**Candida auris** candidemia an emerging threat: A case report and mini review of the literature

K. Sandhya Bhat, King Herald Kisku, Reba Kanungo
Department of Microbiology and Pulmonary Medicine, Pondicherry Institute of Medical Sciences, Puducherry, India

**Abstract**
*Candida auris* (C. auris) is a multidrug-resistant emerging fungal pathogen, which spreads rapidly in health-care settings and has the potential to cause nosocomial outbreaks. The lack of awareness among clinicians and challenges faced for its diagnosis in microbiology laboratories may adversely affect patient outcome. It is resistant to most of the commonly used antifungals for empiric treatment in critical care units. Hence, appropriate identification and antifungal susceptibility-guided treatment can contain infections caused by this organism. Hospital infection prevention and control measures must be in place to prevent nosocomial transmission. We report one such case of bloodstream infection by *C. auris* in a patient with multiple underlying risk factors and morbid obesity, who succumbed to florid sepsis after prolonged hospitalization in spite of aggressive medical management.

**Keywords:** Candida auris candidemia, fluconazole resistance, nosocomial transmission, nucleic acid sequencing

**INTRODUCTION**
*Candida auris* (C. auris) is a recently identified multidrug-resistant (MDR) emerging nosocomial pathogen. It poses a great threat for hospital infection control practices, posing a major threat in critical care units globally. C. auris was first identified from the ear discharge of a Japanese patient in 2009. Since then, infections by this organism have been reported from more than 20 countries including India. It has been associated with a wide spectrum of infections including bloodstream, wound, osteomyelitis, malignant otitis media, ventriculitis, intra-abdominal infections, pleural effusion, pericarditis, and vulvovaginitis.

What makes it more worrisome is its MDR nature. It is resistant to various antifungals agents, including azoles, echinocandins, and amphotericin B. Risk factors implicated for *C. auris* infections include central venous catheter use, recent history of surgery, diabetes, and prolonged use of broad-spectrum antibiotic or antifungal use.

*C. auris* has been commonly misidentified by conventional identification systems as well as by Vitek 2 automated microbial identification system (bioMérieux, France) as *Candida haemulonii*. Misidentification of this MDR yeast can be challenging to medical care. Prompt and accurate identification, followed by timely management, can improve...
the clinical outcome. DNA sequencers or matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) biotypers can help in accurate rapid identification of this MDR yeast.[1]

CASE REPORT

A 62-year-old male patient presented to this hospital with gradually worsening breathlessness and cough for 2 weeks and right-sided retrosternal nonradiating type of pain with high-grade fever for 2 days. He also had bilateral pedal edema and lower limb paresthesia. He had been diagnosed to have obstructive sleep apnea (OSA), rheumatic heart disease with mitral stenosis, hypothyroidism, and cholelithiasis. A provisional diagnosis of community-acquired pneumonia (CAP) of the right lower and middle lobe with morbid obesity was made, and he was started on noninvasive ventilation and bilevel positive airway pressure due to the respiratory failure. On the 2nd day of admission, amoxicillin/clavulanic acid (intravenous dose, 1.2 g, 8th hourly) and azithromycin (500 mg, once daily (OD), oral) were started empirically in view of fever and signs of sepsis. Due to continuing respiratory failure, he developed CO₂ narcosis, and in view of a low Glasgow Coma Scale, he was intubated. Electroencephalography showed abnormal recordings with hemispherical dysfunction, following which tracheostomy was done (on day 17 of admission). During his course in the hospital, he developed high-grade fever spikes, thrombophlebitis at the site of central lines, and reduced urine output.

On examination, his temperature was 39°C, pulse rate was 109 beats/min, blood pressure was 154/109 mmHg, and the respiratory rate was 33 breaths/min. His blood samples and endotracheal (ET) aspirates were sent (on day 20 of admission) for the microbiological and cytological analysis. Investigations revealed hemoglobin of 9.2 g/dl, total leukocyte count of 22,300/μl (polymorphs 89%, lymphocytes 4%, eosinophils 7%, and monocytes 1%), with normal platelet, and red blood cell counts and a positive C-reactive protein (183 mg/L). Renal function tests were deranged with blood urea (121 mg/dL) and serum creatinine (1.3 mg/dL). Fasting blood sugar level and liver function tests were within the normal limits. His blood gas analysis report showed FiO₂ of 60%.

