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Letter to the Editor

# Outbreak of *Candida auris* infection in a COVID-19 hospital in Mexico

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*To the Editor,*

Since its emergence in December 2019, the rapid spread of coronavirus disease 2019 (COVID-19) has necessitated the expansion and transformation of healthcare facilities worldwide to accommodate the constantly increasing numbers of patients. This situation has provided a potential ground for the transmission of nosocomial infections [1]. *Candida auris* is a multidrug-resistant fungal pathogen with the capability for nosocomial transmission. Some studies have suggested an increased risk for *Candida* sp. in COVID-19 patients, resulting in poor outcomes [2,3].

Here we describe an outbreak of *C. auris* which started in a non-COVID-19 patient at the end of May 2020 (reported previously [4]). This occurred during the transition of the hospital to an exclusive COVID-19 facility; the infection later spread to 12 patients in the intensive care unit (ICU).

We collected the clinical data of all the patients admitted to the hospital from April 2020 to the present date. Characteristics of the patients with a diagnosis of *C. auris* infection were analysed. This study was approved by the Research Ethics Committee of the Hospital San José Tec-Salud (registration number: P000353-COVID-19-TecSalud-CS001).

*C. auris* strains from 12 patients and three environmental isolates from their bedrooms were identified by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry (Bruker Daltonics, MALDI Biotyper) and confirmed by multilocus sequence typing of the ITS1-5.8S-ITS2, D1/D2, RPB1 and RPB2 regions. Sequences were aligned and analysed by MEGA v.7.0.26 and a dendrogram was delineated. Antifungal susceptibility testing for amphotericin B (AMB), fluconazole (FLU), voriconazole (VRC), posaconazole (POS), itraconazole (ITC), isavuconazole (ISA), anidulafungin (ANF) and caspofungin (CAS) was performed using the Clinical and Laboratory Standards Institute (CLSI) broth microdilution method M27-A3/S4.

Our team reported the first case of *C. auris* infection in May 2020. At that time the hospital was transitioning from a general hospital to an exclusive COVID-19 facility which included expansion of the ICU to four areas with 60 beds; this was completed as the last non-COVID-19 patient was discharged.

Three months later an outbreak of COVID-19-associated *Candida auris* infections started in three of the ICUs, affecting 12 patients. All the affected patients were under mechanical ventilation, had peripherally inserted central lines (PICCs), urinary catheters and prolonged hospital stay (20–70 days). *C. auris* was isolated from blood in six patients (6/12; 50%), from urine in eight (8/12; 66.6%), and from both sites in two (2/12; 16.6%). Mortality was 83.3% (5/6) among the patients with candidaemia (Table 1A).

Sequences of the genes used for the 15 *C. auris* isolates clustered together in the dendrogram performed with the sequence previously reported from a non-COVID-19 patient, which belonged to the Clade IV (South American) [4], suggesting a very close relationship. Antifungal susceptibility testing showed that all the isolates (15/15) were resistant to AMB (MIC ≥2 μg/mL), just one isolate was resistant to ANF (MIC ≥4 μg/mL), one to CAS (MIC ≥2 μg/mL)

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**Table 1**
(A) Clinical characteristics of 12 patients with *C. auris* infection and COVID-19 pneumonia. (B) MLST and antifungal susceptibility results of the *C. auris* isolates from the patients and surface sampling from an infusion pump (13) and bed rails (14 and 15)

