

Candida parapsilosis in Late Prosthetic Joint Infections Among Immunocompetent Patients: A Case Series

James C George¹, B Samuel Chittaranjan¹, Subin Babu¹, Koshy George¹

Learning Point of the Article:

Fungal PJI presenting as late infections can mimic early aseptic loosening.

Abstract

Introduction: Fungal prosthetic joint infections (PJIs) are very rare in immunocompetent patients. PJI can present either early, delayed, or as late chronic infections. Diagnosis of fungal PJI presenting late is challenging due to the difficulty in isolation as well as the clinical presentation very similar to an aseptic loosening. There are no clear guidelines regarding the management of these patients.

Case Report: We present five cases of *Candida parapsilosis* PJI presenting as late chronic infections. All five patients were culture-negative preoperatively, immunocompetent, and with good soft-tissue condition. There were three infected knee prostheses and two infected hip hemiarthroplasty. All of them were treated with extensive debridement, meticulous sampling, and extended culture. We treated all of them with long-term antifungals without any disease reactivation or recurrence till the last follow-up.

Conclusion: Fungal infection should be suspected in immunocompetent patients presenting early with features of aseptic loosening but without typical signs of periprosthetic infection. Revision with long-term suppressive therapy can give good results in these patients.

Keywords: *Candida parapsilosis*, revision, hemiarthroplasty, fluconazole, culture-negative infection, knee arthroplasty.

Introduction

Prosthetic joint infections (PJIs) are among the most common causes of revision surgeries in joint arthroplasty. *Staphylococcus* remains the most common organism isolated while fungal PJI accounts for nearly 1% of total PJI [1]. Among the various fungi that can produce PJI, *Candida* species is the most common [2,3]. PJI can present either early, delayed, or as late chronic infections. Any infections presenting after 12 months of the initial surgery are considered late presentation as it is usually due to a hematogenous spread or can be due to infection with low virulent organisms. Diagnosis of fungal PJI is very difficult due to the difficulty in isolation [4] as well as the clinical presentation

very similar to an aseptic loosening.

Only two studies with large cohorts are in the literature on fungal PJI [1,2]. All the remaining are case series and reports. Immunocompromised patients are particularly vulnerable to fungal PJI. *Candida albicans* and *Candida parapsilosis* are fungal pathogens frequently reported in the literature. There are no clear guidelines regarding the management of these patients. We present five more cases of *C. parapsilosis* late PJI in immunocompetent patients treated with single-stage revision and fluconazole monotherapy.

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Author's Photo Gallery



Dr. James C George



Dr. B Samuel Chittaranjan



Dr. Subin Babu



Dr. Koshy George

¹Department of Orthopaedic Surgery, Believers Church Medical College Hospital, Pathanamthitta, Kerala, India.

Address of Correspondence:

Dr. James C George,
Department of Orthopaedic Surgery, Believers Church Medical College Hospital, Pathanamthitta-689 103, Kerala, India.
E-mail: drjamescgeorge@gmail.com

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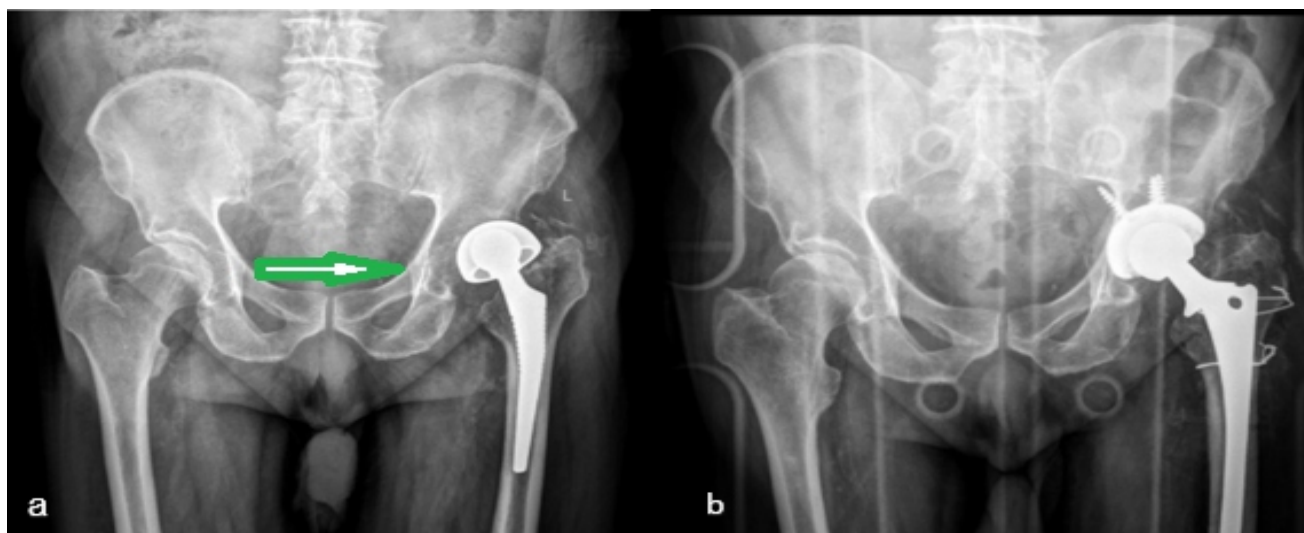


