CASE REPORT
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A rare case of fungemia by *Kodamea ohmeri* in a premature infant

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ABSTRACT

Background: *Kodamaea ohmeri,* is part of the Saccharomycetes that commonly used in the processing of fermented foods, but this fungus can be an emergency when it comes to patients with impaired immune systems so that fungiemia, endocarditis, peritonitis can occur. Many cases have been reported in Asia, America and Europe. This case report aims to present a rare case of fungemia caused by *Kodamera ohmeri* in a premature infant in neonatal intensive care unit (NICU), Prof. Dr. I.G.N.G. Ngoerah, Bali, Indonesia

Case presentation: The baby was born prematurely at 33 weeks of gestation because the mother had severe preeclampsia. The baby was admitted to the NICU with an initial diagnosis of sepsis, then blood cultures were taken and inoculated with sabouraud dextrose agar (SDA) at 37°C for 48 hours. Microscopic examination with lactophenol cotton blue staining was carried out from slide culture for 7 days in which clustered yeast cells were found. Culture results on Saboraud Dextrose Agar (SDA) at 37˚C for 48 hours found growth of colonies that were rough, dry, and white like ivory. Identification results using VITEK-2 compact (bioMérieux®) found *Kodamea ohmeri,* but no antibiotic sensitivity (AST) results. The patient was treated with fluconazole empirically for 11 days, but not routinely therefore the patient got into emergency condition and died.

Conclusion: Patient's condition eventually worsened, possibly due to the ineffective and inappropriate use of fluconazole. The condition of premature babies, most of whom are immunocompromised, can increase the severity of the disease to sepsis and eventually death.

Keywords: fungemia, infant, *Kodamea ohmeri,* premature.
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INTRODUCTION

Kodamaea ohmeri, is a species of fungi that is part of the Saccharomycetes family, originally known as *Pichia ohmeri* or *Yamadazyma ohmeri*.[1-5] This Fungi species is usually used in the processing of fermented foods, such as pickles, fruits, and others but this fungus can be a very serious and very dangerous threat when it comes to patients with impaired immune systems so that various infections can occur such as fungemia, endocarditis, peritonitis.[1,3,6-8] There have been many case reports that have been found and reported in the Asian continent, America, and Europe.[9,10] It was found on Java Island in 1984, in a patient's pleural fluid, however, from expertise conclusion this isolate as contamination.[2,11] Recently it has also been found in Bangladesh, Israel and the latest is a report from Amazon.[11-13] Furthermore, out of all the cases of *K. ohmeri* that were recorded, most of them were from Asia (46/67, 68.5%), particularly from countries in east and southeast Asia (24 in China, 3 in Japan, 6 in Korea, 7 in India, 2 in Turkey, and 1 each in Kuwait, Lebanon, Malaysia, and the Kingdom of Saudi Arabia).[10,11]

K. ohmeri was originally identified from a patient's blood in 1998. A few decades later, the pathogen has emerged as a human danger that can result in potentially fatal infections, particularly in those with weakened immune systems. Worldwide reports of sporadic occurrences of human infections caused by *K. ohmeri* include fungemia, endocarditis, bloodstream infections associated to catheter use, and cutaneous infections, among other illnesses.[12-15] Additionally, reports of nosocomial *K. ohmeri* outbreaks in pediatric intensive care units (PICUs) have been reported. There have been reports of substantial fatality rates from this organism's invasive infections reaching 50%.[16,17] Even though *K. ohmeri* infection is becoming more common in clinical settings, little is known about its clinical and epidemiological features.[11,15,18,19] Furthermore, there have been difficulties in identifying *K. ohmeri* in microbiology laboratory. This is because the various identification techniques that were previously employed by the majority of clinical labs were either inaccurate or time-consuming. In the management of this uncommon fungal infection, early identification of the organism and the use of suitable medication are crucial factors.[20,21]

In this case report we describe a premature male infant with initial diagnosis of sepsis who had been treated in neonatal intensive care unit (NICU), Prof. Dr. I.G.N.G. Ngoerah Hospital, Bali, Indonesia. To the best of our knowledge, this is the first rare case of *K. ohmeri* infection in neonates in Indonesia. This case report also could be the reference for determining the effectiveness of antifungal

therapy breakpoints both in Clinical & Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) for the case of *K. ohmeri* infection. Therefore it could be empirical treatment suggestions based on a thorough examination of the available evidence and issue an advanced identification for microbiologists and physicians to identify *K. ohmeri* as a newly discovered human pathogen.

CASE PRESENTATION

A premature baby from 33 weeks of gestation was delivered by caesarean section because the mother had severe preeclampsia. Baby experiencing asphyxia therefore had been treated in NICU with initial diagnosis of sepsis. Patient had been treated with initial empirical therapy for sepsis, however the condition had not improved. Therefore, a two-side blood sample was collected to be examined in the Clinical Microbiology Laboratory, Prof. Dr. I.G.N.G. Ngoerah Hospital. Blood sample then inoculated in BacT/Alert to observe the growth of any bacteria, then after bacteria showed growth, blood sample the culture on blood agar and MacConkey agar. On the blood agar medium, there was a growth of colonies with large, round, irregular edges, rough, dry and opaque-colored ivory. Because the colony looked like a fungus, the colony culture had been performed in sabouraud dextrose agar (SDA) at 37°C for 48 hours afterwards.

