



Candida auris colonization in an immunocompetent patient: A new threat in medical ICU



Shukla Das^{a,*}, Richa Tigga^a, Gargi Rai^a, Praveen Kumar Singh^a, Shyama Datt^a, Asha Tyagi^b, Narendra Pal Singh^a

^a Department of Microbiology, University College of Medical Sciences, Delhi 110095, India

^b Department of Anaesthesiology and critical care, University College of Medical Sciences, Delhi 110095, India

ARTICLE INFO

Keywords:

Candida auris
Candidemia
Colonization
Intensive care unit
Sequencing

ABSTRACT

Candida auris has become a great challenge in diagnostic, therapeutic and hospital environmental adaptation. With a prevalence of 5.3% in intensive care unit (ICU) acquired candidemia in India, its colonization is very rapid which hastens hospital transmission. Strict surveillance and preventive measures need to be adopted in ICU as it can persist on dry, inanimate object, prompt adaptation and antifungal resistance can pose a future threat of a new drug hospital acquired pathogen.

1. Introduction

Candida auris is an emerging fungal pathogen reported globally as well as from India. As multi-drug resistant yeast, it has been reported to cause bloodstream, wound, urinary and respiratory tract infections since its first isolation from the ear canal of a Japanese patient [1,2]. Its existence in the environment and isolation from healthcare workers, and from skin and mucosa of the hospitalized patients convey its potential to spread horizontally in the hospital [3,4]. Phenotypic features of thermo-tolerance and growth on 0.1% cycloheximide may raise suspicion of *C. auris*; however, its molecular confirmation or detection by MALDI-TOF is mandatory as per national guidelines [5]. The whole genome sequence analysis of various isolates of *C. auris* has shown minimal clonal difference [6,7]. With limitations in the identification, we present a case of *C. auris* from a large tertiary care hospital in Delhi, India, methods adopted to identify the isolates and study the post-hospitalization colonization in the patient

2. Case

A 13-year-old male patient was referred to our tertiary care hospital emergency department from a private nursing home for failure to wean off ventilatory support over 1 week. He had been admitted to the private nursing home with an alleged history of organophosphate poisoning followed by acute respiratory distress syndrome requiring mechanical ventilation; and a cardio respiratory arrest from which he was revived. Upon examination (Day 0) in our emergency department he

was unconscious, not maintaining oxygenation despite endotracheal tube in situ; on ambu ventilation 93% SpO₂ was maintained, with a pulse rate of 92/min. and blood pressure of 120/84 mmHg. The patient was shifted to medical ICU on day 1 immediately for supportive management. Previously, antibiotic therapy initiated at the private nursing home, included empirical tazopip (piperacillin + tazobactam), levofloxacin and augmentin. In addition, injection fluconazole was also started. A single record of total leucocyte count (TLC) of 25,000/mm³ on the first day of admission was available.

Upon admission to the ICU of our hospital, the patient continued to receive mechanical ventilation and his antibiotic therapy was modified to injection tazopip and targocid (teicoplanin) on day 1. Routine blood investigations including haemogram, liver and kidney function tests were performed. Tracheal tube isolate sampled through suction catheter was submitted for a bacteriological culture which grew *Pseudomonas aeruginosa*, sensitive to amikacin, gentamicin, ciprofloxacin, tobramycin, meropenem, imipenem and resistant to ceftazidime, aztreonam, and tazopip. The blood culture (BACTEC, 9120) sent at the same time showed no growth on 5 days of incubation at 37 °C. In view of the failure to extubate and worsening chest condition, respiratory distress and desaturation, ciprofloxacin and amikacin along with metronidazole were initiated at this time, based on the tracheal tip culture report. Despite continuing this therapy, the TLC continued to rise and lack of clinical improvement prompted a repeat blood culture on (Day 7). While awaiting the report of blood culture, blood counts increased to (20,000/mm³) with signs of respiratory distress. A decision to modify treatment was taken, with injection meropenem, levofloxacin

* Corresponding author.

E-mail address: shukladas_123@yahoo.com (S. Das).

