Revision Total Knee Arthroplasty for Chronic *Histoplasma Capsulatum* Prosthetic Joint Infection: A Case Report

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Introduction / Purpose

- Prosthetic joint infections (PJIs) are a devasting, yet relatively common complication following total hip and knee arthroplasty procedures. The overwhelming majority of these infections are bacterial.
- Fungal PJIs only account for 0.9-2.4%, most of which are caused by candida species.(1-3)
- Fungal infections more frequently occur in patients with multiple comorbidities, in those that are immunocompromised, and frequently occur in combination with bacterial PJIs.(4,5,6,7)
- Fungal pathogens can be more difficult and time-consuming to culture and isolate in the lab, which can be obscured by bacterial coinfection.
- The purpose of this case report was to describe a *histoplasma capsulatum* PJI in an immunosuppressed patient successfully treated with a two-stage revision hinged knee prosthesis and planned lifelong suppressive antifungals.

Patient Presentation

Patient History

- 54-year-old female with past medical history of mixed connective tissue disease presented with a chronically painful left total knee since the index surgery 18 months prior to presentation.
- Past medical history was most significant for mixed connective tissue disease including systemic sclerosis, rheumatoid arthritis, polymyositis, and Sjogren's disease managed with daily prednisone, methotrexate, and intravenous immunoglobulin (IVIG).
- Patient had persistent and recurrent effusions, multiple episodes of overlying cellulitis treated with oral antibiotics, and recurrent low-grade fevers.
- Multiple prior joint aspirations obtained without evidence of PJI including negative aerobic and anaerobic cultures, and synovial cell counts.

Patient Exam & Diagnostic Evaluation

- On physical exam, there was moderate tenderness and erythema overlying the patella.
- Radiographs obtained demonstrated a stable implant without evidence of loosening.
- Initial labs demonstrated moderately elevated inflammatory markers:
  - C-reactive protein (CRP) of 39.8 (*reference range 0.1-10.0*)
  - Erythrocyte sedimentation rate (ESR) of 89 (*reference range 0-30*).
- Synovial fluid aspiration and analysis
  - Work-up for atypical pathogens including serum and urine histoplasma testing was negative.
  - Based on *Synovasure*™, 4 of 6 minor criteria were met and decision was made to proceed with elective two-stage revision.

***Synovasure*™**	
Test Item	Value
Alpha defensin	Positive
Neutrophil elastase	Positive
RBCs	11,000
Nucleated Cells	3425
% Neutrophils	57.8%
% Mononuclear cells	42.2%
Microbial Panel	
Staphylococcus	Negative
Candida	Negative
Enterococcus	Negative
Culture data	No growth

Two-Stage Revision

Stage 1 – Explantation with Antibiotic Spacer

- After 6-week antibiotic holiday, patient underwent explantation, irrigation and debridement, and placement of an articulating antibiotic spacer.
- On inspection, the joint surfaces were noted to have a "slime-like" appearance. Operative cultures included synovial fluid, synovium (x2), and tibial bone.
- Temporary components included a *Triathalon* cruciate retaining (CR) femoral component and an all-polyethylene condylar stabilizing (CS) tibial component (*Stryker, Kalamazoo, MI, USA*) (**Figure 1)**
- Implants were cemented with vancomycin and tobramycin impregnated cement (3 g vancomycin, 3.6 grams tobramycin per package).

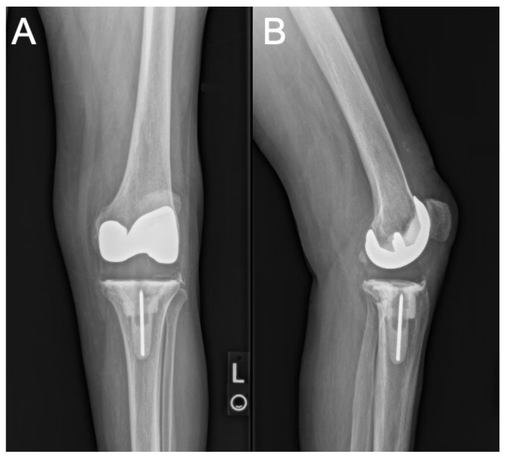

Figure 1. (**A**) Anteroposterior and (**B**) lateral views of the left knee obtained after stage 1 explantation and placement of an articulating antibiotic spacer, cruciate retaining femoral component, and all polyethylene tibial component.

