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ORIGINAL ARTICLE PEDIATRICS

Candida auris infection at a pediatric burn center: Treatment and infection control measures

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ABSTRACT

OBJECTIVE: *Candida auris* (*C. auris*), a novel species, has been increasingly associated with hospital outbreaks worldwide in recent years. *C. auris* is regarded as a global health problem due to issues with the identification of *C. auris*, variable antifungal resistance profiles and the requirement for infection prevention and control (IPC) measures. With this study, we aimed to present our experience with two patients with *C. auris* fungemia who were referred to the Pediatric Burn Center of our hospital at different timepoints and share the antifungal treatment strategy and IPC management policies implemented in the clinic.

METHODS: *C. auris* isolates were identified using MALDI-TOF MS (VITEK MS, bioMérieux, France). Antifungal susceptibility tests were performed at the Turkish Public Health Institution (THSK) using the broth microdilution (BMD) method. The BMD was carried out in accordance with the Clinical and Laboratory Standards Institute procedures.

RESULTS: A patient (3-year-old girl) with *C. auris* which was identified at an external center and negative fungal screening results was transferred to our pediatric burn center. On the 41st day of her hospitalization, she was diagnosed with catheter-related bloodstream infection (CRBSI) by *C. auris*. She received antifungal treatment for a total of 52 days, including caspofungin for 12 days, followed by micafungin for 40 days. Three months after the detection of the index case, a second patient (2-year-old girl) was diagnosed with CRBSI by *C. auris* on the 27th day of hospitalization. This patient received antifungal treatment for a total of 42 days, including 30 days of combination therapy (liposomal amphotericin B and voriconazole). Immediately after the recognition of the index *C. auris* case, infection prevention and control (IPC) measures were formulated and implemented. IPC measures included strict isolation of the patient infected with *C. auris*, and screening of all other patients and the environment. *C. auris* was not detected in any of the patients screened. None of the environmental swabs tested positive for *C. auris*.

CONCLUSION: Collaboration between clinical microbiology laboratories and the IPC committee is essential for making correct and early diagnosis, optimizing the management of precautions and reducing the spread of infection in the hospital.

Keywords: Burn; Candida auris; child; fungemia; infection control.

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Candida auris (*C. auris*) is a fungal pathogen that was first identified in 2009 and has been increasingly reported worldwide since then [1]. As of 2011, sporadic *C. auris* cases and clades have emerged across different parts of the world [2]. Especially in Africa and Asia, *C. auris* has become an endemic pathogen [3]. Prolonged hospitalization in intensive care units is considered as an important risk factor for *C. auris* infection. Transmission has been associated with contact with contaminated surfaces and equipment in healthcare facilities. *C. auris* colonizes in both biotic (skin and other body parts) and abiotic surfaces [4]. *C. auris* has been isolated from many types of specimens including the bloodstream, urine, respiratory secretions, bile, wounds and external ear canal. Patients colonized with *C. auris* may spread *C. auris* to other patients in healthcare settings and may be at risk for invasive *C. auris* infections [5–7].

While *C. auris* causes infection in patients of all ages, it occurs more commonly in males and patients in intensive care units. In general, risk factors for *C. auris* infections are similar to those of other *Candida* spp. These risk factors include advanced age, recent surgery, diabetes mellitus, the presence of an indwelling medical device (e.g., central venous catheter), immunocompromised states, hemodialysis patients, chronic kidney disease, neutropenia, and the use of broad-spectrum antibiotics and/or antifungal drugs [8]. Although *C. auris* is usually multidrug-resistant, antifungal resistance levels may vary widely among isolates. Frequent misidentification of *C. auris* by conventional diagnostic methods makes it difficult to detect and control this pathogen [9].

C. auris is a reportable pathogen and a cause of major concern worldwide because it has been associated with nosocomial outbreaks in intensive care units (ICUs) and ongoing spread despite implementation of infection prevention and control (IPC) measures. With this study, we aimed to present our experience with two patients with *C. auris* fungemia who were referred to the Pediatric Burn Center of our hospital at different timepoints and share the antifungal treatment strategy and IPC management policies implemented in the clinic.

Highlight key points

- *C. auris* is a reportable pathogen and a cause of major concern worldwide.
- It has been associated with nosocomial outbreaks in intensive care units (ICUs).
- This pathogen to harbor or develop multidrug resistance to antifungal agents.

MATERIALS AND METHODS

Our Pediatric Burn Center is a tertiary care clinic at the Children's Hospital affiliated with Ankara Bilkent City Hospital. With 12-bed capacity, our center provides comprehensive multidisciplinary treatment for patients with all kinds of burns, including high-degree burns (second- or third-degree), with each patient placed in single, isolated rooms. Within the burn ward, there is an operating room where wound dressing, debridement and skin grafting procedures are performed.

