Candida Auris Total Knee Arthroplasty Infection in an Immunocompetent Individual: Case Report and Literature Review

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ABSTRACT

Introduction: *Candida auris* (*C auris)*, a multidrug-resistant fungus, was declared by the Centers for Disease Control and Prevention as a serious global health threat in 2016. It is hard to identify, resistant to standard antifungal treatments, and spreads within health care settings, resulting in high morbidity and mortality in critically ill patients.

Case Presentation: We report the case of a 60-year-old immunocompetent male with a protracted course of prosthetic knee joint infections. He received medical care at several health care facilities across 2 Midwestern states culminating in wound dehiscence and *C auris* infection necessitating prolonged antimicrobial treatment.

Discussion: *C auris* has been a pathogen of increasing nosocomial transmission with particular concern for multidrug resistance. Treatment is with prompt irrigation and debridement and polyethylene exchange and systemic antifungal treatment. Local treatment with antimicrobial impregnated cement can be used to reduce treatment duration and mitigate resistance.

Conclusions: With emerging concerns and the prevalence of infection with *C auris*, there should be greater vigilance in evaluating patients with repeat surgeries and health care contacts for fungal infection.

INTRODUCTION

In the last decade, there has been growing concern over the emergence of *Candida auris* (*C auris*) as a multidrug-resistant fungal pathogen. It is often difficult to identify and deadly, with more than 1 in 3 cases of invasive *C auris* infection leading to death.[1] *C auris* was discovered initially in the outer ear canal of a hospitalized patient in Japan in 2009.[2] This multidrug-resistant pathogen has become increasingly common and now globally widespread, with reported cases in over 47 countries. In the United States alone, the percentage of clinical cases increased by 44% in 2019 and 95% in 2021.[3]

Cases of *C auris* infections most often have been reported in critically ill patients admitted to the intensive care unit (ICU) or those with severe comorbidities causing immunosuppression. Typically, like other invasive *Candida* species, *C auris* can be treated with a combination of oral and intravenous azoles, amphotericin B, and echinocandins.[4] Cases of azole-resistant strains of *C auris* have been increasingly common, thus complicating the treatment options for infections and raising concern of particularly deadly infections.

While there is some literature for the *Candida* species, there is limited literature for the treatment of *C auris* specifically. The infection risk and methodology of treatment for *C auris* identified with prosthetic joints are relatively underappreciated within the literature. Adequate understanding of *C auris* within clinical contexts is essential for the accurate treatment and prevention of this infection, ensuring the delivery of safe and effective patient care. In this case report, we present a patient with a history of right knee total arthroplasty complicated by recurrent infections, including *C auris*, leading to multiple revisions.

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CASE PRESENTATION

A 60-year-old male Wisconsinite with a past medical history of obese body habitus, hypertension, and hypothyroidism underwent right proximal tibial osteotomy in 2009 and eventual right total knee arthroplasty (TKA) in December 2015. While he initially responded well with minimal postoperative concern, an infec-

Table. Patient's Medical History Detailing Primary Medical Complaint, Treatment, and Infectious Disease Implication, 2009-2023