Figure 1: (a) Case 1 prosthetic infection with a subluxed hip, (b) 2.5-year follow-up radiograph after revision total hip arthroplasty

Case Report

Between 2018 and 2023, we had eight female patients and one male patient with fungal PJI. Among them, seven female patients had infected knee arthroplasty whereas the remaining two patients had infected hemiarthroplasty. Among the knee arthroplasty patients, one patient who presented 17 months after surgery did not come for treatment after diagnosis, and yet another patient who presented after a revision knee surgery for loosening at 12 months decided not to go ahead with any further intervention. Both patients isolated *C. parapsilosis* sensitive to fluconazole. Excluding these two patients, we had seven cases. Among them, two patients with knee arthroplasty who presented with loosening and discharging sinus grew *C.*

albicans and underwent two-stage revision and arthrodesis. Both these patients were immunocompromised. Finally, we treated five immuno-competent patients with late chronic infection with loosening. Informed consent and institutional review board approval were obtained before the evaluation of these patients.

Pre-operative synovial fluid analysis was done for all five patients. Ultrasound-guided aspiration was done for hemiarthroplasty patients. Synovial fluid and five tissue samples were done intraoperatively for all patients. The fluid culture was done with an automated blood culture system (Bact/ALERT, bioMerieux, Marcy-l'Étoile, France) and tissue culture was done by mounting on Sabouraud dextrose agar

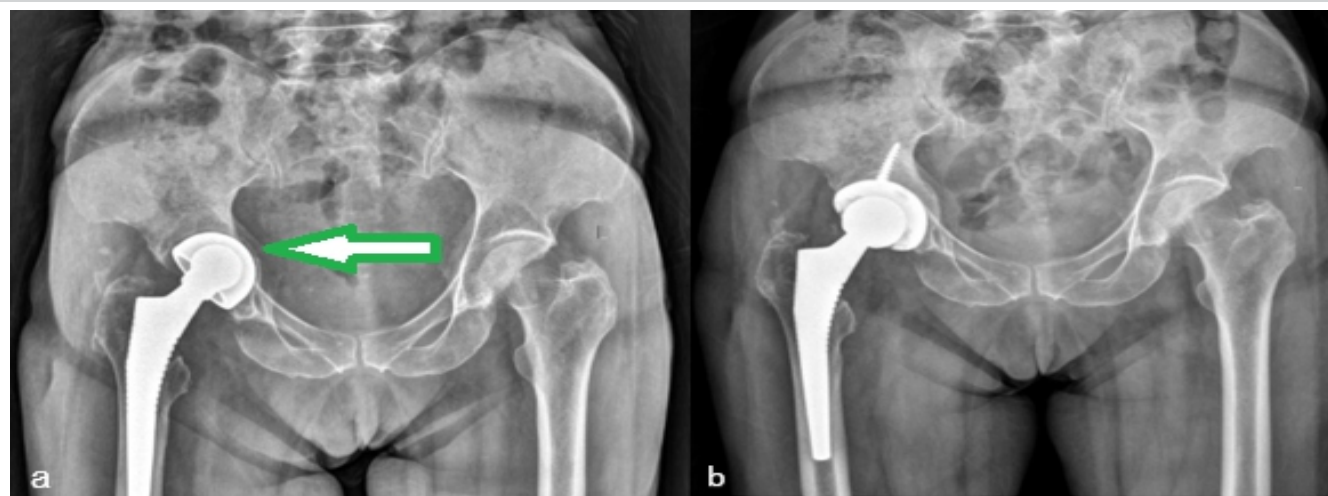


Figure 2: (a) Case 2 infected hemiarthroplasty with protrusion acetabula, (b) 3-year follow-up radiograph after acetabular revision.

