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CASE REPORT

Kodamaea ohmeri fungemia in a newborn. Case Report

Fungemia por Kodamaea ohmeri en un neonato. Reporte de caso

Hernando Pinzón-Redondo[1,2] Valentina Arias-Macea[1,3] Cristina Herrera-Arrieta[1,3] Jairo Jiménez-Rodelo[2] Dilia Fontalvo-Rivera[1,3]

[1] Fundación Hospital Infantil Napoleón Franco - Department of Infectious Diseases - Pediatric Infectious Diseases Research Group - Cartagena - Colombia.
[2] Universidad de Cartagena - Faculty of Medicine - Department of Pediatrics - Cartagena - Colombia.
[3] Universidad del Sinú - Cartagena Campus - Faculty of Medicine - Department of Pediatrics - Basic and Clinical Research Group GIBACUS - Cartagena - Colombia.

Abstract

Introduction: *Kodamaea ohmeri*, considered an emerging human pathogen in recent decades, is a rare infection with a high mortality rate (40-50%). It mainly affects individuals with weak immune systems, such as neonates and older adults.
Case presentation: A 19-day-old male patient with acute fever was taken to a tertiary care children's hospital in Cartagena, Colombia, with no history of disease. The patient came from a rural area in which he lived in an environment where food supplies were traded in small-scale businesses. Physical examination was normal and biomarkers of infection showed C-reactive protein at 4.7mg/L. The patient was admitted to the neonatal intermediate care unit, where treatment with oxacillin and amikacin was started under suspicion of late bacterial sepsis, but this regimen was suspended 2 days later due to a report of yeast growth in fungal blood culture (Saboraud agar), so treatment with caspofungin at 50mg/m² was started due to suspicion of candidemia. Finally, two more days later, the yeast was identified as *K. ohmeri*, which was not resistant to the antifungal agent used. On the fifth day of treatment with the antifungal agent, no fungus was reported in the follow-up blood culture, and the patient was discharged 10 days after initiating treatment without clinical or paraclinical evidence of side effects.
Conclusion: Given its high mortality rate, timely detection and treatment of *K. ohmeri* fungemia is critical. For this reason, it should be suspected in patients with a weak immune system who present with signs of infection in the absence of clinical evidence of other more common infections and in whom exposure to this yeast is a possibility, as was the case of our patient.

Resumen

Introducción. La fungemia por *Kodamaea ohmeri*, un patógeno humano emergente en las últimas décadas, es una infección que, aunque poco frecuente, tiene una alta tasa de mortalidad (40-50%) y afecta principalmente individuos con sistemas inmunes débiles como neonatos y adultos mayores.
Presentación del caso. Paciente masculino de 19 días de edad con fiebre aguda atendido en un hospital infantil de tercer nivel de Cartagena, Colombia, sin antecedentes patológicos, procedente de un área rural en donde habita en un ambiente de comercio minoritario de insumos alimentarios. El examen físico fue normal y los biomarcadores de infección mostraron proteína C reactiva en 4.7mg/L. El paciente fue internado en la unidad de cuidados intermedios neonatales, en donde se inició manejo con oxacilina y amikacina bajo sospecha de sepsis bacteriana tardía, pero este régimen fue suspendido 2 días después por reporte de crecimiento de levaduras en el hemocultivo para hongos (agar Saboraud), por lo que se inició tratamiento con caspofungina a 50mg/m² por sospecha de candidemia. Finalmente, 2 días después la levadura fue identificada como *K. ohmeri* no resistente al antifúngico utilizado y en el quinto día del tratamiento con el antimicótico no se reportó presencia del hongo en el hemocultivo para hongos de control, siendo dado de alta a los 10 días de haber iniciado el tratamiento antifúngico sin evidencia clínica ni paraclínica de efectos secundarios.
Conclusión. Dada su alta tasa de mortalidad, la detección y el manejo oportunos de la fungemia por *K. ohmeri* son fundamentales, razón por la cual se debe sospechar en pacientes con un sistema inmune débil que presentan signos de infección en ausencia de evidencia clínica de otras infecciones más comunes y en los que la exposición a esta levadura es una posibilidad, como fue el caso de nuestro paciente.

