

A *Candida Glabrata*-Associated Prosthetic Joint Infection: Case Report and Literature Review

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Background: *Candida glabrata* (*C. glabrata*) is an opportunistic fungal pathogen that has emerged as a potential risk for orthopedic prosthetic hardware infection. This case report highlights the clinical significance, management strategies, and evolving trends in the treatment of these complex infections.

Case Presentation: A male Vietnam War veteran presented to the emergency department in July 2023 with pain and a large fluid collection over the surgical site on his left hip. The patient had a complex orthopedic history, having undergone total left hip arthroplasty in 1996, in addition to open reduction internal fixation about 9 months prior to presentation. On admission, the patient was afebrile and normotensive, with an elevated erythrocyte sedimentation rate and C-reactive protein. Bedside irrigation and debridement were performed, and synovial fluid analysis revealed an elevated white blood cell count, negative bacterial cultures, and the presence of *C. glabrata*. The patient started receiving intravenous micafungin 100 mg/day as empiric

antifungal therapy. Wound cultures obtained during debridement and implant retention were positive for *C. glabrata*, *Enterococcus faecalis*, *Staphylococcus epidermidis*, and *Corynebacterium tuberculoostearicum*. These findings necessitated a chronic suppressive antibiotic and antifungal regimen, in addition to ongoing local wound care for persistent serosanguinous fluid drainage. The patient opted for a 2-staged revision arthroplasty after shared decision-making with his family and orthopedic surgery team.

Conclusions: This report underscores the importance of a multidisciplinary approach in managing *C. glabrata*-related prosthetic joint infections, along with early detection and initiation of prompt therapy for positive patient outcomes. In addition, this report emphasizes the need for greater awareness and research into this rare but challenging infectious complication in patients undergoing similar orthopedic procedures.

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Prosthetic joint infection (PJI) occurs in about 1% to 2% of joint replacements.¹ Risk factors include immunosuppression, diabetes, chronic illnesses, and prolonged operative time.² Bacterial infections constitute most of these infections, while fungal pathogens account for about 1%. *Candida* (*C.*) species, predominantly *C. albicans*, are responsible for most PJIs.^{1,3} In contrast, *C. glabrata* is a rare cause of fungal PJI, with only 18 PJI cases currently reported in the literature.⁴ *C. glabrata* PJI occurs more frequently among immunosuppressed patients and is associated with a higher treatment failure rate despite antifungal therapy.⁵ Treatment of fungal PJI is often complicated, involving multiple surgical debridements, prolonged antifungal therapy, and in some cases, prosthesis removal.⁶ However, given the rarity of *C. glabrata* as a PJI pathogen, no standardized treatment guidelines exist, leading to potential delays in diagnosis and tailored treatment.^{7,8}

CASE PRESENTATION

A male Vietnam veteran aged 75 years presented to the emergency department in July

2023 with a fluid collection over his left hip surgical incision site. The patient had a complex medical history that included chronic kidney disease, well-controlled type 2 diabetes, hypertension, and osteoarthritis. His history was further complicated by nonalcoholic steatohepatitis with hepatocellular carcinoma that was treated with transarterial radioembolization and yttrium-90. The patient had undergone a left total hip arthroplasty in 1996 and subsequent open reduction and internal fixation about 9 months prior to his presentation. The patient reported the fluid had been present for about 6 weeks, while he received outpatient monitoring by the orthopedic surgery service. He sought emergency care after noting a moderate amount of purulent discharge on his clothing originating from his hip. In the week prior to admission, the patient observed progressive erythema, warmth, and tenderness over the incision site. Despite these symptoms, the patient remained ambulatory and able to walk long distances with the use of an assistive device.

Upon presentation, the patient was afebrile and normotensive. Laboratory testing

revealed an elevated erythrocyte sedimentation rate of 77 mm/h (reference range, 0-20 mm/h) and a C-reactive protein of 9.8 mg/L (reference range, 0-2.5 mg/L), suggesting an underlying infectious process. A physical examination revealed a well-healed incision over the left hip with a poorly defined area of fluctuance and evidence of wound dehiscence. The left lower extremity was swollen with 2+ pitting edema, but tenderness was localized to the incision site. Magnetic resonance imaging of the left hip revealed a multiloculated fluid collection abutting the left greater trochanter with extension to the skin surface and inferior extension along the entire length of the surgical fixation hardware (Figure).