Operative Cultures and Antifungal Treatment

- Operative cultures were sent for gram stain, cell count, aerobic culture, anerobic culture, AFB culture, and fungal culture.
- Two weeks postoperatively, fungal cultures were positive for mold in 3 of 4 specimens, and were subsequently found to be morphologically consistent with *histoplasma capsulatum*.
- Patient was admitted and underwent two-week induction with Amphotericin B (Ambisome 3mg/kg q24 hours) followed by an oral course of itraconazole.
- Repeat aspiration 6 months after stage 1 was negative for aerobic, anerobic, AFB, and fungal growth.

Stage 2 – Revision Left Total Knee Arthroplasty

- 7 months following stage one explant, patient underwent second stage revision with a hinged knee prosthesis (*Stryker Modular Rotating Hinge (MRH) Knee System; Stryker Inc, Kalamazoo, MI, USA*). **(Figure 2)**
- Cement was prepared with 3.6 grams of gentamicin and 200 mg of voriconazole per package of cement.
- Postoperatively, patient was placed on oral voriconazole

Outcomes

- At 7 weeks postoperatively, patient had near symmetric range of motion from full extension to 125 degrees of flexion. She was able to ambulate without pain and was released without restrictions.
- At 18 months postoperatively from stage two, patient was continuing to do well; however, patient had experienced multiple lateral patellar dislocations. These were amenable to self-reduction and treated with a patellar stabilizing brace.
- At the time of most recent follow-up (18 months), patient remained on antifungal therapy with plans for lifelong suppression; however, this necessitated multiple antifungal medication changes due to medications reactions including: itraconazole (diarrhea), posaconazole (rash), and voriconazole (blistering, erythema).
- At the most recent follow-up, the patient was tolerating treatment with isavuconazole without signs of local or systemic recurrence of infection.

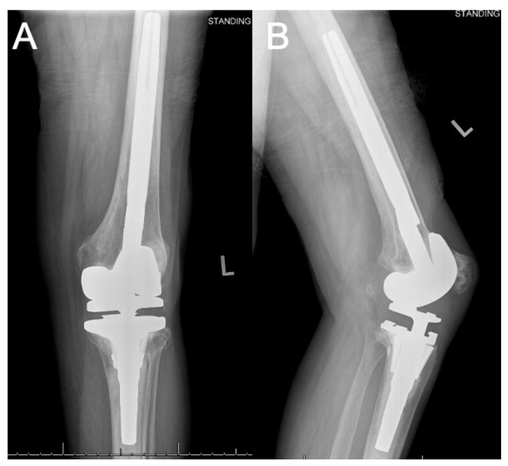

Figure 2. (**A**) Anteroposterior and (**B**) lateral views of the left knee obtained at the most recent follow-up (18 months) after stage 2 revision including placement of a hinged prothesis with both antibiotic and antifungal cement.

Conclusions

- This case represents a prototypical fungal PJI patient that presented with several comorbidities requiring multiple chronic immunosuppressive therapies. She presented with indolent and chronic symptoms, moderately elevated inflammatory markers, and initially repeatedly culture-negative synovial analysis.
- This case emphasizes the need for a high degree of clinical suspicion and often prolonged incubation of cultures in such patients.
- The presented patient underwent a staged revision, received interval systemic antifungal therapy, utilized antifungal cement in the second stage, and received long-term systemic oral antifungal therapy resulting in maintained clearance of infection at the most recent follow-up.

References

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