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Corresponding author: Dilia Fontalvo-Rivera. Grupo de Investigación Básicas y Clínicas GIBACUS, Departamento de Pediatría, Escuela de Medicina, Universidad del Sinú. Cartagena. Colombia. E-mail: diliafontalvor@gmail.com.

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Introduction

In preterm infants, especially among those with very low birth weight, invasive fungal infections (IFI) are associated with significant morbidity and mortality, as they can affect practically any organ and can be rapidly fatal.[1] During the neonatal period, the presence of IFIs is associated with an increased risk of mortality; for example, it has been reported that mortality rates due to candidiasis in neonates with a birth weight of <1 000g range from 19.7% to 35.0% depending on the *Candida* species.[2]

Kodamaea ohmeri is an environmental yeast of the class Ascomycetes that is frequently used in the food industry to facilitate fermentation processes. In recent decades, it has been considered an important emerging human pathogen3 due to its high mortality rate (40-50%).[4]

The following is a case of a full-term newborn with no relevant conditions who developed *K. ohmeri* fungemia.

Case presentation

A 19-day-old male newborn was taken to the emergency room of the Hospital Infantil Napoleón Franco Pareja (a tertiary care center in Cartagena, Colombia) due to a sustained fever (38.8°C) that had been occurring for the past 15 hours, as well as occasional sneezing, and a clear nasal discharge. Regarding the characteristics of the pregnancy, the patient was born at 40 weeks by cesarean section with appropriate anthropometric measurements (weight: 3 253 kilos; height: 53 centimeters) and APGAR score (8/10 at one minute). No complications during pregnancy such as illness or infection were documented.

The newborn metabolic screening results obtained as part of the initial assessment in the emergency room were within normal ranges, with negative results for perinatal infections (syphilis, toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and hepatitis B). Physical examination found oxygen saturation of 98%, weight of 4 300g, height of 53cm, and head circumference of 37cm; the patient was hemodynamically stable. It should be noted that the newborn had a well-defined port wine-colored, painless, smooth-surfaced stain on the left frontal region (Figure 1), which, according to the mother, he had since birth.

Figure 1. Face hemangioma.

After 2 hours of observation in the emergency room and due to the diagnostic suspicion of late neonatal sepsis, the patient was transferred to the neonatal intermediate care unit (NICU). Since his clinical manifestations and the results of imaging and laboratory tests on admission to the NICU (chest X-ray, blood glucose, blood bilirubin, electrolyte panel, arterial blood gases, complete blood count, urinalysis, C-reactive protein [CRP], cerebrospinal fluid [CSF], liver and renal function tests, respiratory pathogens panel) were normal, except for CRP level (4.76mg/L) (Table 1), antibiotic therapy with oxacillin (150mg/kg/day) and amikacin (15mg/kg/day) was started indefinitely until the results of the requested culture tests (blood cultures, urine culture, and CSF culture) were available.

Blood cultures for aerobic and anaerobic bacteria, urine culture, and CSF culture were negative; however, blood culture for fungi on Sabouraud agar showed growth of yeasts at 45 hours.

Table 1. Laboratory tests.

