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Emergence of *Candida auris* in Vietnam: A case series

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Abstract

Candida auris (C. auris), a globally emerging pathogen, has posed a significant threat to hospitalized individuals during the COVID-19 in Vietnam. This case series reported (1) common patterns in five patients with non-multidrug-resistant *C. auris* infections (multiple comorbidities, severe-to-critical illness, use of broad-spectrum antibiotics, or history of surgery/invasive procedures) and (2) high rate of *C. auris*-associated mortality in this medical setting (four deaths out of five cases). Further studies are needed to (1) identify risk factors for *C. auris* infections and mortality and (2) investigate the effects of screening and preventive measures for *C. auris*, especially in low-resource settings.

Keywords

Candida auris, mycosis, fungal infection, antifungal agents, Vietnam

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Introduction

Candida auris (C. auris), first reported in Japan in 2009,[1] is an emerging pathogen that poses serious threats to patient outcomes globally.[2] *C. auris* has been repeatedly found in many infections, including fungemia, skin and soft tissue infections, respiratory tract infections, urinary tract infections, or otomycosis.[1,3] More importantly, it can cause opportunistic infections in immunocompromised individuals,[4] worsen treatment outcomes, and increase the mortality risk in critically ill patients.[5,6]

C. auris infections have been reported in five continents (Africa, America, Asia, Europe, and Oceania).[7] There is a growing number of countries that have isolated *C. auris* from patient samples.[8–10] This can increase the risk of outbreaks, as *C. auris* can spread rapidly and widely following the emergence of the first isolate.[2,11,12] The mortality risk of this fungal infection is even more burdensome, especially in low-resource settings with poor infection control since *C. auris* has been shown to resist many antifungal agents.[11–15]

Given the vulnerability of patients with severe medical conditions, an outbreak of *C. auris* infections has caused a tremendous burden on hospitalized individuals during the COVID-19 in Vietnam. As these were among the first *C. auris* isolates in the country, we reported a single-center case series to describe the impacts of this emerging pathogen on the course of treatment and health outcomes in a middle-income setting. We also reported the antifungal susceptibility of these isolates to clarify the resistant patterns of *C. auris* in this outbreak.

Case series

Starting from the fourth wave of COVID-19 in Vietnam (from August 2021 to January 2023), we recorded five female Vietnamese patients (Asian race; one with moderate COVID-19, one with post-COVID) whose blood

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Table 1. Characteristics of patients with *Candida auris* infections.

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5
Age	40	83	69	85	92
Sex	Female	Female	Female	Female	Female
Comorbidities	Not documented	Hypertension; type 2 diabetes; ischemic stroke; chronic hepatitis B; ovarian cancer; and femoral head fracture	End-stage renal disease; hypertension; post-COVID	Not documented	Hypertension; atrial fibrillation; metastatic colorectal cancer
Date of blood culture	August 26, 2021	November 17, 2021	January 07, 2022	October 13, 2022	December 29, 2022
Diagnosis at the date of blood culture	COVID-19 pneumonia; ARDS; bacteremia	Sepsis; pneumonia; necrotizing fasciitis	COVID-19 pneumonia; bacteremia; cellulitis	Pyelonephritis; pneumonia; bacteremia	ARDS; bacteremia; anemia; cellulitis
Clinical characteristics at the date of blood culture					
Immunosuppression	No	Yes	No	Yes	Yes
Neutropenia	No	No	No	Yes	No
CVC insertion	Yes	Yes	Yes	Yes	Yes
Mechanical ventilation	Yes	Yes	Yes	Yes	Yes
Bacteremia	Yes	Yes	Yes	Yes	Yes
Broad-spectrum antibiotics	Yes	Yes	Yes	Yes	Yes
Parenteral nutrition	Yes	Yes	Yes	Yes	Yes
Surgery within 30 days	No	Yes	No	No	Yes
Candida score	3	4	3	4	4
Treatment for *C. auris* infections					
CVC removal	Yes	Yes	No	No	Yes
Antifungal regimen	Yes (fluconazole)	Yes (caspofungin, micafungin)	Yes (amphotericin B)	Yes (caspofungin)	Yes (caspofungin)
Treatment outcomes					
Microbiological finding	Not tested	Positive for *C. auris*	Negative for *C. auris*	Positive for *C. auris*	Positive for *C. auris*
Survival on day 30	Yes	No	Yes	No	No
Outcome at discharge	Recovered	Death	Poor prognosis	Poor prognosis	Death

ARDS: acute respiratory distress syndrome; COVID-19: coronavirus disease 2019; CVC: central venous catheter.

samples were found positive for *C. auris*. *C. auris* was detected using real-time polymerase chain reaction and rapid clade-identification method (all being clade 1).[16,17] All of these samples were drawn at the intensive care unit (ICU). The isolates of *C. auris* were tested for antifungal susceptibility using the broth dilution method, as described in the document of the Centers for Disease Control and Prevention.[18] The cases were reported as follows (with the characteristics and treatment timelines being summarized in Tables 1 and 2, respectively).