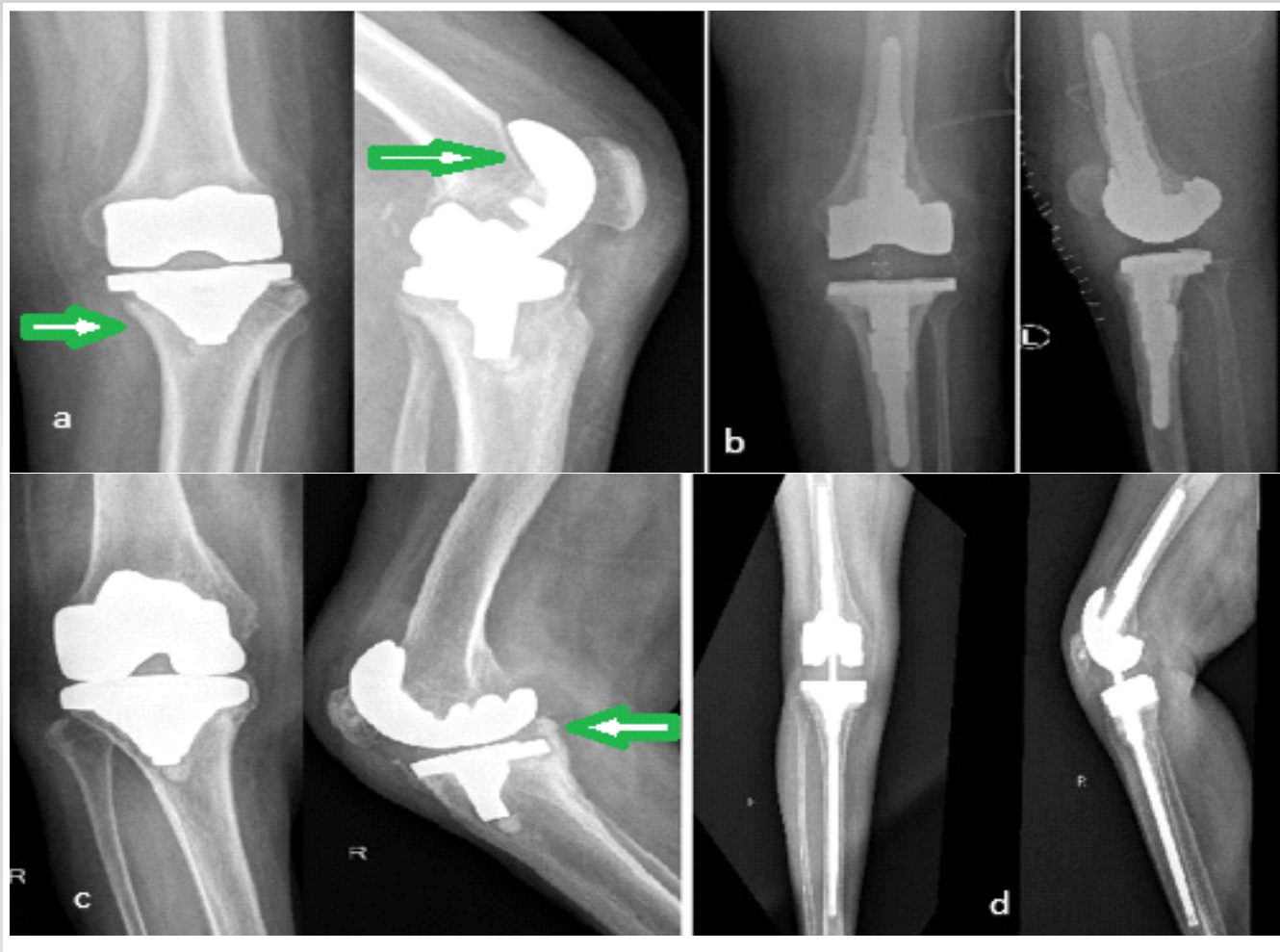


Figure 3: (a) Case 3 pre-operative radiograph showing loosening, (b) 4.5-year follow-up after revision total knee arthroplasty, (c) case 4 infected knee with loosening, (d) 4-year follow-up radiographs of case 4 after revision.