Following detection of *C. auris* infection, a comprehensive screening for *C. auris* was initiated in the burn ward to identify newly infected and colonized patients. All of the patients staying in the unit were screened. During screening, hand hygiene was practiced and medical protective equipment (gloves, gowns and facial masks) was worn by the staff. The swabs were collected with a dry swab (Microcult) using the single swab axilla and groin composite collected method. Cotton swab was first rubbed over both armpits of the patients, swiping back and forth about 4–5 times for each armpit. Then, using the same swab, both groins were rubbed 4–5 times and the swab was immediately sent to the laboratory.

For routine fungal analysis, the specimens were inoculated on Sabouraud Dextrose Agar containing gentamycin and chloramphenicol. Agar plates were incubated for up to 7 days at 28°C and 37°C, respectively. Yeast isolates were identified with VITEK® MS v3.2.0 (bioMérieux), a system that uses Matrix-Assisted Laser Desorption Ionization Time-of-Flight (MALDI-TOF) technology. Antifungal susceptibility tests were performed at the Turkish Public Health Institution (THSK) using the broth microdilution (BMD) method. The BMD was carried out in accordance with the Clinical and Laboratory Standards Institute (CLSI) procedures.

Approval for the study was obtained from the Ankara Bilkent City Hospital 2nd Clinical Research Ethics Committee (date: 18.01.2023, number: E2-23-3180).

RESULTS

Case 1 – A 3-year-old Syrian girl had been admitted to an external hospital in April 2022 due to a burn that occurred after falling into a bucket of hot water. She had been hospitalized in the burn unit for 15 days where *C.*

auris was detected. The patient was referred to our hospital for further examination and treatment after screening cultures were found to be negative. On physical examination, deep, second-degree burns affecting 70% of the total body surface area were observed, involving the entire front and back of the trunk, nearly all of the skin in both hands and arms (in a circular fashion) and both groins and legs. Wound care and escharotomy were performed for the patient on a daily basis in the operating room of the ICU. She received treatment with broad-spectrum antibiotics and fluconazole as antifungal therapy. On the 41st day of hospitalization, *C. auris* growth was detected in the central venous catheter and peripheral blood culture. The antifungal therapy was switched to caspofungin and the catheter was removed. Echocardiography, abdominal ultrasound (US) and eye examination results were normal. All of the measures recommended by the infection control and prevention committee were implemented. Antifungal susceptibility testing showed the following MIC (minimal inhibitory concentration) values: 4 μg/ml for liposomal amphotericin B, 256 μg/ml for fluconazole and 0.25 μg/ml for anidulafungin. The patient received antifungal treatment for a total of 52 days, including 12 days of caspofungin and 40 days of micafungin. Cultures became negative. The patient received burn treatment and followed at our center afterwards.

Case 2 – A Syrian baby girl aged 2 years and 4 months was admitted to our hospital for further examination and treatment after suffering skin burns as well as inhalation burns due to ignition and explosion of a flammable chemical adhesive in August 2022. At the time of physical examination, the patient had third-degree deep burns and second-degree superficial and deep burns affecting 78% of the total body surface area. She was intubated and received wound care and escharotomy on a daily basis. The patient was intubated for a total of 18 days. Upon being diagnosed with a central venous catheter-related bloodstream infection and ventilator-associated pneumonia, the patient received broad-spectrum antibiotic treatment. Fluconazole was administered due to growth of *C. albicans* in the wound culture. On the 27th of hospitalization, antifungal therapy was switched to caspofungin because of detection of *C. auris* growth in the central venous catheter and peripheral blood culture. The catheter was removed. All of the measures recommended by the infection control and prevention committee were implemented. Echocardiography, abdominal US and eye examination results were normal. Liposomal amphotericin B was added to the treatment after 12 days of caspofungin therapy because her blood culture was still positive and fever did not resolve. Antifungal susceptibility testing showed the following MICs: 4 μg/ml for amphotericin B, 256 μg/ml for fluconazole and 0.25 μg/ml for anidulafungin. Caspofungin was discontinued and voriconazole was added to her treatment. Blood culture obtained on the 5th day of liposomal amphotericin B and voriconazole treatment was negative. The patient received antifungal therapy for a total of 42 days, including 30 days of combination therapy. She was monitored in the burn ICU afterwards.

Infection Prevention and Control Measures Implemented at the Pediatric Burn Center Following Detection of *C. auris*

Immediately after identification of the *C. auris* case, a series of decisions were made, taking into account the high potential of this organism to cause large-scale outbreaks. All of the medical devices used by the patients were isolated. It was ensured that the nurse caring the infected patient was not involved in the care of other patients. All ward staff were educated about hand hygiene, isolation measures, cleaning/disinfection practices, use of gloves and urine drainage techniques. The frequency and supervision of daily cleaning and disinfection procedures were intensified in the ICU. The numbers of cleaning workers and housekeepers were increased. Infected patients were bathed with chlorhexidine every other day. It was made sure that infected patients were brought into the operating room as the last patients of the day. Thorough disinfection of the operating room was performed after every surgery. In addition, patient rooms were monitored using fluorescent gel products after cleaning and disinfection.

An extensive screening was initiated for *C. auris* in the burn ward. For each hospitalized patient, a total of two fungal cultures were sent for examination, including one obtained in the first week and the other in the second week. During the screening, *C. auris* was not detected in any of the patients.