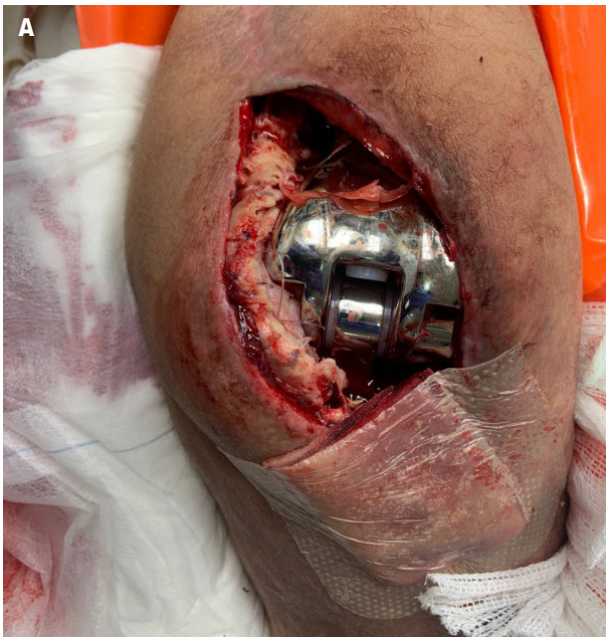
Date	Medical Complaint	Treatment	Infectious Disease Implication
5/2009	Advanced tricompartmental degenerative arthritis	Proximal tibial wedge osteotomy with allograft cellulitis treated with oral cephalexin	Postoperative overlying skin
12/2015	Progression of advanced tricompartmental degenerative arthritis now showing bone-on-bone arthritis	Right TKA	N/A
12/2015	Pruritic rash on right knee and buttock, mild erythema of knee without discharge	Methylprednisolone and cephalexin	Rash vs cellulitis of unknown origin
1/2016	Pruritic rash spread from knee to back of calf	Tramadol and continued cephalexin	Rash vs cellulitis of unknown origin
6/2016	2 weeks of fever and worsening right knee swelling that radiates to hip and is worse with movement	Inpatient vancomycin and ceftriaxone via PICC line	MSSA prosthetic knee infection
6/2016	Right knee hematoma with septic arthritis	Exploratory surgery with I&D and polyethylene exchange	MSSA prosthetic knee infection
6/2016	MSSA infection, erythema, indurated knee	Cefazolin	MSSA infection
7/2016	Improved erythema of anterior knee	Sulfadiazine cream	MSSA infection
8/2016	Septic arthritis requiring revision surgery, cellulitis of the knee	Hospitalized for 2 weeks, hardware removal and placement of antibiotic spacer	MRSA infection
1/2017	Right total knee revision	Hospitalized for 4 days, vancomycin	MRSA infection
1/2019	Serosanguineous drainage from the right knee with overlying cellulitis	Right knee debridement with flap to cover debrided tissue and suppressive vancomycin	MRSA infection
6/2020	Periprosthetic fracture of femoral component of right TKA	Scheduled for revision surgery and placed in knee immobilizer	N/A
7/2020	Revision of right total knee arthroplasty	Physical therapy, Marcaine and Kenalog injections into knee	N/A
5/2021	Fever, erythema and induration of the right knee with pain on passive movement	I&D with poly exchange and polyethylene tibial insert	*Streptococcus agalactiae* on tissue culture – ceftriaxone
4/2022	Left knee total arthroplasty	N/A	N/A
6/2022	Fever, erythema and induration of the right knee with pain on passive movement	I&D necessitating flap coverage by plastic surgery	N/A
8/2022	Right knee infection symptoms	Hospitalized for 1 week	N/A
11/2022	Patient suffers fall and has wound with bloody to purulent draining; fever	I&D with antibiotic beads and primary closure	*Enterococcus faecalis* and *Pseudomonas* on tissue culture – linezolid and levofloxacin suppression
11/2022	Infection symptoms	Daptomycin and oral linezolid	N/A
1/2023	Hospitalized; *C auris* and *Pseudomonas* coinfection	Treatment with cefepime, micafungin, and linezolid	*C auris*/*Pseudomonas aeruginosa* infection confirmed on deep and superficial tissue culture