	Results	Reference values
Blood count	Hemoglobin: 12.7g/dL	13.5±3g/dL
	Hematocrit: 39.2%	39±2%
	MCV: 108 femtoliters (fl)	108±10
	MCH: 35 mg/dL	34±2
	Leucocytes: 12 700	11 400 (5.0-19.0)
	Neutrophils: 47%	41-68%
	Lymphocytes: 45%	26-36%
	Eosinophiles: 4%	0.4-3%
	Monocytes: 4%	1-7%
	Platelets: 270 000	140 000-470 000
C-reactive protein	34.76mg/dL	<1mg/dL
Glucose	78mg/dL	74-107mg/dL
Urinalysis	Clear appearance pH: 6.2; density: 1 015	Clear appearance pH: 6.0; density: 1 025
	Negative: proteins, glucose, ketone bodies	Negative: proteins, glucose, ketone bodies
	Negative: Bilirubin, hemoglobin	Negative: Bilirubin, hemoglobin
	Negative: Nitrites, leukocyte esterase	Negative: Nitrites, leukocyte esterase
	Epithelial cells: scanty	Epithelial cells: negative or scanty
	Leucocytes: 0-3/field (HPF) renal cells: 1-2/c	Leucocytes: 0-2/HPF renal cells: 0-2/HPF
Serum electrolytes	Sodium: 141 milliequivalents (mEq)/liter (L)	134-146
	Potassium: 4.9mEq/L	3.7-5.9
	Chloride: 95mEq/L	96-113
	Calcium: 9mEq/L	8.5-10.2
Bilirubin (B)	Total B: 1.9mg/dL	0.2-1.4
	Direct B: 0.7mg/dL	<0.3
	Indirect B: 1.1mg/dL	
Creatinine	0.40mg/dL	0.2-0.6
Urea nitrogen	6.42mg/dL	3-12
Cytochemistry of cerebrospinal fluid (CSF)	Glucose level: 54mg/dL; protein level: 52mg/dL Leukocyte count: 6cell/mm3 Neutrophils: 20% Lymphocytes: 80%	
Respiratory pathogens panel	Negative for: • Virus: adenovirus, coronavirus HKU1, coronavirus NL63, coronavirus 229E, coronavirus OC43, human metapneumovirus, human rhinovirus/ enterovirus, influenza A, influenza A/H1, influenza A/H1-2009, influenza A/H3, influenza B, parainfluenza 1, parainfluenza 2, parainfluenza 3, parainfluenza 4, respiratory syncytial virus) • Bacteria (*Bordetella pertussis, Chlamydophila pneumoniae, Mycoplasma pneumoniae*)	
Urine culture	Negative	
Blood culture of anaerobic and aerobic bacteria	Negative	
Fungal blood culture	*Kodamaea ohmeri* susceptible to amphotericin B, caspofungin, fluconazole, flucytosine, micafungin, voriconazole	
CSF culture	Negative	

In view of the findings in the admission tests, as well as in the cultures, and the fact that the patient's condition was stable, after 2 days of stay at the NICU he was transferred to the inpatient service (i.e., three days since admission). He was immediately examined by specialists from the infectious disease department, who, suspecting candidemia, suspended antibiotic treatment and started treatment with caspofungin (50mg/m²/day) for 10 days.

That same day, clinical assessment (fundus examination) and imaging tests (cranial ultrasound and renal and urinary tract ultrasound) were performed to look for evidence of fungal colonization, with normal results. Also, an echocardiogram was performed, showing mild tricuspid valve insufficiency without hemodynamic consequences, but no images suggestive of infection were observed. Moreover, on the fourth day of hospital stay, the yeast found in the blood culture was identified as *K. ohmeri*, which was not resistant to the antifungal agent used (VITEK® 2 automated system for detection of microbial agents). Five days into treatment with the antifungal agent, no *K. ohmeri* was reported in the follow-up fungal blood culture.

Abdominal ultrasound performed four days after admission showed no evidence of vascular malformations in the soft internal organs. Then, on the fifth day of hospitalization, specialists from the hematology service examined the macula located in the left frontal region and established that it was a low-risk superficial hemangioma, recommending follow-up and defining the need for a biopsy depending on clinical progression.

On the sixth day of stay, the patient's close relatives (mother and maternal grandparents) were interviewed by professionals from the mental and social health group of the institution. They found that they worked in the petty trade of food supplies and that they lived in a rural area lacking some basic services, which could have increased the newborn's exposure to *K. ohmeri* and the subsequent fungemia.

Since the patient had an adequate clinical course with the antifungal treatment (caspofungin), he was discharged from the hospital after 10 days of treatment, on the 12th day of stay, with the indication to attend follow-up appointments. At his last follow-up appointment at the time of writing this case report (June 2023), the patient exhibited a good health condition with no signs of infection.

