Letter to the Editor
Clinical Microbiology

Ann Lab Med 2015;35:175-177
http://dx.doi.org/10.3343/alm.2015.35.1.175
ISSN 2234-3806 • eISSN 2234-3814

ANNALS OF LABORATORY MEDICINE

Three Cases of Candidiasis Misidentified as *Candida famata* by the Vitek 2 System

Hyun-Young Kim, M.D., Hee Jae Huh, M.D., Rihwa Choi, M.D., Chang-Seok Ki, M.D., and Nam Yong Lee, M.D.
Department of Laboratory Medicine and Genetics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Candida famata is a commensal yeast found in natural substrates and various types of cheese [1]. It is a rare cause of candidiasis and has been described in human infections, including bloodstream infections [2]. Results of commercial microbial identification systems based on biochemical tests, available for *C. famata* identification, are not accurate [3, 4]. Here, we describe three candidiasis cases that were misidentified as *C. famata* by the Vitek 2 system (bioMeriéux, Marcyl'Etoile, France). This study was approved by our Institutional Review Board.

In case 1, an extremely low-birth-weight male infant was delivered at 23 weeks and 3 days of gestation. On postnatal day 49, desaturations, neutropenia, and elevated C-reactive protein level were observed. Peripheral blood and central line (C-line) tip cultures grew *C. famata*, with low discrimination from *C. parapsilosis*. The infant was treated with fluconazole, and blood cultures obtained 1 week later were negative.

In case 2, a 41-yr-old woman had T-cell lymphoma with leptomeningeal seeding. She was undergoing chemotherapy with an Ommaya reservoir in place, and neutropenic fever developed. Meropenem, vancomycin, and caspofungin were empirically administered. Blood cultures obtained from a C-line and peripheral blood were positive for *C. lusitaniae*. Five days after treatment, blood cultures were negative; however, *C. lusitaniae* rebounded 2 days later and was identified in the cerebrospinal fluid. At this point, caspofungin was replaced by liposomal amphotericin B (AmB). Owing to persistent fevers, fluconazole was added to the treatment regimen, and a subsequent blood culture grew *C. famata*. Finally, owing to probable invasive pulmonary aspergillosis, voriconazole alone was administered. The patient died 2 days after the initiation of this treatment.

In case 3, a 68-yr-old woman was hospitalized for treatment of a prosthetic joint infection following a total left knee arthroplasty in 2010. She was treated unsuccessfully with several surgical and antibiotic therapies. In July 2013, *C. parapsilosis* was isolated from the joint fluid, and the patient subsequently underwent open debridement and insertion of an antibiotic-loaded cement spacer in February 2014. Owing to ongoing pain, her joint fluid was cultured the following month, which tested positive for *C. famata*, and fluconazole treatment was initiated.

Because of the discrepancy within these results or low discrimination between species, sequence analyses of the internal transcribed spacer (ITS) and D1/D2 regions of the rRNA gene were performed to identify *C. famata* isolates [5]. In cases 1, 2, and 3, *C. parapsilosis*, *C. lusitaniae*, and *C. parapsilosis* were identified, respectively (Table 1), with no isolate being identified as *C. famata*.

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS)-based identification of clinically relevant yeasts has proven to be superior to identification by phenotypic identification systems [4]. Thus, we subjected the isolates

Received: May 21, 2014
Revision received: July 28, 2014
Accepted: November 14, 2014

Corresponding author: Nam Yong Lee
Department of Laboratory Medicine and Genetics, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 135-710, Korea
Tel: +82-2-3410-2706, Fax: +82-2-3410-2719
E-mail: micro.lee@samsung.com

Table 1. Three cases of candidiasis misidentified as *Candida famata* by the Vitek2 system

No. Case	Age/Sex	Specimen	Clinical information	Previously isolated *Candida* species	Currently isolated *Candida* species		
				Vitek 2	Vitek 2 (% ID)	Bruker Biotyper (score)	DNA sequencing
1	3 months/M	Blood	ELBW	None	*C. famata or C. parapsilosis* (low discrimination)	*C. parapsilosis* (1.70)	*C. parapsilosis*
2	41 yr/F	Blood	Peripheral T-cell lymphoma	*C. lusitaniae*	*C. famata* (93%)	*C. lusitaniae* (1.73)	*Clavispora lusitaniae**
3	68 yr/F	Synovial fluid	Prosthetic joint infection	*C. parapsilosis*	*C. famata* (95%)	NT	*C. parapsilosis*

*Teleomorph of *Candida lusitaniae*.
Abbreviations: ID, identification; ELBW, extremely low birth weight; NT, not tested.