<https://doi.org/10.1016/j.mmcr.2018.05.004>

Received 28 March 2018; Accepted 9 May 2018

Available online 10 May 2018

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with amikacin was administered for next 6 days. The blood culture meanwhile grew MRSA (Methicillin-Resistant *Staphylococcus aureus*) that was sensitive to vancomycin, tetracycline and resistant to erythromycin, clindamycin, ceftioxin, ampicillin. Consequently, vancomycin was added, to which the patient responded and became afebrile. Thereafter the TLC normalized and the patient was weaned off the ventilator, although with a tracheostomy tube in situ. Treatment with meropenem and levofloxacin continued for a total of 10 days.

The patient continued to stay in the ICU when a repeat blood culture was sent on day 14 which grew yeast, while tracheal suction tip isolates grew *Acinetobacter baumannii* which was resistant to cefotaxime, ciprofloxacin, amoxicillin-clavulanic acid, tigecycline, piptaz. On phenotypic characterization as per conventional techniques, the yeast was identified as non-albicans *Candida* (later confirmed as *C. auris*). As per our hospital ICU protocol of sending bi-weekly blood culture, a repeat sample on day 17 also grew *Candida non-albicans* species. The patient eventually responded to treatment and was shifted out of ICU. The patient started accepting feeds but continued to maintain respiration with a tracheostomy. On obtaining blood culture positive for *C. auris*, an attempt was made to identify the sites of colonization. One swab each was collected from the patient's axilla (right and left), groin, tracheostomy opening for culture. Environmental sampling was also done which included suction nozzle, patient's bed railings, linen, wash basin, tap and ventilator machine. The swabs were inoculated on blood agar, Sabouraud dextrose agar (SDA) with chloramphenicol and with/without cycloheximide. *C. auris* grows at 42 °C but fails to grow in the presence of 0.1% cycloheximide. MRSA and yeast were isolated from tracheostomy site discharge, both axilla and groin. The yeast was identified on MicroScan (BioRad, California, USA) as *C. famata*. The cultures from water tap grew *Klebsiella pneumoniae*; from wash basin we isolated *Acinetobacter baumannii*. All the *C. famata* isolates (from blood, tracheostomy site and groin) were subjected to DNA extraction using commercially available DNA extraction kit (HiYield Genomic DNA Kit, RBC, Taiwan). Genomic DNA was subjected to PCR using panfungal primers; ITS1 (5'-TCCGTAGGTGAACCTGCGG-3') and ITS4 (3'-TCCTC CGCTTATTGATATGC-5') to amplify the internal transcribed spacer (ITS) region of 18S rRNA. Purification of the PCR products and DNA sequencing was done commercially. The sequencing was done and compared with sequences deposited in GenBank by using the Blast program to find identical or similar sequences. DNA sequencing analysis of the ITS region showed 100% identity with *C. auris* and all isolates were submitted to GenBank and assigned accession numbers MG679898, MG679899 and MG679900. The isolate from blood culture was deposited at the National Reference and Research Laboratory, Mycology division; Post Graduate Institute of Medical Education Research (PGIMER), Chandigarh, India for further confirmation. The antifungal susceptibility was performed using E strip (HiMedia, Mumbai) method. The MIC for fluconazole was 2 µg/ml, amphotericin B 0.75 µg/ml and 0.0025 µg/ml for caspofungin.

The patient was eventually discharged when repeat blood culture was reported sterile on day 20. He was advised 2% chlorhexidine body wash to counter the fungal load of *C. auris*. From the environmental surveillance it was evident that MRSA from patient bed, *Acinetobacter baumannii* from the wash basin, *Streptococcus viridans* from suction nozzle and *Klebsiella pneumoniae* from taps were the major microbial agents inhabiting the medical ICU. No microbe was isolated from ventilator machine. All the culture isolated was subjected to manual speciation and Microscan identification.