A. Clinical characteristics of 12 patients with *C. auris* infection and COVID-19 pneumonia.

| No. Patient | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age | 51 | 54 | 55 | 51 | 64 | 64 | 54 | 60 | 58 | 36 | 66 | 46 |
| Sex | M | M | M | M | M | M | F | F | M | M | M | M |
| Co-infections | *Pseudomonas aeruginosa* | *Pseudomonas aeruginosa, Klebsiella pneumoniae* | *Pseudomonas aeruginosa, Candida glabrata* | *Pseudomonas aeruginosa, Candida glabrata, Enterococcus faecalis* | *Pseudomonas aeruginosa* | *Candida glabrata* | None | *Pseudomonas aeruginosa* | *Pseudomonas aeruginosa* | Cytomegalovirus | *Pseudomonas aeruginosa, Stenotrophomonas maltofilia* | None |
| Risk factors | HBP, DM2, Obesity | HBP, DM2, Obesity, Asthma | HBP, DM2, CAD | Obesity | AKI | HBP, Smoking, Obesity, Hipothyroidism | HBP, Obesity. | Obesity | HBP, Obesity | DM2, Obesity | HBP, DM2, CAD, VHD | Obesity |
| Antibiotics | CTR, CAZ/ABI, MEM, LZD | MEM, LZD, VAN, TZP, VAN, CTZ/TAZO | CRO, MEM, LZD, CAZ/ABI | CRO, MEM, LZD, CTZ/TZP, CST | CRO, LZD, CAZ, MEM, CAZ/ABI | CRO, CAZ, TZP | AZM, LZD, CRO, VAN, CTZ/TZP | CRO, LZD, CAZ, CAZ/ABI, VAN | CTZ/TZP, VAN, CRO, CST | CRO, LZD, CAZ, MEM, VGV | TZP, MEM, CTZ/TZP, METRO | CRO, MEM, CAZ/ABI, LZD |
| SARS-CoV-2 treatment | LPV/RTV, RBV, BARI, PLASMA | LPV/RTV, RBV, BARI | LPV/RTV, RBV, BARI | LPV/RTV, RBV, BARI, PLASMA | LPV/RTV, RBV, BARI | LPV/RTV, RBV, BARI, TOCI, PLASMA | LPV/RTV, RBV, BARI, | LPV/RTV, RBV, BARI, PLASMA | LPV/RTV, RBV, BARI | LPV/RTV, RBV, BARI, TOCI, PLASMA | LPV/RTV, RBV, BARI | LPV/RTV, RBV, BARI |
| Steroids | Dex 6mg QD Hidro 100mg BID | Dex 6mg QD Metil 60mg BID | Dex 6mg QD Hidro 100 BID | Dex 6mg QD | Metil 40mg BID | Metil 40mg BID | Dex 6mg QD | Metil 125mg BID | Hidro 100mg TID | Metil 60mg BID Hidro 100mg TID | Dex 6mg QD Metil 60mg BID | Dex 6mg QD Metil 60mg BID |
| Cumulative dose of steroids (mg prednisone) | 1480mg | 1580 | 1360 | 1440 | 1300 | 1000 | 1240 | 5000 | 2025 | 2550 | 1320 | 3280 |
| Antifungals | CAS, ANF | ISA, CAS | ANF | ISA, ANF | CAS, VRC, AMB (intravesical) | ANF, ISA | AMB, CAS, VRC | CAS, ANF, VRC | ANF | CAS | VRC, CAS | VRC, CAS |
| Interleukin 6 (pg/mL) | 270.5 | NA | 89.56 | 192.2 | 9.29 | 44.13 | 798.3 | NA | 235.9 | 203.6 | NA | NA |
| D dimer (ng/mL) | 831 | 383 | 254 | 2000 | 5516 | 150 | 2117 | 143 | 16,111 | 448 | 280 | 84 |
| Ferritin (ng/mL) | 1563 | 3187 | 1701 | 11,007 | 4163 | 3694 | 1199 | 658 | 2235 | 3292 | 2030 | 1307 |
| Culture | Blood | Urine | Blood | Urine | Blood and Urine | Blood, PIC line and Urine | Blood | Urine | Urine | Urine | Urine | Blood |
| *Days to 1st. positive culture | 37 | 17 | 29 | 36 | 13 | 10 | 31 | 16 | 27 | 22 | 11 | 27 |
| Outcome | Died | Survived | Died | Died | Died | Died | Died | Died | Died | Survived (Hospital transfer) | Survived | Survived |

B. MLST and antifungal susceptibility results of the *C. auris* isolates from the patients and surface sampling from an infusion pump (13) and bed rails (14 and 15).

| No. Isolate | GenBank accession numbers (ITS-D1/D2-RPB1-RPB2) | ST cluster | MIC (μg/mL) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | AMB | FLC | VRC | POS | ITC | ISA | ANF | CAS |
| 1 | MW087107-MW089312-MW091400- MW113720 | IV | 4 | 64 | 1 | 0.5 | 2 | 0.5 | 1 | 1 |
| 2 | MW087108-MW089313-MW091401- MW113721 | IV | 4 | 16 | 0.25 | <0.03 | 0.25 | 0.06 | 1 | 1 |
| 3 | MW087109-MW089314-MW091402- MW113722 | IV | 2 | 16 | <0.03 | <0.03 | 0.5 | 0.25 | 0.5 | 0.5 |
| 4 | MW087110-MW089315-MW091403- MW113723 | IV | 2 | 16 | 0.5 | 0.06 | 2 | 0.5 | 1 | 1 |
| 5 | MW087111-MW089316-MW091404- MW113724 | IV | 2 | 64 | 0.25 | 0.06 | 0.125 | 0.125 | 0.5 | 1 |
| 6 | MW087112-MW089317-MW091405- MW113725 | IV | 2 | 16 | 0.125 | 0.03 | 0.25 | 1 | 1 | 0.5 |
| 7 | MW087113-MW089318-MW091406- MW113726 | IV | 4 | 64 | 0.5 | 0.5 | 1 | 0.5 | 0.5 | 1 |
| 8 | MW087114-MW089319-MW091407- MW113727 | IV | 2 | 32 | 0.25 | 0.03 | 0.5 | 0.125 | 0.5 | 1 |
| 9 | MW087115-MW089320-MW091408- MW113728 | IV | 4 | 64 | 1 | 0.125 | 0.50 | 0.125 | 0.5 | 1 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 10 | MW087116-MW089321-MW091409- MW113729 | IV | 4 | 32 | 0.125 | 0.125 | 0.125 | 0.06 | 0.5 | 1 | |
| 11 | MW087117-MW089322-MW091410- MW113730 | IV | 4 | 8 | 0.06 | <0.03 | 0.06 | 0.125 | 4 | 0.5 | |
| 12 | MW087118-MW089323-MW091411- MW113731 | IV | 2 | 8 | 0.125 | <0.03 | 0.06 | 0.125 | 0.5 | 1 | |
| 13 | MW087119-MW089324-MW091412- MW113732 | IV | 4 | 32 | 0.06 | 0.06 | 0.125 | 0.25 | 1 | 2 | |
| 14 | MW087120-MW089325-MW091413- MW113733 | IV | 4 | 16 | 0.125 | 0.06 | 0.125 | 0.25 | 2 | 0.5 | |
| 15 | MW087121-MW089326-MW091414- MW113734 | IV | 4 | 32 | 0.125 | 0.25 | 0.5 | 0.5 | 1 | 1 | |