Table 2. Case reports of *Candida famata* infections in Korea

Year	N of isolates	Isolated organism	Specimen	Identification method	Clinical information	Treatment	Outcome
1998 [6]	1	*C. famata*	Blood	ATB 32C System	Esophageal cancer	FLU	Improved
2001 [7]	1	*C. famata (C. parapsilosis)*	Central line tip (Blood)	ND	ELBW	AmB	Improved
2007 [8]	1	*C. famata*	Tissue biopsy	ND	Cervical spine OM	AmB	Improved
2009 [9]	2	*C. famata*	Blood	ND	VLBW	AmB	Improved
2014 [10]	1	*C. famata*	Blood	ND	ESRD, IE	AmB	Died

Abbreviations: ND, not described; ELBW, extremely low birth weight; OM, osteomyelitis; VLBW, very low birth weight; ESRD, end-stage renal disease; IE, infective endocarditis; FLU, fluconazole; AmB, amphotericin B.

from cases 1 and 2 to MALDI-TOF MS (Bruker Biotyper, Bruker Daltonik, Bremen, Germany). The results were consistent with those obtained by sequencing; however, based on the manufacturer's breakpoints, the identification confidence score (1.70) allowed for only a genus-level identification in both cases [4].

In recent molecular identification studies, phenotypic methods initially identified isolates as *C. famata*, including strains of *C. guilliermondii*, *C. lusitaniae*, *C. parapsilosis*, and *C. palmioleophila* [1, 3]. Moreover, the ARTEMIS and SENTRY surveillance programs that identified 53 isolates as *C. famata* were disproven when sequencing analysis was performed by Castanheira *et al*. [4], suggesting that phenotypic identification of *C. famata* is almost certainly incorrect. The results of these studies are consistent with those of the three cases presented herein. Therefore, it is possible that, in the absence of confirmatory assays (e.g., sequencing), previous case reports may have misdiagnosed *C. famata* infection. To date, six such cases have been reported in Korea (Table 2), and the data presented here suggest the possibility of misidentification.

General antifungal susceptibility patterns of *C. famata*, *C. parapsilosis*, and *C. lusitaniae* are different. *C. famata* exhibits good susceptibility to AmB but reduced susceptibility to echinocandins and azoles. Therefore, liposomal AmB is recommended as the initial therapy [2]. *C. parapsilosis* is highly susceptible to most antifungal agents, but exhibits higher minimal inhibitory concentrations to echinocandins. *C. lusitaniae* is usually susceptible to azoles and echinocandins; however, it rapidly acquires resistance to AmB *in vitro*. Therefore, although misidentification of *C. famata* in our cases did not have a significant impact on the patients' treatment, this could have led to misinterpretation of antifungal susceptibility and incorrect selection of the initial antifungal agent.

In conclusion, it is important to be aware of the potential misidentification of *C. famata* by commercial systems. For more accurate identification of these isolates, sequencing analysis of ITS and D1/D2 may be helpful.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

REFERENCES

1. Desnos-Ollivier M, Ragon M, Robert V, Raoux D, Gantier JC, Dromer F.

http://dx.doi.org/10.3343/alm.2015.35.1.175

Debaryomyces hansenii (Candida famata), a rare human fungal pathogen often misidentified as Pichia guilliermondii (Candida guilliermondii). J Clin Microbiol 2008;46:3237-42.
2. Beyda ND, Chuang SH, Alam MJ, Shah DN, Ng TM, McCaskey L, et al. Treatment of Candida famata bloodstream infections: case series and review of the literature. J Antimicrob Chemother 2013;68:438-43.
3. Meletiadis J, Arabatzis M, Bompola M, Tsiveriotis K, Hini S, Petinaki E, et al. Comparative evaluation of three commercial identification systems using common and rare bloodstream yeast isolates. J Clin Microbiol 2011; 49:2722-7.
4. Castanheira M, Woosley LN, Diekema DJ, Jones RN, Pfaller MA. Candida guilliermondii and other species of candida misidentified as Candida famata: assessment by vitek 2, DNA sequencing analysis, and matrix-assisted laser desorption ionization-time of flight mass spectrometry in two global antifungal surveillance programs. J Clin Microbiol 2013;51: 117-24.
5. CLSI. Interpretive criteria for identification of bacteria and fungi by DNA target sequencing; Approved guideline. CLSI document MM18-A. Wayne, PA: Clinical and Laboratory Standards Institute, 2008.
6. Lim JG, Son JS, Jang IH, Uh Y, Yoon KJ, Lee JI. A case of fungemia caused by Candida famata. J Clin Pathol Qual Control 1998;20:373-7.
7. Kim DH, Lee JA, Jo HS, Park KR, Park JD, Kim BI, et al. Systemic candidiasis in neonatal intensive care unit: a 8-yr experience. J Korean Soc Neonatol 2001;8:33-45.
8. Seok H, Kim SH, Kim DH, Kim TH, Kim HK. Cervical osteomyelitis and radiculopathy due to candida: a case report. J Korean Acad Rehabil Med 2007;31:482-5.
9. Lee SW, Lee JE, Lee J, Lee HS, Lee JH, Sung IK. Systemic candida infection in very low birth weight infants: epidemiological features over 5 years. J Korean Soc Neonatol 2009;16:190-6.
10. Kim JG, Whang HC, Jang JY, Ha SE, Kim DH, Choi BS. A case of infective endocarditis in an end-stage renal disease patient caused by Candida famata. Korean J Med 2014;86:349-52.