3. Discussion

C. auris, an emerging pathogenic fungus frequently associated with drug resistance has been recently reported from critically ill hospitalized patients admitted to the public sector with underlying respiratory illness or undergone vascular surgery and medical intervention and prior antifungal exposure and prolonged ICU stay, as major risk factors

for acquiring this pathogen [3]. It has a strong potential for nosocomial transmission and most of the invasive infections have been reported from four major continents [8,9]. Several reports have misidentified it as *C. haemulonii* or *Rhodotorula glutinis*, *C. sake* or *Saccharomyces cerevisiae*, *C. famata*, *C. lusitaniae*, *C. guilliermondii* by API or other automated systems. *C. auris* in the United States reported 112 cases till 2017 as global emerging threat and continue a constant surveillance with CDC's Antibiotic Resistance Laboratory Network (ARLN) under the Emerging Infections Program (EIP) [10]. In India, a study from PGIMER Chandigarh observed in one year period (April 2011- September 2012) out of 1400 patients diagnosed with ICU acquired candidaemia, 5.3% (74 patients) were due to *C. auris*. The majority (52, 70.3%) of these *C. auris* cases were adult patients [7]. In another investigation reported by Biswal et al., observed three cases of *C. auris* bloodstream infection over a period of three months. Other patients admitted at the same time, in the same area, were also found to be colonized by *C. auris*. A thorough surveillance detected *C. auris* contamination of environmental surfaces and hands of healthcare workers. Prompt interventions with chlorhexidine washing and use of disinfectants *C. auris* was successfully eradicated from patients and hospital environment [11].

Based on our experience, we observed that colonization of *C. auris* at different anatomical sites (axilla, groin, tracheostomy, etc.) is influenced by prolonged ICU stay, continuous use of intravenous broad-spectrum antibiotics, poor de-escalation policy, excessive use of medical device and poor surveillance strategies. In our case, the blood culture isolate was identified as *C. famata* which prompted us to collect skin swabs from various sites and look for similar growth. Interestingly, the patient was extensively colonized at various sites viz. groin, the skin around tracheostomy tube and axilla, indicating the most probable source causing bloodstream infection. It is well documented that previous use of antifungals and transfer from the private hospital may facilitate the carriage of *C. auris*, as was evident in our case. Hence, isolation of *C. auris* from any patient should raise an alarm, and alert the infection control team to become watchful for *C. auris* colonization amongst the other hospitalized patients in the ICU. The antifungal susceptibility test showed MIC 2 µg/ml for fluconazole and 0.75 µg/ml for amphotericin B and 0.0025 µg/ml for caspofungin. Since the breakpoints for *C. auris* are not yet defined, the cut off suggested for yeast in CLSI M27-S3 were used to interpret the MICs values [12]. Though this isolate was sensitive to the antifungals, however, literature documents the potential ability of *C. auris* to exhibit multi drug resistance and its clonal existence in a hospital environment.

CDC guideline provides alert regarding strict isolation of patients harbouring *C. auris* to prevent horizontal transfer to other patients in the hospital, however in a resource-limited setting, like our tertiary care hospital which caters to a large population from low socioeconomic strata, the possibility of isolation and cohorting patients, is far from reality. The best affordable steps that may be immediately taken under such constraint, is to provide local decolonization with a suitable disinfectant like chlorhexidine or others [11]. In our case, the clinician was educated to use 2% chlorhexidine or similar disinfectant and also advised to use topical antifungal at the tracheostomy site of this patient before discharge. Schelenz et. al., recommend regular environmental and equipment cleaning with high strength chlorine-based agents and hydrogen peroxide vaporization to expedite the reduction of *C. auris* in the environment [13]. It is important to remember that patients admitted to Medical ICU are generally critical, with overwhelming bacterial infection; peritonitis and sepsis, secondly, empirical use of broad-spectrum antibiotics provide a favorable ground for the emergence of drug-resistant pathogens. Though *C. auris* may not be directly associated with high mortality, but emergence and proliferation of this bug will create a niche for the survival of yet another multi-drug resistant organism, with the additional threat in hospital units homing immunocompromised patients.

Very little is known about the factors promoting environmental resilience and transmission, the mechanisms of resistance to antifungal

drugs or disinfectants and properties contributing to prolonged host colonization, hence the management of outbreaks by *C. auris* in healthcare facilities will remain a difficult challenge [13]. Strict vigilance and infection control adherence are future endeavors to reduce the burden of infection in ICU and high dependency sections of the hospital.

Acknowledgements

The authors are thankful to Dr. Arunaloke Chakraborty, Professor Department of Medical Microbiology, and Centre of Advanced Research in Medical Mycology, Post Graduate Institute of Medical Education and Research, Chandigarh, India for confirming our isolate species.

Conflict of interest

There are none.

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