CTR: ceftaroline; CAZ: ceftazidime; CAZ/ABI: ceftazidime/abivactam; CRO: ceftriaxone; CTZ/TZP: ceftolozane/tazobactam; CST: colistin; AZM: azithromycin; VAN: vancomycin; MEM: meropenem; MTZ: metronidazole; TZP: piperacillin/tazobactam; ISA: isavuconazol; ANF: anidulafungin; CAS: caspofungin; AMB: amphotericin B; VRC: voriconazole; LPV/RTV: lopinavir/ritonavir; VGV: valganciclovir; Metil: methylprednisolone; Hidro: hydrocortisone, DEX: dexametasone; BARI: baricitinib; TOCI: tocilizumab; CAD: coronary artery disease; VHD: valvular heart disease; HBP: high blood pressure; DM2: diabetes mellitus type 2; AKI: acute kidney injury; NA: not available; PIC: peripherally inserted central catheter.
AMB: amphotericin B; FLC: fluconazole; VRC: voriconazole; POS: posaconazole; ITC: itraconazole; ISA: isavuconazole; ANF: anidulafungin; CAS: caspofungin; MIC: minimal inhibitory concentration; ST: sequence typing.
* Number of days elapsed from hospital admission to the first positive culture for *C. auris*.

and eight isolates (8/15; 53.3%) were resistant to FLU (MIC ≥32 μg/mL). Eight isolates were multidrug-resistant (resistance to two major classes of antifungals) (Table 1B).

Numerous reports have described COVID-19 co-infections by fungal pathogens, especially in critically ill patients. As stated in the work of Arasthefar et al. [5], classic risk factors commonly found in these patients include diabetes mellitus, use of multiple antibiotics, renal failure, and use of central venous catheters, but other factors specifically associated with COVID-19—such as excessive corticosteroid use, which has an immunosuppressive effect on neutrophils and macrophages—might also contribute to this problem. Nonetheless, a lot of interest still exists in elucidating a relationship between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immune response and predisposition to *Candida* infection [2].

In our report 12 patients have presented COVID-19-associated *C. auris* infection, and so far only three environmental samples have yielded this pathogen. The prolonged lag between the first case 3 months ago and current cases is thought to be due to measures taken during the transformation process from a general hospital to a COVID-19-exclusive facility, such as reinforcement of hand washing compliance and use of personal protective equipment (PPE). Chowdhary et al. [6] theorized that transmission of COVID-19-associated *C. auris* by health personnel is unlikely because of the use of PPE. The 15 isolates of *C. auris* were non-susceptible to AMB and FLU, which are the main antifungal drugs used in most of the hospitals in Mexico.

This study has some limitations as it was conceived as a description of an outbreak; as such, there is no control group, and findings may not be generalizable to other populations. Nonetheless mortality in patients with COVID-19-associated *C. auris* bloodstream infection was exceedingly high, five of six patients died even with antifungal treatment; strict control of risk factors, such as central line care bundles, corticosteroids and antibiotic stewardship, must therefore be implemented to avoid the lethal combination of these two emergent infectious threats.

## Author contributions

HV-L, RJT-R and GMG contributed to drafting and revising the article, as well as in the conception and design of the study. RL-M, MTR-E and NG-Ch contributed to the acquisition and interpretation of data. FC-L, MCA-B, CEG-L and GT-A contributed to revision and final approval of the report. MFM-R participated in the analysis and interpretation of data, drafting and final approval of the version to be submitted.

## Transparency declaration

All authors declare no conflicts of interest. This work was supported by internal resources of the department.

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