On day 28 of hospital admission, his paired blood samples (from both central line and peripheral line) grew Pseudomonas aeruginosa (sensitive isolate) and Candida species. ET aspirate grew MDR Acinetobacter baumannii sensitive only to polymyxin B. The patient was diagnosed to have polymicrobial sepsis (Pseudomonas and Candida spp.) and ventilator-associated pneumonia due to MDR A. baumannii. On the 29th day following admission, he was started on injection polymyxin B (6 lakh units, 12th hourly), oral fluconazole (400 mg, Ryles Tube, once daily), and injection meropenem (1 g, 12 hourly). In spite of vigorous medical management, he developed acute kidney injury for which dialysis was started on dopamine 10 μg/kg/min. His hemodynamics and respiratory mechanics did not improve in spite of aggressive medical care. He succumbed to florid sepsis after 37 days of hospitalization.

Yeast identification

Gram-stained smear from the positive blood culture by BacT-ALERT showed oval budding yeast-like cells. Sabouraud dextrose agar (SDA) showed cream-colored colonies, and CHROMagar Candida (HiCrome™ Candida Differential Agar from HiMedia) showed cream colonies with purple tinge after 48 h of incubation. SDA plate incubated at 42°C also grew yeast-like pasty colonies. Carbohydrate fermentation and assimilation tests were carried out with glucose, maltose, lactose, sucrose, galactose, and trehalose, and the results were inconclusive, with only glucose was fermented, and all other carbohydrates were neither fermented nor assimilated. Antifungal susceptibility testing (done on day 32) showed resistance to fluconazole (by disc diffusion), and later, on day 37, sensitivity to echinocandin (by E-strip test, from HiMedia) was tested with MIC of 0.25 μg/mL (susceptible). Two weeks after the death of the patient, isolate was identified as C. auris with nucleic acid sequencing of the ITS and D1/D2 regions of the 28S subunit of the ribosome at the WHO Mycology Reference Laboratory, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India.

DISCUSSION AND REVIEW OF LITERATURE

C. auris, a new MDR yeast pathogen, was first detected in the external ear canal of a female patient in Tokyo, Japan, in 2009.[3] Hence, it was named as C. auris. It is globally emerging as an MDR yeast that can cause fatal invasive infections. Accurate identification of this organism is possible by DNA sequencing or MALDI-ToF. Laboratories lacking these facilities fail to identify the organism, leading to inadequate treatment of life-threatening infections.

Here, we report a case of C. auris fungemia in a patient with multiple underlying risk factors which included CAP of the right lower and middle lobe of the lung, OSA with chronic type II respiratory failure, hypothyroidism, and morbid obesity. This was compounded with acute kidney...
injury and multisystem organ failure leading to prolonged hospital stay and long-term central venous catheters and MDR P. aeruginosa sepsis.

Most recent cases report similar multiple comorbidities precipitating C. auris infection in patients with a prolonged hospital stay.[5,15] C. auris is commonly misidentified as C. baemulonii, Candida famata, Candida sake, Rhodotorula glutinis, and Saccharomyces cerevisiae by the conventional systems including API 20C and automated identification systems such as Vitek 2 and Phoenix, which can lead to inadequate treatment and poor outcome.[1,3,8,10] The present isolate grew at 42°C, and the conventional methods of identification were inconclusive. The growth of C. auris on CHROMagar (HiCrome Candida differential agar from HiMedia) may be pale purple or pink or white-to-cream-colored smooth colonies or no characteristic colored colonies, which could be due to varied incubatory conditions. On Gram staining, they may appear in single, paired, and/or sometimes, grouped as oval-to-elongate budding cells of varied size without pseudohyphae.[4,11] The thermoresistance of C. auris that allows it to grow between 30°C and 40°C–42°C and inability to grow on cycloheximide-containing medium may be possibly used as a marker for the identification of this pathogenic yeast.[11,12]