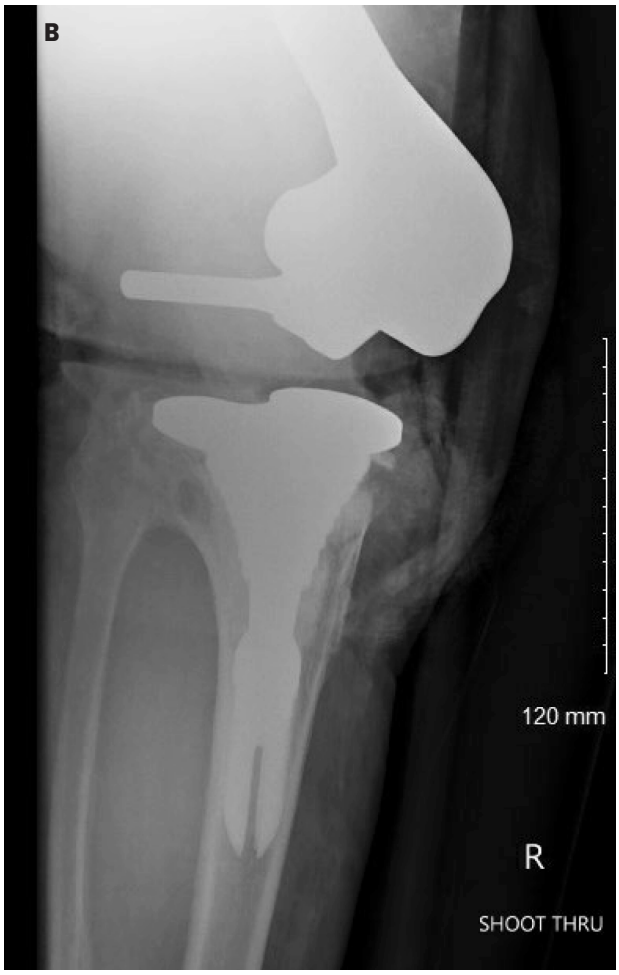
Abbreviations: TKA, total knee arthroplasty; PICC, peripherally inserted central catheter; MSSA, methicillin-susceptible *Staphylococcus aureus;* I&D, incision and drainage; MRSA, methicillin-resistant *Staphylococcus aureus*.

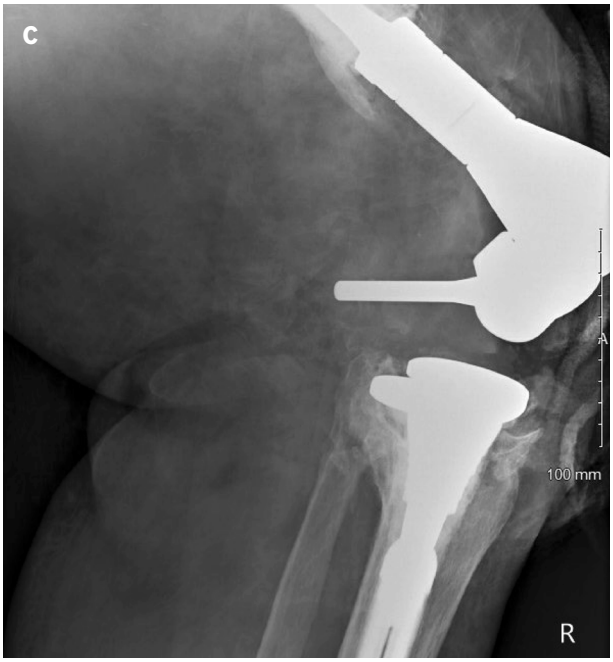
tious complications ensued 6 months status-post right TKA, including *Echinococcus faecalis*, methicillin-resistant *Staphylococcus aureus*, and *Streptococcus agalactiae* septic knee arthritis (Table). He underwent several additional years of complex care for his right TKA involving revision surgeries related to infection and hardware complications in 2019 and 2020, respectively. He was asymptomatic and underwent left TKA in April 2022. Soon after in June, he began to present with new symptoms concerning for reinfection of his right knee, for which he underwent right knee incision and drainage with polyethylene exchange. His postoperative period was complicated when he sustained a ground-level fall culminating in a laceration over his right knee requiring incision and drainage and flap coverage with long-term, broad-spectrum antibiotic treatment. He gradually improved to his baseline status of being a community ambulator with a cane.