(SDA). Clinical isolates of *Candida* species obtained from Bact/ALERT were subcultured on SDA after identifying Gram-positive budding yeast on Gram stain of positive culture broth. The suspected colonies of *Candida* were confirmed through Gram stain and Germ tube test and then were identified with Vitek 2 Compact using Vitek ID-YST cards. Anti-fungal susceptibility testing was performed with Vitek AST-YS08 cards. Five samples were taken for culture from every patient. Positive cultures from at least two samples were required for consideration PJI. When the culture came positive for *C. parapsilosis*, all patients received 2 weeks of IV fluconazole followed by oral fluconazole 200 mg twice daily for 3 months. A liver function test was done routinely for all patients every 1 month and none of them developed any derangement.

We had two patients with hip pain and three patients with knee pain after hemiarthroplasty and total knee arthroplasty,

respectively. None of these patients had any fever or any constitutional symptoms to suspect infection. Except for an elevated erythrocyte sedimentation rate (ESR), all of them had a normal blood picture (Table 1). Pre-operative synovial fluid analysis did not grow any microorganisms in any patients. Intraoperative tissue and fluid cultures of all five patients grew *C. parapsilosis* and was given antifungal therapy with fluconazole for 3 months. None of them developed reactivation till the last follow-up (Tables 2-4).

Case 1 was a 79-year-old man, with type 2 diabetes mellitus, benign prostatic hyperplasia, and coronary artery disease with progressive hip pain becoming worse for 3 months. He had undergone an uncemented bipolar hemiarthroplasty 14 months ago. His radiograph showed a subluxated hip prosthesis with a well-integrated uncemented femoral stem (Fig. 1a). The femoral stem was extracted with an extended

Pre-operative results				Last follow-up results	
Cases	Total WBC count (4800–10,800 μ L)	Erythrocyte sedimentation rate (15 mm/h)	C-reactive protein (<10 mg/dL)	C-reactive protein (<10 mg/dL)	Erythrocyte sedimentation rate (15 mm/h)
Case 1	8100	45	8	10	33
Case 2	5700	50	12	8	25
Case 3	4600	94	13.6	3.1	35
Case 4	8600	28	8	5	26
Case 5	9400	65	10	6	28
WBC: White blood cell					

Table 1: Blood investigations.

trochanteric osteotomy. Revision surgery was performed with DePuy Pinnacle Acetabulum and Solution stem after meticulous debridement. The patient was followed up for 2.5 years without any reactivation (Fig. 1b). At the last follow-up, his Harris Hip score was 59.45 (Table 2). He developed a cerebrovascular accident (major stroke) and passed away due to reasons unrelated to the revision surgery.

Case 2 was a 70-year-old lady with right hip pain for 4 months after an uncemented bipolar hemiarthroplasty done for a neck of femur fracture 18 months back. X-ray showed grade 3 protrusio hip (Fig. 2a). The femoral stem was well fixed without any loosening. The stem was retained and acetabular protrusio was filled with allograft and the cup was revised with a Depuy Pinnacle cup. Her Harris Hip score improved to 87.45 at the 3 years at follow-up without any reactivation (Table 2). X-ray showed good integration (Fig. 2b).

Patient	Before surgery	Follow-up
Case 1	16.95	59.45
Case 2	18.6	87.45

Table 2: Harris hip score at initial presentation and last follow-up.

Case 3 was a 65-year-old diabetic lady who presented to us 25 months after left knee arthroplasty surgery, pain effusion reduced flexion range (90°) for the last 6 months. Knee radiographs showed tibial loosening in all zones as per Knee Society guidelines and in 1–4 zones of the femur (Fig. 3a and b). After thorough debridement, she underwent a revision knee arthroplasty using bone cement incorporated with gentamycin and vancomycin. Her post-operative knee society scores at 4.5-year follow-up are shown in Table 3.

Case 4 was a 64-year-old lady without any medical comorbidities presented with an 18-month history of knee effusion and painful knee flexion to 70° . Her knee arthroplasty was done 3 years back (Fig. 3c). She underwent revision knee surgery with azithromycin-loaded bone cement. Her knee society score improved (Table 3) and the radiograph did not show any loosening at the 4-year follow-up (Fig. 3d).