Case 1

A 40-year-old female with no medical conditions was hospitalized for fever, cough, dyspnea, and diarrhea, and had a diagnosis of moderate COVID-19 (classified by the National Institute of Health[19]) upon admission. As the disease progressed severely, she developed acute respiratory distress syndrome and bacteremia. The patient was inserted central venous catheter (CVC), was mechanically ventilated, and received midazolam, rocuronium, enoxaparin, broad-spectrum antibiotics (for *Acinetobacter baumannii* and *Pseudomonas aeruginosa*), dexamethasone, tocilizumab, and parenteral nutrition. On day 22, *C. auris* was isolated (antifungal susceptibility in Table 3). Fluconazole was initiated for *C. auris* on day 27 (upon receiving a positive culture result), with a loading dose of 800 mg and a maintenance dose of 400 mg, q24h. Clinical status started to improve after 3 days (ventilator weaning, clinical sobriety, and oral nutrition). By day 41, when fluconazole was discontinued, no other blood culture had been tested for *C. auris*. The patient recovered and was discharged on day 45. We found no re-hospitalization or any other adverse events within 90 days of discharge.

Table 2. Timelines of primary events of the five cases.

Date	Event
Case 1	
August 4, 2021	Admission to the ICU
August 23, 2021	CVC insertion
August 26, 2021	Blood culture test for fungal pathogen
August 30, 2021	Detection of *Candida auris*
August 31–September 14, 2021	Fluconazole, loading dose of 800 mg (first day) and maintenance dose of 400 mg, q24h
September 15, 2021	CVC removal
September 18, 2021	Discharge
Case 2	
September 1, 2021	Admission to the ICU
November 8, 2021	Blood culture test for fungal pathogen
November 11, 2021	Detection of *C. albicans*
November 12–November 26, 2021	Caspofungin, loading dose of 70 mg (first day) and maintenance dose of 50 mg, q24h
November 17, 2021	Second blood culture test for fungal pathogen
November 21, 2021	Detection of *C. auris*
November 27–November 28, 2021	Micafungin 100 mg, q24h
November 29, 2021	Death
Case 3	
December 13, 2021	Admission to the hospital
December 22, 2021	Admission to the ICU
January 7, 2022	Blood culture test for fungal pathogen
January 10, 2022	Detection of *C. auris*
January 10–24, 2022	Amphotericin B 50 mg, q24h
January 18–February 6, 2022	Blood culture tests were negative for *C. auris*
February 8, 2022	Discharge with poor prognosis
Case 4	
September 28, 2022	Admission to the ICU
September 29, 2022	CVC insertion
October 10, 2022	Blood culture test for fungal pathogen
October 13, 2022	Detection of C. *auris*
October 14–October 24, 2022	Caspofungin, loading dose of 70 mg (first day) and maintenance dose of 50 mg, q24h
October 21, 2022	The blood culture test was positive for *C. auris*
October 24, 2022	Discharge with poor prognosis
Case 5	
November 1, 2022	Admission to the hospital
November 7, 2022	Admission to the ICU
November 8, 2022	CVC insertion
December 29, 2022	Blood culture test for fungal pathogen
January 3, 2023	Detection of C. *auris*
January 3–January 15, 2023	Caspofungin, loading dose of 70 mg (first day) and maintenance dose of 50 mg, q24h
January 5, 2023	CVC removal. The blood culture test was positive for *C. auris*
January 11, 2023	The blood culture test was negative for *C. auris*
January 16, 2023	Death

CVC: central venous catheter; ICU: intensive care unit.

Case 2

An 82-year-old female with a history of hypertension, ischemic stroke, chronic hepatitis B, ovarian cancer, and femoral head fracture was hospitalized for sepsis, pneumonia, and necrotizing fasciitis in the buttocks. Treatment included debridement and drainage (for the necrotizing fasciitis), broad-spectrum antibiotics through CVC, parenteral nutrition, and mechanical ventilation. After debridement, the patient received intensive resuscitation, wound care, and low-dose norepinephrine. On day 67, *C. albicans* was isolated from a blood sample. Caspofungin was initiated for *C. albicans* on day 71 (upon receiving positive culture result), with a loading dose of 70 mg and maintenance dose of 50 mg, q24h. On day 76, *C. auris* was also isolated (antifungal susceptibility in Table 3), although the patient was receiving standard antifungal therapy. After a

Table 3. Antifungal susceptibility of *Candida auris* isolates.