Discussion

Nosocomial fungemia is usually associated with factors such as the use of broad-spectrum antibiotics, insertion of a central venous catheter, transplantation, and the development of neutropenia and decreased cell-mediated immunity.[5]

K. ohmeri is a yeast that is considered an emerging human pathogen, which can cause life-threatening infections, especially in immunocompromised patients.[3] This bacterium has been used in the food industry because of its fruit and vegetable fermentation properties.[3,4,6] In the same way as other yeasts, its environmental dissemination has been influenced by multiple factors such as climate change[7] and the widespread use of fungicides in agriculture.[8]

It has been established that *K. ohmeri* can cause serious diseases such as fungemia, peritonitis, funguria, endocarditis, cellulitis, catheter-related bloodstream infections, and cyanosis.[3,9] A mortality rate as high as 50% has been reported for invasive infections caused by this microorganism.[3]

Regarding the populations at risk for *K. ohmeri* infection, according to the 2021 systematic review performed by Zhou *et al.*[3] (51 studies), of the 67 patients included in the studies, 10 were children (54 days-11 years), 22 were adults, 24 were older adults, and 11 were newborns.

Furthermore, according to these authors, there were 2 outbreaks of this fungemia: 1 in China (6 newborns) and another in Turkey (2 children aged 8 months and 10 years).

In Colombia, cases of *K. ohmeri* infections have also been reported in the pediatric population. For example, a case was reported by Alvarado-Socarras *et al.*[10] in a 12-day-old full-term newborn, and another case was reported by Vivas *et al.*[11] in a 54-day-old premature newborn (35 weeks). It is worth mentioning that, in these cases, both patients survived despite requiring care at the NICU.

In our case, the patient was a newborn with persistent fever, no history of infectious perinatal exposure, no apparent risk factors associated with his age, and laboratory and imaging tests that did not show evidence of infectious agents common to the neonatal stage. However, he received antibiotic therapy (oxacillin and amikacin) for 2 days due to the possibility of late neonatal sepsis, which was discontinued due to the growth of yeast in the blood culture that was initially considered as candidiasis, since *K. ohmeri* can be mistaken for *Candida sp.* when only traditional methods of identification are used. In unclear cases, the identification of the pathogenic agent is achieved through genotyping.[12]

For the identification of the fungus, no genotyping was used in this study due to limitations in the access to this type of tests in our health institution. However, this was not a problem for the proper treatment of the patient because by day 4 of hospital stay, using the VITEK2 automated microbial agent detection system, it was possible to identify the yeast reported in the blood culture as *K. ohmeri* not resistant to the antifungal agent used, and as of day 5 of the antifungal treatment, initiated based on the preliminary report of yeasts, the follow-up fungal blood culture did not show the presence of this yeast.

Accordingly, in a study conducted at a pediatric care center in India in 398 culture-proven fungemia cases (median age 87 days), it was reported that of 148 isolates that had been initially identified as *Candida tropicalis*, 38 (25.7%) were re-identified as *K. ohmeri* by genotypic characters.[13] In our case, Saboraud Agar culture medium was used for isolation and identification of the fungus, as it has been successfully used for this purpose in other studies.[4,14]

K. ohmeri may cause both invasive and non-invasive infections, the former being more common (92.5%).[3] Among invasive infections, fungemia (74.2%) is the most frequent, followed by endocarditis (11.3%), and peritonitis (6.4%). Other less frequent types of infection caused by this microorganism are urinary tract infection, pneumonia, keratitis, cellulitis, and subcutaneous infection.[3]

As for dermatological findings, the patient reported here had a port-wine stain on the left frontal region which, according to the hematology service assessment, was considered to be a low-risk superficial hemangioma. Although the literature has not reported a direct relationship between the presence of hemangiomas and a greater susceptibility to *K. ohmeri* fungemia, there are cases in which a possible association between this type of neoplasm and infection has been reported. For example, Okorie *et al.*[15] described the occurrence of late ulceration of a hemangioma in a 2-year-old child infected with SARS-CoV-2.

In terms of the treatment of *K. ohmeri* infections, according to the systematic review by Zhou *et al.*,[3] amphotericin B was the most frequently used antifungal drug (44.6%), followed by fluconazole (35.4%), caspofungin (13.8%), voriconazole (7.7%), micafungin (4.6%), and itraconazole (4.3%). Moreover, combined treatment was used in 24.6% of cases, the most common combination being amphotericin B+fluconazole (13.8%), followed by fluconazole+equinocandins such as caspofungin and micafungin (4.6%). In this regard, Alvarado-Socarras *et al.*[10] reported the case of a full-term newborn who developed *K. ohmeri* infection while receiving clinical care at the hospital due to a mediastinal mass

that required multiple interventions, for which he was treated with amphotericin B, resulting in a satisfactory resolution of the fungemia.