Case 5 was a 60-year-old lady presented 21 months after knee arthroplasty with recurrent effusion and pain. The radiology was normal with well-fixed implants. The lower end of the incision scar was tender and erythematous. Her aspirate did not grow any microorganisms. Her pain and effusion were not reduced after anti-inflammatory medicines and empirical antibiotics for 10 days. Her joint was aspirated again and cultured which grew *C. parapsilosis* at 7 days. She underwent debridement and implant retention. Intraoperative tissue cultures were also positive for *Candida*. At the final follow-up of 18 months, she had no loosening or recurrence of infection.

Patient	Expectation (15)	Satisfaction (40)	Function (100)	Symptoms (25)	Objective (75)	Total (255)
Case 3	11	30	39	16	70	166
Case 4	13	28	44	19	72	176
Case 5	13	35	60	20	70	198

Table 3: Knee society score at last follow-up.

Discussion

Fungal PJI is rare and the limited literature available makes it difficult to adopt a planned approach to its management. Since fungal PJI most commonly is associated with the immunocompromised state, a healthy patient with a loosened implant without any signs of sepsis can get labeled as aseptic loosening [5]. However, post-operatively, it may turn out to be culture-positive after extended culture and meticulous tissue sampling.

This unexpected positive culture (UPC) is not very uncommon in literature. Neufeld had encouraging results with a prevalence of 9.2% (110) of 1196 aseptic THA revisions with a 2- and 5-year infection-free implant survival of 93.1% and 86.8%, respectively [6]. Another article with fewer patients where pre-operative cultures after aspiration were negative showed a prevalence of 44% (7 out of 16) of UPC among

hemiarthroplasty patients [5]. All patients had an elevated ESR similar to that observed in our patients. To date, there is no fungal UPC published in the literature. Our study must be the first fungal UPC published so far.

Diagnosis of fungus is also quite challenging. All our patients except for a rise in ESR appeared as aseptic loosening or rather culture-negative infections. Parvizi et al. have outlined new evidence-based and validated criteria for the diagnosis of PJI preoperatively and intraoperatively [7]. Our patients did not fit into the pre-operative criteria but did have two intraoperative cultures positive for the same *C. parapsilosis* after extended culture in BACTALERT and Sabouraud dextrose agar.

Even though *C. albicans* is the most common fungal PJI, Klatt found that all of his fungal PJI of the knee were infected with *C. parapsilosis* [8]. Azzam et al. [3] in their meta-analysis also identified *C. parapsilosis* as the most common organism,

Patient	Age (years)	Medical issues	Index surgery	Time to onset of symptoms (months)	Plain radiograph	Surgery	Follow-up (months)	Functional score
Case 1	79	DM, BPH, CAD	Hemiarthroplasty	14	Subluxation	Single-stage revision THA	30	59.45 Harris hip
Case 2	70	Nil	Hemiarthroplasty	18	Protrusion acetabuli	Single-stage revision THA	36	87.45 Harris hip
Case 3	65	DM	TKA	25	Loosening, deformity	Single-stage revision TKA	54	166 knee society
Case 4	64	Nil	TKA	36	Loosening, deformity	Single-stage revision TKA	48	176 knee society
Case 5	60	Nil	TKA	21	Normal	DAIR	18	198 knee society

DM: Type II diabetes, BPH: Benign prostatic hypertrophy, CAD: Coronary artery disease, THA: Total hip arthroplasty, TKA: Total knee arthroplasty, DAIR: Debridement and implant retention

Table 4: Patient demographics.

representing 39% of infections [2]. Hwang et al. detected *C. parapsilosis* in 50% of their 30 fungal PJI. Our series with culture-negative low-grade PJI presenting late also showed *C. parapsilosis* as the most common pathogen

Bacterial PJI can be treated with two-stage or single-stage exchange arthroplasty. Two meta-analyses have shown that one-stage exchange arthroplasty may provide superior outcomes, including lower reinfection rates and superior function, in a selected group of patients (absence of severe immunocompromised state and significant soft-tissue or bony compromise and concurrent acute sepsis) [9]. The rate of recurrent infection ranged from 0% to 18%, at a minimum of 2-year follow-up [9]. For fungal PJIs, most authors recommend a two-stage revision. The rates of recurrent infection vary widely and may be up to 25% [3], especially in patients with discharging sinus and immunocompromised states. The patients reported here were not immunocompromised and had a near-normal soft-tissue envelope. The five patients in our series with single-stage revision surgery did not develop any reinfection till the last follow-up.