Antifungal agents	MIC (μg/mL)					
	Breakpoint[a]	Case 1	Case 2	Case 3	Case 4	Case 5
Amphotericin B[b]	⩾2	8	4	—[c]	8	8
Fluconazole[b]	⩾32	1	2	—[c]	1	2
Voriconazole	N/A	⩽0.12	⩽0.12	—[c]	⩽0.12	⩽0.12
Caspofungin[b]	⩾2	0.25	0.25	—[c]	⩾8	0.25
Micafungin[b]	⩾4	0.12	0.12	—[c]	0.12	0.12
5-Flucytosine	N/A	⩽1	⩽1	—[c]	—[c]	—[c]

[a]These breakpoints were tentative at that time and did not imply any definitive resistance status of *C. auris*.
[b]Only these antifungal agents were available as intravenous products at that time.
[c]No test was conducted.
MIC: minimal inhibitory concentration; N/A: not available.

14-day course of caspofungin, the patient was switched to micafungin 100 mg, q24h (on day 85). Despite intensive treatment, the clinical status continued to deteriorate. On day 88, the patient died of sepsis, pneumonia, multiple organ dysfunction syndrome, and fungemia.

Case 3

A 69-year-old female with post-COVID and end-stage renal disease (currently on conventional hemodialysis) was admitted to the ICU for critical COVID-19 pneumonia, bacteremia, cystitis, cellulitis in two arms, and upper gastrointestinal bleeding. The patient was mechanically ventilated and received broad-spectrum antibiotics with intermittent hemodialysis. The patient's fevers persisted after a 7-day course of standard antibiotics (38.0°C–41.0°C). On day 16, *C. auris* was isolated. Amphotericin B was initiated for *C. auris* on day 19 (upon receiving a positive culture result), with a standard dose of 50 mg, q24h, for 15 days. Blood cultures were negative for *C. auris* on days 27, 33, and 45. On day 42, clinical status started to deteriorate as the patient had signs/symptoms of sepsis and a low platelet/red blood cell count. On day 47, the patient was discharged with a poor prognosis (severe sepsis and septic shock) upon the family's request. The patient died after 1 day of discharge.

Case 4

An 85-year-old female with left ureterolithiasis and pyelonephritis was indicated by contrast-enhanced multislice computed tomography. After the procedure, the patient had symptoms of iopromide-suspected grade-2 anaphylaxis and was admitted to the ICU for further management. At the ICU, the patient's infection progressed severely under anaphylaxis management, which required CVC insertion, antibiotics for the complicated urinary tract infection, and intensive care. The patient was then placed with a JJ stent through the left ureter. During the treatment course at the ICU, the patient was ventilated due to respiratory failure, which resulted in ventilator-associated pneumonia that required broader-spectrum antibiotics and parenteral nutrition. On day 17, caspofungin was initiated for the isolated *C. auris* (antifungal susceptibility available on day 28, Table 3), with a loading dose of 70 mg and maintenance dose of 50 mg, q24h. On day 24, *C. auris* was still isolated from the blood culture. Clinical status continued to deteriorate (septic shock on day 25). On day 27, the patient was discharged with a poor prognosis upon the family's request. The patient died after 1 day of discharge.

Case 5

A 92-year-old female with bowel obstruction due to metastatic colorectal cancer was hospitalized for a colostomy. After the procedure, the patient was admitted to the ICU, ventilated, inserted a CVC, and received broad-spectrum antibiotics with intensive care. On day 63, caspofungin was initiated for the isolated *C. auris* (antifungal susceptibility in Table 3), with a loading dose of 70 mg and maintenance dose of 50 mg, q24h. Blood culture was positive for *C. auris* on day 66 but was negative on day 71. Caspofungin was discontinued on day 76. The patient died on day 77 with septic shock and *C. auris* fungemia as attributable causes.

