Arrival of *Candida auris* Fungus in Singapore: Report of the First 3 Cases

Dear Editor,

Candida auris is an emerging fungus that is of increasing global concern. Healthcare-associated outbreaks and cases have been reported in 5 continents[1-2] and the number of countries involved is growing. This is alarming as *C. auris* is commonly multidrug-resistant with some isolates displaying pan-resistance to the available antifungal drugs.[3] Here, we report the first 3 cases of *C. auris* isolated from a tertiary hospital in Singapore. Table 1 summarises the clinical characteristics, management, outcome and antifungal susceptibilities of these cases.

Case 1

The first case was detected back in 2012. A 52-year-old local-born Chinese lady was transferred from India following a road traffic accident. She sustained multiple bilateral lower limb fractures. External fixation was performed for the right femur fracture in India and the patient received multiple

Table 1. Clinical Characteristics, Management, Outcome and Antifungal Susceptibilities of the 3 Cases of *Candida auris*

Case/Year	**1/2012**	**2/2016**	**3/2017**
Transferred from overseas hospital/country	Yes/India	Yes/Bangladesh	Yes/Bangladesh
Main diagnosis	Traumatic fractures	Metastatic carcinoma	Infective exacerbation of COPD
CP-CRE screening*/type of carbapenemase(s)† identified	Positive/NDM-1	Positive/NDM and OXA-232	Positive/OXA-232
C. auris isolation site	Right femur tissue	Blood	Blood
Antifungal therapy			
Prior *C. auris* isolation	Yes. Fluconazole for 10 days.	Yes. Fluconazole was given in Bangladesh. Duration not known.	Not known back in Bangladesh. Not given upon arrival in Singapore.
Post *C. auris* isolation	Yes. Fluconazole for 6 days before *C. auris* antibiogram was known.	Yes. Anidulafungin for 1 day prior discharge to Bangladesh.	No. Palliative care.
Outcome	Survived	Not known	Death
Antifungal Susceptibility Testing	**Antifungal MIC in µg/ml (Interpretation)‡**		
Fluconazole	256 (R)	≥256 (R)	256 (R)
Voriconazole	1 (NA)	1 (NA)	2 (NA)
Itraconazole	0.25 (NA)	0.12 (NA)	0.12 (NA)
Posaconazole	0.06 (NA)	0.06 (NA)	0.06 (NA)
Caspofungin	≥8 (R)	0.06 (S)	0.12 (S)
Anidulafungin	0.5 (S)	0.12 (S)	0.12 (S)
Micafungin	0.25 (S)	0.12 (S)	0.06 (S)
Amphotericin B	2 (R)	2 (R)	1 (S)
Flucytosine	0.25 (NA)	≤0.06 (NA)	≤0.06 (NA)

COPD: Chronic obstructive pulmonary disease; CP-CRE: Carbapenemase-producing carbapenem-resistant *Enterobacteriaceae*; MIC: Minimum inhibitory concentration; NA: Not available; NDM: New Delhi metallo-β-lactamase; OXA: Oxacillinase; R: Resistance, S: Susceptible

*Screening was performed from stool or rectal swab on admission.
†NDM and OXA.
‡There are currently no established susceptibility breakpoints for *C. auris*. Interpretation is based on the US CDC tentative MIC breakpoints for *C. auris* (Centres for Disease Control and Prevention. Recommendations for identification of *Candida auris*. Available at: https://www.cdc.gov/fungal/diseases/candidiasis/recommendations.html. Accessed on 1 February 2018.) Fluconazole ≥32 µg/ml (R), amphotericin B ≥2 µg/ml (R), anidulafungin ≥4 µg/ml (R), caaspofungin ≥2 µg/ml (R), micafungin ≥4 µg/ml (R).

antibiotics prior to transferring to Singapore for further management at day 5. Patient underwent external fixation to the left tibia fracture in Singapore on the following day with the right external fixator left in-situ. Unfortunately, the wound at the pin track site of the right femur shaft fracture was infected and intraoperative tissue cultures grew multiple organisms including *C. auris* on hospital day 78. Both antibiotics and antifungal were initiated. However, fluconazole was discontinued after 1 week when *C. auris* was tested to be resistant to it (Table 1). Due to an improvement in the inflammatory markers, no further antifungal drug was given. Blood cultures remained sterile throughout the hospitalisation. Patient was discharged 4 months later with the wounds healing well.

Case 2

A 24-year-old Bangladeshi male flew to Singapore in 2016 to seek further medical management. He had been admitted to 3 hospitals in Bangladesh for a total of 21 days for metastatic carcinoma of unknown origin and was given antibiotics including fluconazole before transferring to Singapore. Chemotherapy was initiated upon arrival but patient turned septic and was cultured and covered with antibiotics. Anidulafungin was added subsequently when blood culture taken at day 9 grew *C. auris* (Table 1). However, the patient discharged against medical advice and returned to Bangladesh the following day.

Case 3

A 69-year-old United States' male citizen suffered infective exacerbation of chronic obstructive pulmonary disease (COPD) while touring in Bangladesh in late 2016. He was admitted into the intensive care unit (ICU) in Bangladesh and treated with broad-spectrum antibiotics before transferring to Singapore in early 2017 for further management.

The patient suffered from a series of medical complications including cardiac arrest and brain infarcts during his hospitalisation here. Septic workup grew *C. auris* from the blood culture taken on day 9 of admission (Table 1). Antifungal therapy was not initiated as patient was not for active management after discussion with family members. He deteriorated rapidly and passed away shortly after.

The identification of *C. auris* was confirmed by sequencing of the internal transcribed spacer (ITS). Antifungal susceptibilities were performed using Sensititre™ YeastOne® microdilution panel (TREK Diagnostic Systems Ltd, Thermo Scientific). Although there are currently no established Clinical Laboratory Standard Institute (CLSI) and European Committee for Antimicrobial Susceptibility Testing (EUCAST) susceptibility breakpoints for *C. auris*, the United States Centers for Diseases Control and Prevention (US CDC) does provide tentative minimum inhibitory concentration (MIC) breakpoints for certain antifungals as a general guide.[4] It must be emphasised that these breakpoints are not definitive and an elevated MIC does not necessarily preclude the use of an antifungal drug. *C. auris* isolates uniformly display high fluconazole MICs and about one-third of them have raised MICs to voriconazole and amphotericin B which are similar to the cases here.[5-6] As such, echinocandins are the empiric drugs of choice for *C. auris* infections, although they have no activity against *C. auris* biofilms.[6] Coincidentally, all 3 cases were screened positive for carbapenemase-producing carbapenem-resistant *Enterobacteriaceae* (CP-CRE) and were isolated with contact precautions (Table 1).

C. auris has not been previously reported in Singapore.[7] These 3 cases all appear to be imported. This highlights the need for a screening policy for *C. auris* in patients transferred from overseas hospitals, especially from countries reported to have this yeast in order to prevent its establishment and spread within the institution. Despite our first case in 2012 and not doing active surveillance, we were fortunate not to experience any outbreaks of *C. auris* infection during this period. This may be due to the heightened infection control for all 3 cases which were screened positive for CP-CRE. The isolation of CP-CRE may also indicate the high probability of co-colonisation with *C. auris* in patients transferred from overseas hospitals. This was not surprising as some of these countries were reported to have high incidence of CP-CRE too.[8] With the propensity of *C. auris* to cause outbreaks in healthcare settings,[2,9] institutions may have to do risk assessment to consider including this fungus into their screening protocols and further strengthen infection control measures to prevent it from becoming a major global public health issue.

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