In January 2023, the patient pivoted while taking a step in his kitchen and felt his knee "give out," leading to wound dehiscence with resultant hardware exposure and extensor mechanism lateral dislocation (Figure 1A). At this time, he had been on chronic antibiotic suppression consisting of 600 mg of linezolid twice a day and levofloxacin 750 mg daily for 2 months at the recommendation of an infectious disease specialist at an outside hospital. Further workup in the emergency department included a dose of 2 grams of cefazolin and right lower extremity radiographs (Figures 1B and 1C), at which point the patient was taken to the operating room (OR) emergently overnight for irrigation and debridement. In the OR, 2 superficial wound tissue cultures and 1 deep wound synovial tissue culture polyethylene were taken. The polyethylene was noted to have dislocated posteriorly and there was a partial avulsion of the medial tibial tubercle with the remainder of the hardware well fixed. A mixture of 2 grams of vancomycin and 3 grams of tobramycin were placed in the wound and the polyeth-

Figure 1.







A. Dehiscence Wound of Right Total Knee Arthroplasty with Exposed Hardware from Emergency Department Visit, January 2023

B/C. Anterior/Posterior (B) and Lateral (C) Radiographs of the Right Knee Status Post Ground-level Fall, January 2023

ylene was exchanged, demonstrating that the knee was stable to varus and valgus stress. The wound closed primarily with a wound vacuum set to 75 mmHg of continuous suction with overlying ace bandage, at which point he was placed in a hinged knee brace that was locked in extension.

The day after surgery, all 3 intraoperative cultures demonstrated *Pseudomonas* growth and the deep wound culture developed 2+ growth of unknown yeast. The patient was placed on 600 mg of daily oral fluconazole, 600 mg of linezolid twice a day, and 2 g cefepime three times a day in exchange for his home levofloxacin pending susceptibilities. On hospitalization day 3, the fungus was speciated to *C auris*. Fluconazole was discontinued and replaced with 200 mg IV micafungin. He was discharged on hospital day 7 on 6 weeks of IV cefepime and micafungin via a peripherally inserted central catheter (PICC) line and continued indefinitely on his oral linezolid.

Upon follow-up in February, the patient was healing well from surgery with no complications or signs of infection. A month

later, he completed his IV antibiotic course at which point his PICC line was removed. He began his current and indefinite treatment regimen of his previous 600 mg linezolid twice a day, 400 mg oral fluconazole daily and 500 mg ciprofloxacin twice a day for long-term suppression based on susceptibilities. Three months after discharge, he had had routine visits with his orthopedic surgeon and with infectious disease, with his improvement supported by decreased trending inflammatory markers and a promising clinical course.

DISCUSSION

Since its initial identification in 2009, *C auris*, a major multidrug-resistant fungal pathogen has emerged on a global scale.[1] From 2019 to 2021, *C auris* spread rapidly across the United States, with 17 states reporting their first cases.[3] During the same period, the number of clinical cases increased each year, with a 95% surge observed in 2021 alone. The number of Americans colonized by the fungus rose by 21% from 2019 to 2020 and by 209% from 2020 to 2021, despite only an 80% increase in screening measures.[3] Despite this increased prevalence, *C auris* likely remains underreported and underdiagnosed without universal screening precautions across the United States, in addition to the continued incorrect identification of *C auris* as other phylogenetically similar strains such as *Candida haemulonii* and *Rhodotorula glutinis*.[5,6] The clinical presentation of *C auris* is typically nonspecific and emulates other types of systemic fungal infections.[7] The majority of cases have been seen in adults, with those who are critically ill and, in the ICU, boasting a higher prevalence rate likely due to the concomitant presence of risk factors, such as urinary catheters, central venous catheters, malignancy, chronic kidney disease, and neutropenia. Interestingly, the COVID-19 pandemic led to multiple reported outbreaks of SARS-CoV-2 and *C auris* coinfections, specifically in patients who had received azithromycin or use of tetracycline antibiotics, as well as other second-generation tetracycline derivatives.[4] Additionally, those on long-term broad-spectrum antibiotics are also likely at greater risk of resistant fungal infection, which has been demonstrated in the intestine and was likely the driving factor in our case.[8]