Upon admission, orthopedic surgery performed a bedside aspiration of the fluid collection. Samples were sent for analysis, including cell count and bacterial and fungal cultures. Initial blood cultures were sterile. Due to concerns for a bacterial infection, the patient was started on empiric intravenous (IV) ceftriaxone 2 g/day and IV vancomycin 1250 mg/day. Synovial fluid analysis revealed an elevated white blood cell count of 45,000/ μ L, but bacterial cultures were negative. Five days after admission, the fungal culture from the left hip wound was notable for presence of *C. glabrata*, prompting an infectious diseases (ID) consultation. IV micafungin 100 mg/day was initiated as empiric antifungal therapy.

ID and orthopedic surgery teams determined that a combined medical and surgical approach would be best suited for infection control. They proposed 2 main approaches: complete hardware replacement with washout, which carried a higher morbidity risk but a better chance of infection resolution, or partial hardware replacement with washout, which was associated with a lower morbidity risk but a higher risk of infection persistence and recurrence. This decision was particularly challenging for the patient, who prioritized maintaining his functional status, including his ability to continue dancing for pleasure. The patient opted for a more conservative approach, electing to proceed with antifungal therapy and debridement while retaining the prosthetic joint.

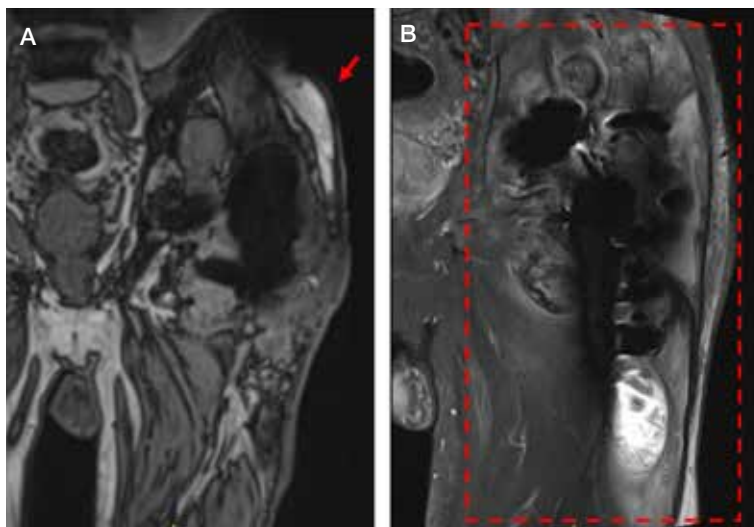


FIGURE. Multiplanar Multisequence Magnetic Resonance Imaging of the Femur With and Without IV Contrast

A, Red arrow indicates peripherally enhancing fluid collection abutting the left trochanter and extending to the skin surface. B, Extent of multiloculated fluid collection extending along entire length of the surgical fixation hardware can be seen within red box.

After 11 days of hospitalization, the patient was discharged with a peripherally inserted central catheter for long-term antifungal infusions of micafungin 150 mg/day at home. Fungal sensitivity test results several days after discharge confirmed susceptibility to micafungin.

About 2 weeks after discharge, the patient underwent debridement and implant retention (DAIR). Wound cultures were positive for *C. glabrata*, *Enterococcus faecalis*, *Staphylococcus epidermidis*, and *Corynebacterium tuberculostrictum*. Based on susceptibilities, he completed a 2-month course of IV micafungin 150 mg daily and daptomycin 750 mg daily, followed by an oral suppressive regimen consisting of doxycycline 100 mg twice daily, amoxicillin-clavulanate 2 g twice daily, and fluconazole initially 800 mg daily adjusted to 400 mg daily. The patient continued wound management with twice-daily dressing changes.

Nine months after DAIR, the patient remained on suppressive antifungal and antibacterial therapy. He continued to experience serous drainage from the wound, which greatly affected his quality of life. After discussion with his family and the orthopedic surgery team, he agreed to proceed with a 2-staged revision arthroplasty involving prosthetic explant and antibiotic spacer placement. However, the surgery was postponed

due to findings of anemia (hemoglobin, 8.9 g/dL) and thrombocytopenia (platelet count, $73 \times 10^3/\mu\text{L}$). At the time of this report, the patient was being monitored closely with his multidisciplinary care team for the planned orthopedic procedure.