In our patient, treatment was based on the administration of caspofungin at 50mg/m² for 10 days, also achieving a good response. A study on the pharmacokinetics and safety of this antifungal in 18 children under 3 months of age with candidiasis showed that caspofungin at a dose of 25mg/m² once daily was well tolerated by the participants, reaching plasma levels similar to those obtained in adults receiving doses of 50mg/day.[16]

On this matter, caspofungin has been reported to be an effective and safe treatment option for candidemia in low-birth-weight neonates. For example, Jeon & Sin,[17] in a study performed in 7 extremely premature newborns (gestational age: 23-24 weeks; birth weight: 530-825g) with systemic candidiasis refractory to liposomal amphotericin B, reported that therapy with caspofungin (2mg/kg/day) allowed complete resolution of candidemia without adverse effects in all cases. Moreover, according to these authors, there were no recurrent episodes of candidemia after discontinuation of caspofungin.

Similarly, Natarajan *et al.*,[18] in a study that reviewed the cases of 13 infants (birth weight: 530-5 600g; 12 preterm [24-28 weeks] and 1 at term), report that the addition of caspofungin to conventional antifungal therapy (liposomal amphotericin B and/or fluconazole or flucytosine) for the treatment of refractory candidemia resulted in sterilization of blood cultures in 11 of these patients after a median time of 3 days after its addition. However, it should be pointed out that several adverse events were reported in this study, such as thrombophlebitis, hypokalemia and elevated liver enzymes, and 3 newborns presented a second episode of candidemia.

Furthermore, the use of high doses of caspofungin (50mg/m²) in very low birth weight preterm newborns with candidemia refractory to administration of liposomal amphotericin B, fluconazole and the conventional dose of this antifungal (2mg/kg/day) has also been reported, with no adverse events, as in the case reported by Seo *et al.*[19] Despite the foregoing, it has been reported that the use of caspofungin in children and infants may cause adverse effects such as alteration of blood parameters, fever, vomiting, diarrhea, thrombophlebitis, hypercalcemia, hypokalemia, elevated transaminases, hyperbilirubinemia, rash, hypotension, nephrotoxicity, and chills.[20] However, our patient did not develop any of these complications, neither in the short nor in the medium term.

Finally, one important matter to consider is that the patient lived in a rural area that lacked some basic services and that the economic activity of the relatives who lived with him, in other words, the people who were in constant direct contact with him, was the petty trade of food supplies. This suggests that it is likely that the *K. ohmeri* infection was the result of his increased exposure to infectious agents, given that *K. ohmeri* is an environmental yeast commonly used in fruit and vegetable fermentation and has been considered an emerging human pathogen in recent decades.[3] Additionally, the patient had a short stay at the NICU and did not require the use of a central venous catheter or any type of device (oxygen therapy, mechanical ventilation, gastrointestinal or urinary catheters, or drains) associated with risk of nosocomial infection.

Conclusion

Although *K. ohmeri* fungemia is a rare infection, its timely detection and treatment is critical given its high mortality rate (40%-50%) and the fact that it mainly affects populations with weak immune systems, such as newborns and older adults. In that sense, its presence should be suspected in patients with a weak immune system who

present signs of infection when there is no clinical evidence of other more common infections (identification of other microorganisms or presence of risk factors such as prolonged hospital stay, use of invasive medical devices, extensive use of broad-spectrum antibiotics, associated diseases, among others) and in whom exposure to this yeast is a possibility. Such was the case of the patient reported here, a newborn who lived in a rural area lacking several basic services and whose family was engaged in the petty trade of food supplies, which may have increased his risk of exposure to this yeast, as *K. ohmeri* is frequently used in the food industry to facilitate fermentation processes.

Ethical considerations

The informed consent of the patient's family was obtained for the preparation of this case report.

Conflicts of interest

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