Infect Chemother. 2018 Dec;50(4):362-366
https://doi.org/10.3947/ic.2018.50.4.362
pISSN 2093-2340·eISSN 2092-6448

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Case Report

Successful Treatment of Catheter Related Blood Stream Infection By *Millerozyma farinosa* with Micafungin: A Case Report

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Received: Nov 12, 2017
Accepted: Dec 27, 2017

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Conflict of Interest
No conflicts of interest.

Author Contributions
Conceptualization: SIH, OHC. Methodology: JHS. Writing - original draft: SIH, OHC. Writing - review & editing: YSS, HOK, IGB.

ABSTRACT

Millerozyma farinosa (formerly *Pichia farinosa*) is halotolerant yeast mainly found in food and ubiquitous in the environment. It was a rare yeast pathogen, but it has recently emerged as a cause of fungemia in immunocompromised patients. Optimal therapy for invasive fungal infection by this pathogen remains unclear. We report a case of catheter related blood stream infection caused by *M. farinosa* in a 71-year-old patient who recovered successfully after removal of the central venous catheter and treatment with micafungin.

Keywords: Catheter-related infection; Fungemia; Micafungin; *Millerozyma farinosa*

INTRODUCTION

Millerozyma farinosa, formerly known as *Pichia farinosa,* is a yeast belonging to the *Saccharomycetaceae* family [1]. *M. farinosa* is a halotolerant diploid yeast that can produce high yields of glycerol and xylitol. It can adjust osmotic pressure by accumulating glycerol which endows tolerance to 3 M NaCl [2]. *M. farinosa* produces a salt-mediated killer toxin that can kill competitive strains [3]. It is commonly found in food such as fermented alcoholic beverages, soybean paste, and miso. It has been used for food production and fermentation [4].

M. farinosa is a rare opportunistic pathogen. It has been identified as a cause of fungemia. Only two cases of human infections with *M. farinosa* have been described [5]. Since the number of patients with host susceptibility is increasing, the incidence of opportunistic yeast infections is expected to increase [6]. And sensitive laboratory isolation techniques including 18S ribosomal RNA (rRNA) sequencing have greatly improved the ability to report these infections. Here, we report one case of catheter related blood stream infection (CRBSI) caused by *M. farinosa* identified by 18S rRNA sequencing in a 71-year-old patient. The infection was successfully treated with micafungin.

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CASE REPORT

A 71-year-old man with bladder cancer was admitted to the emergency department for hematuria. The patient had been diagnosed with bladder cancer 3 years earlier. He had undergone transurethral resection of bladder cancer five times. Five months ago, results of abdomen computed tomography (CT) suggested progression of bladder cancer. Therefore, chemoport was inserted into the right jugular vein. The patient received five courses of palliative chemotherapy with gemcitabine and cisplatin. After his hematuria and general condition were improved, the 6th cycle of chemotherapy was administered. After seven days of chemotherapy, his body temperature had been abnormal for six days, reaching 38.6°C at the highest point without any significant symptoms or signs. Complete blood counts revealed myelosuppression with absolute neutrophil count of 890/mm^3, hemoglobin of 10.3 g/dL, and platelet count of 45,000/mm^3. His C-reactive protein level was 200.7 mg/dL and procalcitonin level was 0.47 ng/mL. Chest and abdominal contrast-enhanced CT showed no abnormal findings except bladder cancer and bilateral pleural effusion. Three sets of blood cultures (two from a peripheral vein, one through the chemoport, 5 ml each) were collected and treatment with broad-spectrum antibiotic agents was started.

Growth of yeasts was detected in three out of three sets on the first day and the third day after fever onset. With a consideration of chemoport related blood stream infection, the chemoport was removed and micafungin 100mg daily intravenously was started on day 5 after fever onset. Blood culture (Vitek-2; Biomérieux, Durham, NC, USA) isolation revealed *M. farinosa* and semiquantitative catheter-tip culture was positive for the same microorganism (≥15 colony-forming units). Because *M. farinosa* is a rare fungal pathogen, we also performed 18S rRNA sequencing analysis to confirm the identification of the organism in the blood isolates. Universal eubacterial primer pair of pITS-F (5′-GTCGTAACAAGGTT AACCTGCGG-3′) and pITS-R (5′-TCCTCCGCTTATTGATA TG C-3′) were used. PCR products were purified and sequenced was performed using an ABI 3730XL sequencer (Applied Biosystems, Foster City, CA, USA). Sequence similarity searches were performed using BLAST tool at NCBI (http://www.ncbi.nlm.nih.gov/blast). The sequence was 100% identical to that of *M. farinosa* deposited at GenBank (accession number: KY204280). Minimum inhibitory concentrations (MIC) were: amphotericin B, 0.5 μg/ml; fluconazole, 32 μg/ml; voriconazole, 0.125 μg/ml; micafungin, 0.015 μg/ml; and caspofungin, 0.125 μg/ml.

On day 7 after fever onset, blood cultures obtained after 3 days of intravenous therapy with micafungin were negative. Micafungin was continued for 14 more days. On day 28, he was discharged from the hospital with improved condition.