Available options for rapid and accurate identification of C. auris are DNA sequencers or matrix MALDI-TOF biotypers. Two platforms for MALDI-TOF MS are available, namely Bruker Biotyper and Vitek MS, which can detect C. auris within few minutes and are 100% sensitive and specific. DNA sequencing also could confirm the identification as described in various other studies.[4,5,13-15] A detailed description of sequenced C. auris by Chakrabarti et al. and Sharma et al. showed that the C. auris genome is different from that of Candida albicans by 99.5% and had the closest homology with the genome of Candida lusitaniae (85.9%–86.4%).[16,17]

Resistance to all three classes of antifungals has been reported in various studies; fluconazole resistance is maximum (up to 90%), voriconazole (50%), amphotericin B (35%), and to echinocandins (2%–8%).[4,5,18] It has a very close phylogenetic relationship with Candida krusei, C. baemulonii, Candida pseudohaeumlonii, and C. lusitaniae, which are intrinsically resistant to azoles and amphotericin B. This could be a probable reason for the similarly higher resistance of C. auris to these classes of drugs.[5,19] A higher rate of resistance to flucytosine and echinocandins (caspofungin, micafungin, and anidulafungin) has been also well-documented.[13,16] Thus, MDR nonalbicans Candida isolate should be considered as a possible indicator of potential C. auris infection. The optimal therapeutic option for C. auris infections is currently unknown. However, due to relatively low resistance to echinocandins, they can be recommended for the empirical therapy. The management of infections caused by these superbugs should be guided by antifungal susceptibility results.[14,11,16]

C. auris can be transmitted by multiple modes. Due to its ability to persist on both dry and moist surfaces, floors, sinks, bedding materials, the air, on the skin, and in nasal cavities etc., it colonizes and spreads rapidly in health-care settings and can cause nosocomial outbreaks.[11,13] Very short contact time of 4 h is sufficient enough for the acquisition of C. auris from a colonized patient, and within 48 h of admission into ICUs, invasive infections have been acquired.[7]

C. auris has been associated with a variety of invasive fungal infections. Invasive C. auris infection may range from candidemia (mainly associated with central venous catheter use) to pericarditis, respiratory tract, and urinary tract infections, especially occurs in critically ill patients, as we have found in this case.[7,9,11,16] Health-care workers can also be possible agents of transmission; hence, isolation of the patient as well as contact precaution is necessary. The decontamination of instruments and strict adherence to hand hygiene may play an important role in preventing transmission of this hardy fungus.[1,7,19]