The colony morphology that had been cultured on SDA was round, irregular edges, rough, dry, and opaque-colored ivory. Identification and antimicrobial susceptibility testing (AST) which was made through VITEK-2 Compact (bioMérieux®) showed *Kodamea ohmeri* however there were no AST results. In addition, microscopic examination was done by lactophenol cotton blue staining (LPCB) which was taken from a 7-days slide culture. LPCB staining showed clustered yeast-like with dark-colored tear-like spores. Due to absence of AST result, clinical microbiologist suggested fluconazole as empirical antifungal therapy. From the patient's medical record retrospectively, the patient was given fluconazole parenterally for 13 days in which at a dose of 3 mg/kg body weight every 48 hours for 7 days, followed by a dose of 5.2 mg/kg body weight every 24 hours for 6 days. However, the patient's condition has worsened to an emergency that eventually led to the patient's death when the blood sample was collected.

DISCUSSION

In the last two decades, infections caused by rare fungi have increased significantly, one of which is *K. ohmeri*. The majority of infection by *K. ohmeri* were found in immunocompromised patients with cancer (including lymphoma, leukemia, and other solid tumors), rheumatoid arthritis, diabetes, HIV, HBV, HCV, and other chronic viral infections, or other serious infectious diseases like bacterial sepsis, meningitis, pneumonia, and organ dysfunction syndrome (of which renal and hepatic insufficiency are the most common).[17-22] Immunosuppressive medication was frequently necessary for patients with certain underlying illnesses, which compromised immune system performance.[16,23,24] The most frequent conditions among the instances that have been reported are infectious diseases, followed by cancer and diabetes mellitus. A further significant prevalence is attributable to rheumatoid arthritis and organ failure. It should be mentioned that, albeit far less commonly, *K. ohmeri* infections have been found in immunocompetent people. *K. ohmeri* caused both invasive and non-invasive infections, with invasive infections (62/67, 92.5%) of the cases reported. The invasive infections including fungemia (74.2%), endocarditis (11.3%), peritonitis (6.4%), urinary tract infection, pneumonia, keratitis, and one case of disseminated have been reported worldwide.[21,22,25-28]

Since fungemia was the most prevalent

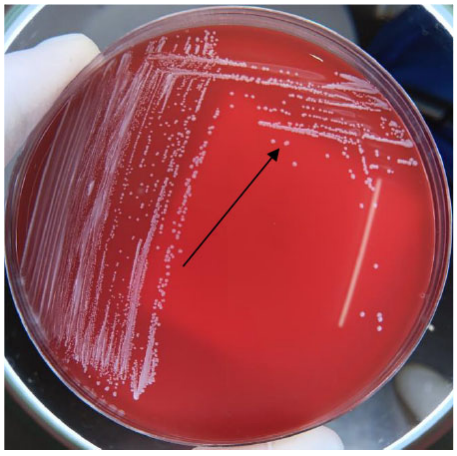

Figure 1. Colony growth on blood agar showed round morphology with irregular edges, rough, dry, and opaque-colored ivory.

Figure 2. Colony growth on SDA showed, large round colonies with uneven edges, opaque, rough, and dry.

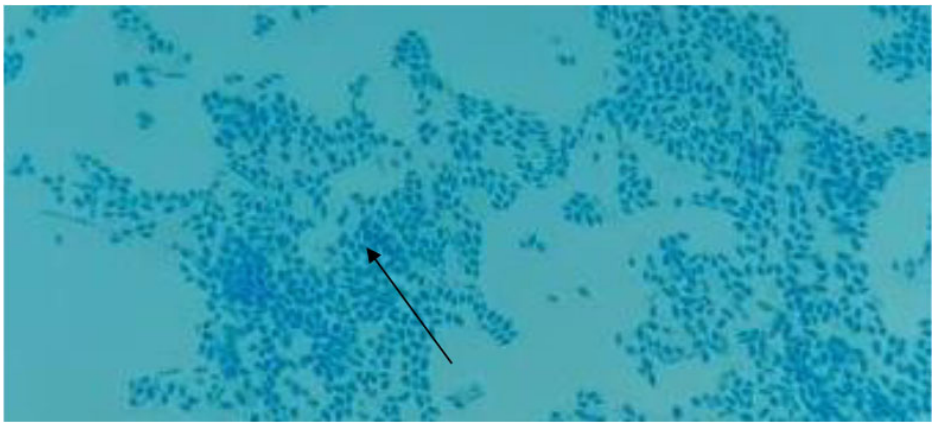

Figure 3. Microscopic examination sfter LPCB staining, with 40X magnification showed dark-colored tear-like spores.