Apart from the prophylactic antibiotics, most culture-negative patients receive antibiotics till the definitive culture reports arrive. Fungal cultures take 7–10 days to be ready and therefore the definitive antifungal treatment will be delayed for 1 week. Oral fluconazole has a high bioavailability equivalent to amphotericin. Oral fluconazole is less toxic and has shown good synovial fluid and serum concentrations comparable to

amphotericin while treating *Candida* infections [10, 11]. The Infectious Diseases Society of America recommends giving antifungals for 6–12 months for osteomyelitis and 6 weeks for septic arthritis. We gave intravenous fluconazole (200 mg twice daily) for 2 weeks and oral fluconazole for 3 months. All the patients had normal CRP preoperatively. Postoperatively the CRP elevated and normalized by 6 weeks. There was no loosening or reactivation of infection during the follow-up.

Conclusion

All immunocompetent patients presenting with an early prosthetic loosening should be evaluated for fungal elements if the culture is negative. *C. parapsilosis* is a common fungal PJI, especially in knee joints. Single-stage revision and fluconazole monotherapy have prevented the reactivation and recurrence of *C. parapsilosis* in immunocompetent patients with good soft tissues in our series.

Clinical Message

Meticulous debridement of all revision surgeries is required in an immunocompetent patient with suspected aseptic loosening considering emerging positive fungal cultures. Send samples for extended cultures and fungal cultures for all prosthetic loosening presenting early irrespective of normal-appearing blood picture.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

References

- Theil C, Schmidt-Braekling T, Gosheger G, Idelevich EA, Moellenbeck B, Dieckmann R. Fungal prosthetic joint infection in total hip or knee arthroplasty: A retrospective single-centre study of 26 cases. *Bone Joint J* 2019;101:589-95.
- Hwang BH, Yoon JY, Nam CH, Jung KA, Lee SC, Han CD, et al. Fungal peri-prosthetic joint infection after primary total knee replacement. *J Bone Joint Surg Br* 2012;94:656-9.
- Azzam K, Parvizi J, Jungkind D, Hanssen A, Fehring T, Springer B, et al. Microbiological, clinical, and surgical features of fungal prosthetic joint infections: A multi-institutional experience. *J Bone Joint Surg Am* 2009;91 Suppl S6:142-9.
- Basu S, Bose C, Ojha N, Das N, Das J, Pal M, Khurana S. Evolution of bacterial and fungal growth media. *Bioinformation* 2015;11:182-4.
- Neufeld ME, Lanting BA, Shehata M, Howard JL, MacDonald SJ, Teeter MG, et al. Prevalence and outcomes of unexpected positive intraoperative cultures in presumed aseptic revision hip arthroplasty. *J Bone Joint Surg Am* 2021;103:1392-401.
- Cichos KH, Detweiler M, Parvizi J, McGwin G Jr., Heatherly AR, Ghanem ES. The fate of positive intraoperative cultures following conversion total hip arthroplasty. *Hip Int* 2022;32:17-24.
- Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C,



Chen AF, et al. The 2018 definition of periprosthetic hip and knee infection: An evidence-based and validated criteria. *J Arthroplasty* 2018;33:1309-14.e2.

8. Klatt TO, Kendoff D, Kamath AF, Jonen V, Rueger JM, Frommelt L, et al. Single-stage revision for fungal periprosthetic joint infection: A single-centre experience. *Bone Joint J* 2014;96:492-6.

9. Thakrar RR, Horriat S, Kayani B, Haddad FS. Indications for a single-stage exchange arthroplasty for chronic prosthetic joint infection: A systematic review. *Bone Joint J* 2019;101-B 1

SupplA:19-24.

10. Rex JH, Bennett JE, Sugar AM, Pappas PG, Van der Horst CM, Edwards JE, et al. A randomized trial comparing fluconazole with amphotericin B for treatment of candidemia in patients without neutropenia. *Candidemia study group and the national institute. N Engl J Med* 1994;331:1325.

11. Brammer KW, Farrow PR, Faulkner JK. Pharmacokinetics and tissue penetration of fluconazole in humans. *Rev Infect Dis* 1990;12 Suppl 3:318-26.

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