogram, the antibiotics were changed to ciprofloxacin and tigecycline. A peripheral puncture was made, and concentrated red blood cells (15 ml) were introduced; the baby was then placed in contact precaution and transferred to another bed. From then on, the patient presented worsening clinical and laboratory signs, with death being the final outcome on October 19 and 31 days of life.

The second case of *C. magnoliae* occurred in a female neonate born on August 28, 2017, at 37 weeks of gestation. The birth was a cesarean delivery because the neonate presented gastroschisis. The patient was born with an Apgar score of 7/9, weighing 1.625 g, and presenting cyanosis in the extremities, and the silo was placed soon after. After being admitted to the NICU, culture collection was realized and a peripheral puncture was made through which the analgesic and antibiotic ampicillin and gentamicin were administered. The following day, the closure of the abdominal wall was surgically performed, and tests were conducted; the results showed an increased CRP level and a normal blood count. However, the abdomen was distended and painful to touch and the orogastric tube presented bilious residue. The PICC was inserted on the same day. The patient continued to present a distended abdomen with time, which was painful to the touch, with bilious residue and the CRP remained altered, however, diminished. On day 6, the culture result was positive for oxacillin-resistant *Staphylococcus epidermidis,* and the antibiotic was changed to vancomycin (treatment for 15 days). Subsequent cultures were performed, all presenting negative results. Because of the persistence of symptoms, the absence of positive culture results, and the continuity of an altered CRP level, cefepime was administered (treatment for 11 days) on day 10. As the newborn showed improvement, an abdominal ultrasound was performed on day 14, which showed the presence of distended handles with liquid content in their interior. Given this result, it was decided to perform a new surgical intervention on September 16. During the surgical intervention, the release of the flanges and an appendectomy were carried out. On the day following surgery, the patient presented a large volume of bilious residue and thrombocytopenia. On September 21, the newborn initiated episodes of regurgitation, hypoactivity, and tachycardia and presented a distended and painful abdomen. The patient remained in this state for two more days until new examinations were performed; the results continued to show thrombocytopenia and an elevated CRP level. A new culture was collected after obtaining negative results, and the antibiotic treatment was changed to meropenem and vancomycin. During the following days, the patient presented worsening clinical and laboratory signs, with death as the final outcome on October 1. On the patient's final day, cultures were collected, and results proved positive, postmortem, for *C. magnoliae*.

3. Discussion

A prospective study found 89 cases of candidemia in neonatology. The average age was 16 days at the start of the infection (1–28 days). The main species isolated were *C. albicans* (44%), *Candida parapsilosis* (27%), *Candida tropicalis* (15%), and *Candida guilliermondii* (5%) [8]. Epidemiological studies have shown that non-*C. albicans* species have emerged as important agents causing fungemia [9]. The incidence of candidemia is 3% in neonates with weight between 751 and 1000 g and 1% in neonates with weight between 1001 and 1500 g [10]. In October 2007, a clinically related *Candida* species appeared in the blood culture of a 42-year-old Chinese patient with stomach cancer [7]. The species observed, *C. magnoliae*, is commonly used in the food industry because of its high capacity to produce erythritol and mannitol, which are used as functional substitutes for sugar in various foods [11,12]. This microorganism has the ability to quickly consume fructose and grow in various pH levels (2.5–8.0) [13,14].

C. magnoliae infections are rare. In literature, to date, two cases of *C. magnolia* infection have been described. Low birth weight, preterm neonates present high morbidity and mortality rates because of the immaturity of their lungs, the immune system, and other factors [15]. In our maternity unit, we use the MALDI-TOF MS method for microbiological identification. In these two cases, we did not have the opportunity to confirm the results by another microbiological identification method. The treatment for one of the cases was done with amphotericin B deoxycholate; however, there was a fatal evolution similar to that of the other case. The antibiogram showed sensitivity to echinocandins. Amphotericin was not tested because of the lack of a kit at the local laboratory. The result for the second case was received postmortem; therefore, antifungal treatment was not administered. There are few cases for us to be able to arrive at a conclusion, but there remains a doubt regarding the lethality that this yeast possesses in neonates. Both neonates had worsening clinical and laboratory conditions, and this led us to use a broad-spectrum antibiotic.

The first step before infection is colonization, and the time between two culture collections was 7 days, which suggests a possible common source of contamination. The children were fed with natural milk, which discarded the possibility of contamination through milk bank. In the case of contaminated parenteral nutrition, this would have presented more cases, given that the majority of neonates from the sector are premature with low birth weight and also susceptible to developing infection through the same agent. Another possibility may be the ingestion of industrialized products by family members or health professionals who transmitted the colonizing yeasts to the neonates. This hypothesis, however, remains difficult to prove, given that when receiving the microbiological result, 120 hours after the start of the infection, the colonization had already passed, thus making causal/root research impossible. The two cases represented an outbreak for us. Hence, NICU and laboratory teams were alerted to initiate a more in-depth investigation if another case appeared, but fortunately, this did not occur. We did not perform a culture of milk, parenteral nutrition, or any other kind of parenteral medication.

4. Conclusion

Neonatal infection from *C. magnoliae* is a rare condition. We had two cases in a short period of time, both with a fatal evolution. To

date, the sensitivity of these microorganisms to antifungal agents existent on the market is unknown. Further pharmacological and clinical research is necessary to elucidate the best treatment in these cases.

Conflict of interest

The corresponding author on behalf of all the authors declares that there is no conflict of interest.

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