Environmental swabs were collected to identify possible sources of *C. auris* outside of the immediate surroundings of the patients. These swabs were collected from stationary surfaces and equipment, medical and mobile devices such as carts and supplies trolleys used for patient care and the areas used for dressing and surgery in the operating room. None of the environmental swabs tested positive for *C. auris* growth.

DISCUSSION

One of the reasons why the emergence of *C. auris* is of major concern is the potential of this pathogen to harbor or develop multidrug resistance to antifungal agents. In fact, some isolates have exhibited high MIC values against all currently available antifungal drug classes, suggesting that treatment options for pan-resistant isolates will be extremely difficult, if not impossible. Although *C. auris* isolates resistant to fluconazole and amphotericin are common, isolates resistant to echinocandins (e.g., caspofungin) are relatively infrequent and some *C. auris* strains are resistant to all available antifungal drug classes [2, 8, 10]. In a murine *C. auris* candidemia study, micafungin showed the highest effectiveness when compared with fluconazole and amphotericin B [11]. In vitro studies examining synergistic use of antifungal agents have produced the first promising data for the use of combination therapy with micafungin and voriconazole against multidrug-resistant isolates [12].

The site of infection is critically important for the choice of antifungal agents to be used for invasive infections. Echinocandins should not be preferred for the treatment of central nervous system (CNS) and urinary tract infections due to their high molecular weight. 5-flucytosine and amphotericin B preparations have been recommended for use in urinary tract infections [13]. For CNS disease, as with other *Candida* species, some success has been achieved with optimization of treatment with empirical amphotericin B and 5-flucytosine, as demonstrated by susceptibility testing [14]. The optimal treatment regimen for *C. auris* has not been established. Since the majority of *C. auris* isolates identified in the United States have been susceptible to echinocandins, treatment with a drug from this class is recommended for initial therapy [15]. While our first case was successfully treated with echinocandins (caspofungin and micafungin), combination antifungal therapy was required for our second case due to ongoing growth of *C. auris* in the cultures and refractory fever.

Identification of *C. auris* at the species level is challenging. *C. auris* can be easily misidentified as *C. haemulonii* or other yeast species using conventional phenotypic and biochemical methods. MALDI-TOF MS can readily distinguish *C. auris* from other fungal species but correct identification of *C. auris* is dependent on the reference databases supplied with the MS device [8]. Upon growth of yeast in cultured urine and/or blood specimens from our cases, identification at the species level was performed with MALDI-TOF MS (VITEK® MS v3.2.0, bioMérieux, France) at our hospital's microbiology laboratory. BMD and antifungal susceptibility tests were done by the THSK Laboratory.

Rapid spread of *C. auris* coupled with high mortality rates and detection of high antifungal resistance underscore the importance of timely implementation of infection prevention and control measures to prevent transmission. Thanks to the multidisciplinary teamwork approach that we have adopted since the outset of coronavirus disease 2019 (COVID-19) pandemic, we were able to act fast and implement a series of effective IPC measures in an organized fashion. As such, we educated physicians and other healthcare professionals on the epidemiology, biology and transmission of *C. auris*. Pediatric infectious diseases specialists and nurses supervised and actively supported the implementation of IPC measures in the ward on a daily basis. Contrary to other reports on outbreaks, we did not detect environmental contamination with *C. auris* [16–18]. No evidence of *C. auris* was observed within three months after implementation of the IOC measures as appropriate. However, about 3 months later, we identified the same fungal agent in another patient in the same unit. *C. auris* is highly contagious among patients, possibly due to its tendency to persistently colonize the skin and other body parts and contaminate the environment. Patients undergoing invasive procedures or placement of invasive devices are at an increased risk of acquiring bloodstream infection with *C. auris* [19–21]. Colonization persisting for more than one year has been reported in some patients infected with *C. auris* [22]. We think that the identification of *C. auris* in our second case was possible due to its epidemiological and biological characteristics. We also believe that invasive procedures such as wound dressing, debridement and grafting operations of second- and third-degree burns involving large areas carried out in the tertiary-care burn ICU made it easier for us to be aware of our second case. Since the Centers for Disease Control and Prevention (CDC) does not recommend routine re-assessment of *C. auris* colonization, repeated screening activities were not performed. However, identification at the species level was continued for one more month upon detection of *Candida* spp. growth in specimens from non-sterile sites. None of the specimens sent for examination showed the presence of *C. auris*.

Conclusion

In conclusion, C. *auris* is an emerging public health threat across the world. Although there are currently no established species-specific breakpoints, all suspected or confirmed cases should be reported to public health authorities and antifungal susceptibility testing done for invasive infections. Based on available MIC data, echinocandins seem to be the best choice for first-line therapy. Collaboration between clinical microbiology laboratories and the IPC committee is essential for making correct and early diagnoses, optimizing the management of precautions and reducing the spread of infection in the hospital.

Ethics Committee Approval: The Ankara Bilkent City Hospital 2nd Clinical Research Ethics Committee granted approval for this study (date: 18.01.2023, number: E2-23-3180).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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