Candida infections typically are treated with a combination of azoles, echinocandins, and amphotericin B. However, *C auris* has extremely variable susceptibility patterns and frequently exhibits resistance to the common treatments at the time of diagnosis.[9] National surveillance data have demonstrated that 3 times the number of *C auris* cases with echinocandin-resistant infections were reported in 2021 than the previous 2 years.[3] *C auris* displays a wide variety of resistance mechanisms. It can form biofilms, undergo filamentation, and phenotypically change between specific cell types.[4] Interestingly, *C auris* has multiple resistance mechanisms unique to *Candida* species. *C auris* can grow at high temperatures (>40 °C) and high salt concentrations (>10% sodium chloride, weight/volume). These resistance mechanisms contribute to the survival and persistence of *C auris* on organic and inorganic surfaces. This persistence may contribute to the commonly observed nosocomial transmission of *C auris*.[10] This combination of both novel and known resistance mechanisms found in *C auris* makes it an increasingly dangerous pathogen that recently has emerged on a global scale.

While reports of *C auris* infections are becoming more common, there have been few documented cases of *C auris* in joint replacement procedure–particularly in the context of complex postoperative complications. Documented fungal prosthetic joint infections (PJIs) are rare, occurring in only 0.3% to 2.3% of all infections, with *Candida* species being responsible for about 90% of all fungal PJIs, though epidemiology and etiology vary by geography.[11] There is limited literature on optimal management, and at the time of this writing, there is 1 case of a left ankle *C auris* PJI following open reduction and internal fixation for an open right ankle fracture that was successfully treated with an amphotericin B-molded cement spacer and postoperative micafungin for 2 weeks, followed by oral fluconazole.[12] At our facility, antifungal susceptibility testing for *C auris* was performed. The minimum inhibitory concentrations (MICs) were as follows: amphotericin B, 1.000 μg/mL; fluconazole, 8.000 μg/mL; micafungin, 0.060 μg/mL; and voriconazole, 0.060 μg/mL. While the antibiotic management was similar to our case, the use of amphotericin B cement spacer may mitigate the potential for further resistance by reducing the duration of azole therapy to only 2 weeks versus our case's 6 weeks. According to the Infectious Disease Society of America (IDSA), medical therapy alone is unlikely to be successful, and the addition of antifungals, such as amphotericin B and fluconazole to bone cement for osteomyelitis and loaded cement spacers for PJIs, can have some utility as an adjunctive therapy. However, this practice is controversial as cement spacers may be unable to elute antifungals at a clinically significant rate.[13,14] The current IDSA standard of treatment in most cases consists of removal of hardware and 12 weeks of antifungal therapy, followed by reimplantation with another 6 weeks of antifungal therapy.

CONCLUSIONS

This unique case presentation illustrates the evaluation, treatment, and management of *C auris* in a patient with a right total knee arthroplasty, complicated by multiple revision surgeries and significant comorbidities. The multitude of resistance mechanisms displayed by *C auris*, combined with the increased effort required for identification, makes it an incredibly challenging pathogen to treat. The complexity of care needed for *C auris* joint infections necessitates a multidisciplinary approach, including both infectious disease and orthopedic specialists. Given the alarming surge in *C auris* cases in 2021, improved detection and treatment are imperative to prevent long-term morbidity and mortality. Further research, cross-specialty collaboration, and the establishment of

screening protocols are essential to enhance future identification and management of this fungal pathogen. High clinical suspicion is particularly important in critically ill patients or those with chronic prosthetic joint infections.

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