CONCLUSION

C. auris is an emerging MDR pathogen which is a diagnostic challenge in clinical laboratories. Any multi-drug resistant Candida species isolated from blood sample of a critically ill patient with underlying morbidities, which has been difficult to identify by the conventional diagnostic methods, should raise the suspicion of possibility of C. auris infection. Appropriate identification is the key to treat and contain infections caused by this organism. Treatment should be guided by susceptibility reports in consultation with infectious disease specialists. Appropriate infection control measures, including isolation and strict hand hygiene practice, should be instituted to prevent transmission and contain this emerging threat.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will
not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgment
The authors would like to thank Dr. Shivaprakash M. Rudramurthy, Professor, Department of Medical Microbiology, PGIMER, WHO Mycology Reference Laboratory, Chandigarh, for providing accurate identification by nucleic acid sequencing of the ITS and D1/D2 regions of the 28S subunit of ribosome.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Rudramurthy SM, Chakrabarti A, Paul RA, Sood P, Kaur H, Capoor MR, et al. Candida auris candidaemia in Indian ICUs: Analysis of risk factors. J Antimicrob Chemother 2017;72:1794-801.
2. Alatoom A, Sartawi M, Lawlor K, AbdelWareth L, Thomsen J, Nusair A, et al. Persistent candidemia despite appropriate fungal therapy: First case of Candida auris from the United Arab Emirates. Int J Infect Dis 2018;70:36-7.
3. Satoh K, Makimura K, Hasumi Y, Nishiyama Y, Uchida K, Yamaguchi H, et al. Candida auris sp. nov: A novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. Microbiol Immunol 2009;53:41-4.
4. Chowdhary A, Anil Kumar V, Sharma C, Prakash A, Agarwal K, Babu R, et al. Multidrug-resistant endemic clonal strain of Candida auris in India. Eur J Clin Microbiol Infect Dis 2014;33:919-26.
5. Lockhart SR, Eiteen KA, Vallabhaneni S, Farooqi J, Chowdhary A, Govender NP, et al. Simultaneous emergence of multidrug-resistant Candida auris on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. Clin Infect Dis 2017;64:134-40.
6. Lee WC, Shin JH, Uh Y, Kang MG, Kim SH, Park KH, et al. First three reported cases of nosocomial fungemia caused by Candida auris. J Clin Microbiol 2011;49:3139-42.
7. Jeffery-Smith A, Taori SK, Schelenz S, Jeffery K, Johnson EM, Borman A, et al. Candida auris: A Review of the literature. Clin Microbiol Rev 2018;31. pii: e00229-17.
8. Parra-Giraldo CM, Valderrama SL, Cortes-Fraile G, Garzón JR, Ariza BE, Moro F, et al. First report of sporadic cases of Candida auris in Colombia. Int J Infect Dis 2018;69:63-7.
9. Tian S, Rong C, Nian H, Li F, Chu Y, Cheng S, et al. First cases and risk factors of super yeast Candida auris infection or colonization from shenyang, China. Emerg Microbes Infect 2018;7:128.
10. Sears D, Schwartz BS. Candida auris: An emerging multidrug-resistant pathogen. Int J Infect Dis 2017;63:95-8.
11. Osei Sakyere J. Candida auris: A systematic review and meta-analysis of current updates on an emerging multidrug-resistant pathogen. Microbiologysopen 2018;7:e00578.
12. Centres for Disease Control and Prevention. Candida auris Candida Fungal Diseases. Centres for Disease Control, 2017. Available from: https://www.cdc.gov/fungal/Candida-auris/index.html. [Last accessed on 2019 Sep 18].
13. Centre for Disease Prevention. Candida auris in Healthcare Settings – Europe. Available from: https://ecdc.europa.eu/sites/portal/files/documents/RRA-Candida-auris-European-Union-countries.pdf. [Last accessed on 2018 Oct 28].
14. Mohd Tap R, Lim TC, Kamarudin NA, Ginsapu SJ, Abd Razak MF, Ahmad N, et al. A fatal case of candida auris and Candida tropicalis candidemia in neutropenic patient. Mycopathologia 2018;183:559-64.
15. Yang A, Carlton DA, Hamula C, Patel G, Iloreta AM. First prospectively identified case of Candida auris in the United States. Otolaryngol Case Reports 2017;5:6-7. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2468548817300875 [Last accessed on 2018 Oct 28].
16. Chakrabarti A, Sood P, Rudramurthy SM, Chen S, Kaur H, Capoor M, et al. Incidence, characteristics and outcome of ICU-acquired candidemia in India. Intensive Care Med 2015;41:285‑95.
17. Sharma C, Kumar N, Meis JF, Pandey R, Chowdhary A. Draft genome sequence of a fluconazole-resistant Candida auris strain from a candidemia patient in India. Genome Announc 2015;3. pii: e00722‑15.
18. Schwartz IS, Hammond GW. First Reported case of Multidrug-Resistant Candida auris in Canada; 2017. Available from: https://www.cdc.gov/fungal/Candida-auris/index.html. [Last accessed on 2018 Oct 24].
19. Cendejas-Bueno E, Kolecka A, Alastrauey-Izquierdo A, Theelen B, Groenewald M, Kostrzewa M, et al. Reclassification of the Candida haemulonii complex as Candida haemulonii (C. haemulonii group I), C. douglasiae (C. haemulonii group II), and C. haemulonii var. Vulsena var. Nov. J Clin Microbiol 2012;50:3641-51.