Discussion

In this case series, we identified many patterns that have been reportedly risk factors for *C. auris* infections, including multiple comorbidities, severe-to-critical illness, admission to the ICU, exposure to broad-spectrum antibiotics, or history of surgery/invasive procedure.[2,12,20–23] While *C. auris* has been cultured from many organs or sites within the human body,[24,25] we only found its isolates in the blood samples. This suggests that some invasive procedures or surgeries could have facilitated the entry of *C. auris* into the bloodstream or sterile sites from the internal (patient's skin) or external sources (caregiver or hospital environment), as reported in previous studies.[20,22,25,26] The risk of invasive *C. auris* infections is even greater if the patients have moderate-to-critical COVID-19, are on steroid therapy, or are admitted for intensive treatment at the ICU.[14,22–25,27–30] The joint

effects of these factors could be observed clearly in case 1 of this study, where the patient did not have any significant medical conditions before admission. Moreover, the use of broad-spectrum antibiotics, as for all five cases in this study, could cause dysbiosis, which is likely associated with the in vivo intestinal colonization and dissemination of *C. auris*.[31] Noticeably, prior use of antifungal therapy may also induce selective pressure of resistant *C. auris*, as reported in case 2 of this study, thus increasing the risk of invasive infections.[23,24,27] These factors, combined with the inadequate infection control strategies and long survival of *C. auris* on many surfaces,[32] have partially explained the outbreak of this pathogen in our facility.

Other reported *C. auris* outbreaks worldwide also had similar patterns.[33,34] This suggests that in high-risk settings, for example, at the ICU, the emergence of one *C. auris* isolate may trigger a series of *C. auris* infections, leading to potential outbreaks in patients with multiple risk factors. While predicting such infections is challenging or even unfeasible in low-middle-income countries, it is more practical to prevent the outbreaks following these cases by implementing extensive infection control strategies.[24] However, screening for *C. auris* is still useful if resources are available and affordable. This is particularly important if a patient exposed to risk factors of *C. auris* gets transferred to another cleaned setting. The two cases reported in Australia and Taiwan are typical examples of this screening program.[35,36] In the context of global threats posed by emerging pathogens, it is also essential that low-middle-income countries establish a central reporting system for effective monitoring, surveillance, and prevention of infections, ensuring timely interventions and coordinated public health responses.

As *C. auris* is notorious for its high resistance against many antifungal agents (especially amphotericin B, fluconazole, etc.),[11–15] treatment options are often limited, with echinocandin drug as the recommended initial therapy.[37] While all isolates in this case series were sensitive to most available antifungal agents and most patients were given optimal regimens, only one case recovered. Since this study design was not appropriate to draw any confirmative conclusion, we hypothesized that in patients with *C. auris* infections, effective antifungal regimens alone might not improve treatment outcomes. This is based on the fact that these infections are more likely to develop in patients with severe-to-critical illness or multiple comorbidities. These factors themselves are strongly associated with poor prognosis, which can confound the effect of antifungal regimens on survival or recovery. Therefore, management of *C. auris* infections should include both intensive and extensive care with multisectoral collaboration. As for our setting, we have implemented the following measures to limit and prevent other outbreaks of *C. auris* infections: enhancing infection control practices (hand hygiene, environmental cleaning, and isolation of infected patients), active surveillance and screening programs, and strengthening laboratory capacity for accurate and timely diagnosis.

Conclusion

In this first case series about *C. auris* in Vietnam, we reported five patients with severe illness who developed *C. auris* fungemia after more than 10 days of treatment at the ICU; four out of five patients died or were discharged with poor prognosis. We found some common patterns that could be the risk factors for *C. auris* infections among these cases, including multiple comorbidities, disease severity, use of broad-spectrum antibiotics, or history of surgery/invasive procedures. However, as our study was not designed or powered to detect such statistical associations, further studies are needed to confirm these hypotheses. Screening and preventive measures for *C. auris* should also be investigated, especially in low-resource settings.

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None.

Author contributions

H.T.P., T.H.T., and A.H.V.: conceptualization, writing—original draft preparation, writing—review and editing, patient care. M.-T.N.S. and H.H.N.: writing—original draft preparation, writing—review and editing. M.-H.T.: conceptualization, writing—original draft preparation, writing—review and editing, supervision.

Data availability statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: H.T.P. reported receiving speaking fees and travel reimbursement from Servier Vietnam Ltd and Pfizer Vietnam Ltd, grants from Servier Vietnam Ltd outside the submitted work. M.-H.T. reported receiving travel reimbursement from Pfizer Vietnam Ltd, speaking fees, and grants from Servier Vietnam Ltd outside the submitted work. The other authors declare no competing interest.

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Ethical considerations

Ethical approval to report this case series was obtained from the Ethics Committee of Nhan Dan Gia Dinh Hospital (approval number 61-2021/NDGD-HDDD).

Informed consent

Written informed consent was obtained from the patient (for case 1) and from the legally authorized representatives (for cases 2, 3, 4, and 5 of the DECEASED subjects) for their anonymized information to be published in this article.

Consent to participate

Not applicable.

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