DISCUSSION

To the best of our knowledge, our case is the third published case of human infection caused by *M. farinosa*. The first reported case of human disease due to *M. farinosa* was reported in 1989 by Anaissie et al. in a 12-year-old girl with teratoma due to catheter-related fungemia. It was resolved after removing the catheter [5]. The second case was described in a 13-year-old boy with anaplastic large-cell lymphoma who had apparent catheter related fungemia with tunnel infection. It was resolved after removal of the catheter and treatment with amphotericin B deoxycholate [7]. Colonization of the oral cavity with *M. farinosa* has been found in two immunocompromised patients [8, 9].

https://doi.org/10.3947/ic.2018.50.4.362

Serious infections due to less commonly recognized opportunistic yeasts are increasing. Changing epidemiology of human fungal infections is partly due to the use of antimicrobial chemoprophylaxis and the increase of patients with host susceptibility such as prolonged hospitalization and intensive care, malignancy, mucositis, neutropenia, T-cell depletion, corticosteroid use, malnutrition, abdominal surgery, hyperalimentation, and prematurity [6]. Furthermore, the development of clinical microbiology has enhanced the detection and identification of rare fungal organisms. In recent years, the number of human infections caused by *Pichia* species has been also increased [7]. The clinical features of the 10 reported cases of *Pichia* species infection other than *M. farinosa* in adult patients are summarized in **Table 1**.

Few data are available on *M. farinosa*. Data on its antifungal susceptibilities are limited. The breakpoint of its susceptibility test is defined by the Clinical Laboratory Standards Institute. The optimal treatment strategy for *M. farinosa* has not been determined yet. Currently there are no evidence-based guidelines for treatment of *M. farinosa* infections. All three cases of human infection were catheter related blood stream infections. For all three patients, the central venous catheter was removed. No antifungal treatment was used in the first case while amphothericin B was used for the second case. Both patients successfully recovered.

In the clinical guideline for the management of candidiasis, echinocandin is recommended as the first choice for candidemia. Lipid formulation of amphotericin B is a less attractive alternative due to its potential toxicity [10]. Although no previous data were available about treatment of *M. farinosa* with micafugin, it might be a reasonable treatment option considering our antifungal susceptibility result of micafugin for this pathogen.

This case shows that *M. farinosa* appears to be an emerging pathogen in immunocompromised hosts. Micafungin therapy and catheter removal may be used to improve patient outcome.

Table 1. Clinical features of reported *Pichia* species fungemia in adult patients other than *Millerozyma farinosa*

Case	Reference (year)	Infection	Age (years)/sex	Pre-existing conditions	Source of Pichia species infection	Antifungal treatment	Outcome
1	[11] (2003)	*Kodamaea ohmeri*[a] BSI	59/M	VP shunt infection, pneumonia	Phlebitis at skin site and blood	AMB	Survived
2	[12] (2006)	*Kodamaea ohmeri* BSI	58/F	Accelerated phase of CML	Blood and CVC tip	AMB	Survived
3	[13] (2009)	*Kodamaea ohmeri* BSI	71/M	DM, tinea pedis, cellulitis	Blood	FLC then AMB	Survived
4	[14] (2010)	*Kodamaea ohmeri* BSI	34/M	Asthma, alcohol abuse, thrombophlebitis, transesophageal fistula	Blood	MIF	Survived
5	[15] (2017)	*Kodamaea ohmeri* BSI	58/F	RA, acute pancreatitis	Blood and CVC tip	MIF	Survived
6	[16] (2013)	*Pichia anomala* BSI	21/M	Sickle cell disease	Blood	FLC then MIF	Survived
7	[17] (2006)	*Cyberlindnera fabianii*[b] BSI	46/M	Morbid obesity, alcohol and nicotine abuse, pneumonia, cholecystectomy, CVVHD	Blood	FLC then CAF	Died
8	[18] (2008)	*Cyberlindnera fabianii* endocarditis	40/M	Congenital combined aortic incompetence of the mitral valve, craniectomy	Blood	FLC	Survived
9	[19] (2012)	*Cyberlindnera fabianii* BSI	53/F	Mesenteric ischemia, Continuous hemofiltration	Blood	CAF then FLC	Survived
10	[20] (2013)	*Cyberlindnera fabianii* BSI	47/F	Plasma cell myeloma, ASCT	Blood and CVC tip	AMB then CAF	Died

BSI, bloodstream infection; M, male; VP, ventriculoperitoneal shunt; AMB, amphotericin B deoxycholate; F, female; CML, chronic myelogenous leukemia; CVC, central venous catheter; DM, diabetes mellitus; FLC, fluconazole; MIF, micafungin; RA, rheumatoid arthritis; CV VHD, continuous venovenous hemodiafiltration; CAF, caspofungin; ASCT, autologous stem cell transplantation.
[a]Previously known as *Pichia ohmeri*.
[b]Previously known as *Pichia fabianii*.

https://doi.org/10.3947/ic.2018.50.4.362

ACKNOWLEDGEMENTS

The pathogen resource for this study was provided by Gyeongsang National University Hospital (GNUH), as the Branch of National Culture Collection for Pathogens (NCCP).

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