DISCUSSION

PJI is the most common cause of primary hip arthroplasty failure; however, fungal species only make up about 1% of PJIs.^{3,9-11} Patients are typically immunocompromised, undergoing antineoplastic therapies for malignancy, or have other comorbid conditions such as diabetes.^{12,13} *C. glabrata* presents a unique diagnostic and therapeutic challenge as it is not only rare but also notorious for its resistance to common antifungal agents. *C. glabrata* is known to develop multidrug resistance through the rapid accumulation of genomic mutations.¹⁴ Its propensity towards forming protective biofilm also arms it with intrinsic resistance to agents like fluconazole.¹⁵ Furthermore, based on a review of the available reports in the literature, *C. glabrata* PJIs are often insidious and present with symptoms closely mimicking those of bacterial PJIs, as it did in the patient in this case.¹⁶

Synovial fluid analysis, fungal cultures, and sensitivity testing are paramount for ensuring proper diagnosis for fungal PJI. The patient in this case was empirically treated with micafungin based on recommendations from the ID team. When the sensitivities results were reviewed, the same antifungal therapy was continued. Echinocandins have a favorable toxicity profile in long-term use, as well as efficacy against biofilm-producing organisms like *C. glabrata*.^{17,18}

While there are a few cases citing DAIR as a feasible surgical strategy for treating fungal PJI, more recent studies have reported greater success with a 2-staged revision arthroplasty involving some combination of debridement, placement of antibiotic-loaded bone cement spacers, and partial or total exchange of the infected prosthetic joint.^{4,19-23} In this case, complete hardware replacement would have offered the patient the most favorable outlook for eliminating this fungal infection. However, given the patient's advanced age, significant underlying comorbidities, and functional status, medical management with

antifungal therapy and DAIR was favored.

Based on the discussion from the 6-month follow-up visit, the patient was experiencing progressive and persistent wound drainage and frequent dressing changes, highlighting the limitations of medical management for PJI in the setting of retained prosthesis. If the patient ultimately proceeds with a more invasive surgical intervention, another important consideration will be the likelihood of fungal PJI recurrence. At present, fungal PJI recurrence rates following antifungal and surgical treatment have been reported to range between 0% to 50%, which is too imprecise to be considered clinically useful.²²⁻²⁴

Given the ambiguity surrounding management guidelines and limited treatment options, it is crucial to emphasize the timeline of this patient's clinical presentation and subsequent course of treatment. Upon presentation to the ED in late July, fungal PJI was considered less likely. Initial blood cultures from presentation were negative, which is common with PJIs. It was not until 5 days later that the left hip wound culture showed moderate growth of *C. glabrata*. Identifying a PJI is clinically challenging due to the lack of standardized diagnostic criteria. However, timely identification and diagnosis of fungal PJI with appropriate antifungal therapy, in patients with limited curative options due to comorbidities, can significantly improve quality of life and overall outcomes.²⁵ Routine fungal and mycobacterial cultures are not currently recommended in PJI guidelines, but this case illustrates it is imperative in immunocompromised hosts.²⁶

This case and the current paucity of similar cases in the literature stress the importance of clinicians publishing their experience in the management of fungal PJI. We strongly recommend that clinicians approach each suspected PJI with careful consideration of the patient's unique risk factors, comorbidities, and goals of care, when deciding on a curative vs suppressive approach to therapy.

CONCLUSIONS

This case report highlights the importance of considering fungal pathogens for PJIs, especially in high-risk patients, the value of obtaining fungal cultures, the necessity of a multidisciplinary approach, the role of antifungal susceptibility testing,

and consideration for the feasibility of a surgical intervention. It underscores the challenges in diagnosis and treatment of *C. glabrata*-associated PJI, emphasizing the importance of clinician experience-sharing in developing evidence-based management strategies. As the understanding of fungal PJI evolves, continued research and clinical data collection remain crucial for improving patient outcomes in the management of these complex cases.

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Ethics and consent

The patient provided oral informed consent to the authors.

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