Table 1. Antifungal susceptibility profiles of *K. ohmeri* isolates[5]

Antifungals	MIC range (mg/L)	MIC_{50} (mg/L)	MIC_{90} (mg/L)
Fluconazole	1- >128	8	32
Voriconazole	0.015-2	0.06	0.5
Itraconazole	0.008- <2	0.125	0.5
Posaconazole	0.012-0.06	0.03	0.06
Micafungin	0.03-1	0.06	0.125
Caspofungin	0.125- ≥16	0.25	4
Anidulafungin	0.06-1	0.125	1
Amphotericin B	0.008-1	0.25	0.5
5-flucytosine	<0.02-4	0.5	2
Ketoconazole	0.06	-	-
Miconazole	0.5	-	-

presentation of *K. ohmeri* infections, blood was the most often used isolation source (51/67, 76.1%), with catheter tip culture coming in second (20.9%, 14/67) of the cases. Peritoneal fluid (4/67, 6.0%) was the third most often reported source of isolation and was reported in all four cases of peritonitis. In addition, *K. ohmeri* was isolated from nail or skin cultures in three cases—one each of onychomycosis, phlebitis, and subcutaneous infections. The bacterium was identified from oral swabs, urine, bronchoalveolar fluid, wound tissue, and respiratory secretions. It is noteworthy to remark the possibility tahat *K. ohmeri* was also isolated from the mother's high vaginal swab in a case of neonatal fungemia, suggesting a potential infection route from immunocompromised mother.[7-10] Like other non-candida yeasts, *K. ohmeri* can cause life-threatening infections, primarily in immunocompromised people, and can accelerate the mortality of patients suffering from fungal diseases.[12-17,23]

In 43.3% of the cases, the traditional culture-based approach CHROMagar was used. The most popular commercial biochemical procedures were VITEK 2 compact (62.7%) and API 20C (46.3%). 6.0% (4/67) of the cases involved the use of ATB ID 32C and matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS).[6,9,11,25] As the gold standard for *K. ohmeri* identification, gene sequencing was carried out in over half of the cases that were studied here (40/67, 59.6%). 47.5% (19/40) of the instances employed the internal transcribed spacer (ITS) region (ITS1 and/or ITS2 genes) most frequently, followed by 5.8S rDNA (30.0%), the D1/D2 area of 28S rDNA (27.5%), and 18S rDNA (20.0%). More than one gene was sequenced in 27.5% of the instances in order to correctly identify the species. The sequenced gene was not identified in two of the cases. When two or more identification methods were applied concurrently, as was the case in most cases (52/67, 77.6%), the rate of misidentification was lower than when one approach was applied solely.[19-25]

K. ohmeri infections were treated with a variety of antifungal regimens. Previous study compared the minimum inhibitory concentration (MIC) values to the breakpoints of Candida species, as *K. ohmeri* did not have any breakpoints. While amphotericin B frequently showed a low MIC value, the organism's susceptibility to fluconazole varied between experiments. Contrary results were found for strains isolated from an outbreak in India, where 86.8% of the isolates had a relatively higher MIC of amphotericin B (1 mg/L).[5,8,10,17] This could be because the antifungal medication is widely used in India because to its low cost. The limited data available also showed good in vitro action for echinocandins. Five out of the six patients in the nosocomial newborn infection in China responded well to caspofungin treatment. Some studies reported for instances where patients treated with in vitro susceptible antifungal medications (fluconazole and amphotericin B) were unable to eradicate the fungemia. It should be highlighted, nonetheless, that a drugs in vitro antifungal susceptibility does not always convert into an effective in vivo context because the antifungal effectiveness is influenced by various factors, including the patient's tolerance and the infection site.[21-25-28]

Treatment strategies for *K. ohmeri* infections are similar to those developed to address fungemia brought on by Candida species or other pathogens that resemble yeast. While there were not many *K. ohmeri* isolates that have been tested against echinocandins, micafungin and and anidulafungin may be useful alternative drugs in patients where the isolate is either resistant to azoles or use of amphotericin B is not suitable due to renal insufficiency.[3-7,22] There have been documented cases of clinical failure following the start of fluconazole therapy, requiring a switch to amphotericin B or caspofungin. Additionally, the choice of various AST techniques can have a significant impact on the MIC values. Previous surveillance studies have shown that variations in MIC values can result from the use of some established methods in addition to the standard broth microdilution.[21,22] Therefore, the conventional broth microdilution approach might be more precise and dependable for rare fungi like *K. ohmeri*. Instead of using empirical drug use, the susceptibility report should be rapidly considered when adjusting the clinical antifungal treatment strategy.[27,28] Effective management of *K. ohmeri* requires early identification and heightened awareness of this organism by microbiologists and clinicians as an emergent human disease.

CONCLUSION

K. ohmeri has been known for decades to be a fungal contamination which now has been regarded as an emerging human pathogen and has caused various types of infections with high mortality. Children were found to have vulnerability to the infection more frequently than adults in which the antifungal medications most frequently given were fluconazole and amphotericin B. Further study needed to assess the accurate identification of clinical isolates and the importance of validating antifungal susceptibility.

CONFLICT OF INTEREST

The authors affirmed that there were no conflicts of interest in this study.

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ETHICAL STATEMENT

Authors have secured informed consent regarding patient data for this publication.

AUTHOR CONTRIBUTION

All authors contributed equally in this study and publication of this manuscript.

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