

Fungal Prosthetic Joint Infection Following Total Knee Arthroplasty: A Case Report

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Learning Point of the Article:

Although rare, Fungal infection post Total Knee Replacement needs clinical suspicion and a two-stage revision with systemic and local anti-Fungal.

Abstract

Introduction: Prosthetic joint infection (PJI) is a rare complication of total knee replacement (TKR), yet it is a serious and debilitating condition. Bacterial infection accounts for the majority of cases and fungal infection is estimated to cause 1% of all prosthesis infection.

Case Report: This case presents a 60-year-old female, who presented to our outpatient orthopedic clinic complaining of right knee pain, swelling, and hotness. The physical examination revealed redness, hotness, restricted range of movement, and tibial loosening, 9 months following TKR revision. Culture of the joint aspirate showed growth of "Candida parapsilosis" and second aspirate confirmed the diagnosis. The patient then underwent two stages revision surgery with placement of amphotericin B loaded cement, to maintain high local antifungal concentration in addition to decrease the side effects of amphotericin B infusion such as thrombophlebitis and the more serious systemic effect as nephrotoxicity. The post-operative course was uneventful, with gradual improvement and restoration of normal movement range.

Conclusion: Fungal PJI is a rare complication of TKR, yet it results in severe debilitating symptoms and impairment of the patient functional capacity. Careful evaluation of the patient followed by a detailed workup is necessary for the identification of the underlying causative micro-organism. Two-stage revision surgery with antifungal loaded cement spacer and antifungal therapy currently is the standard of management. To the best of our knowledge, this is the first fungal PJI following total knee arthroplasty reported in Jordan.

Keywords: Fungal prosthetic joint infection, fungal infection, total knee replacement, total knee replacement complication.

Introduction

Prosthetic joint infection (PJI) is one of the main reasons for knee prosthesis failure. Most of the PJI is caused by bacterial species, particularly staphylococcal and Gram-negative micro-organisms. Moreover, fungi, particularly candida species responsible for a minority of the PJI cases, yet it is a serious and debilitating complication of knee arthroplasty. The incidence of fungal PJI is expected to rise due to increasing number of patients undergoing arthroplasty [1]. Despite the use of standardized operation procedure and strict infection control strategies, the risk of infectious complication following joint replacement is 1–2%. Of which, fungal infection is estimated to cause 1% of all prosthesis infection [2].

The most commonly isolated candida was *Candida albicans*, followed by *Candida parapsilosis*, *Candida glabrata*, and *Candida tropicalis*.

The pathogenicity of these organisms is considered a result of their ability to secrete hydrolytic enzymes and to form a biofilm on the prosthesis surface that protect them from the systemic antifungal and permits their growth.

[1, 3]. Three different modes prescribe the possible mechanism of candida prosthetic infection: (1) The hematogenous route, (2) direct inoculation from the previously infected native joint with candida, and (3) extension from adjacent infected soft tissue [2].

Author's Photo Gallery



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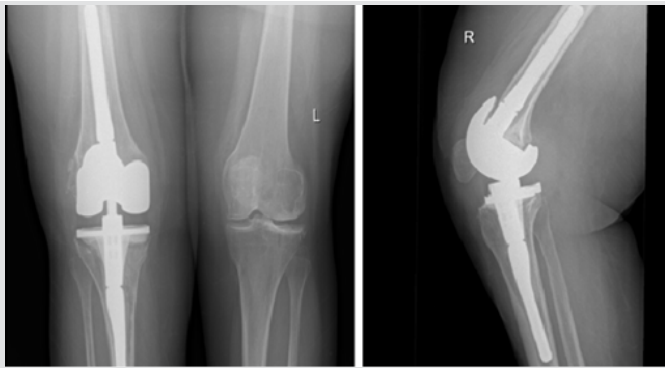


Figure 1: Perioperative radiography of the infected prosthesis.

The development of symptoms in candida PJI is often indolent, whether it was acute or chronic infection. Symptoms include local signs of inflammation (erythema, hyperthermia, swelling, and pain), fever, fistula, and purulent discharge which are consider to be specific for prosthesis infection. The most important diagnostic criteria are the presence of pain at the site of the implant [4].

Case Report

This report presents a 60-year-old non-diabetic, non-hypertensive female whom had experienced a fungal infection on her prosthetic knee post total knee replacement (TKR). Two years ago, the patient underwent right TKR for her osteoarthritis which was then followed by conventional physiotherapy. The patient post-operative period was uneventful for the subsequent 8 months.

Eight months later, the patient presented with the right knee pain, associated knee swelling, and restricted range of motion. She was admitted for suspected bacterial infection of the prosthetic knee. The culture of the joint aspiration was done, and the result was positive for bacterial infection with “Streptococcus viridans”. Following the confirmation of bacterial PJI, the patient underwent TKR revision with the removal of the infected prosthesis and placement of cement spacer, all covered with a plethora of antibiotics, including

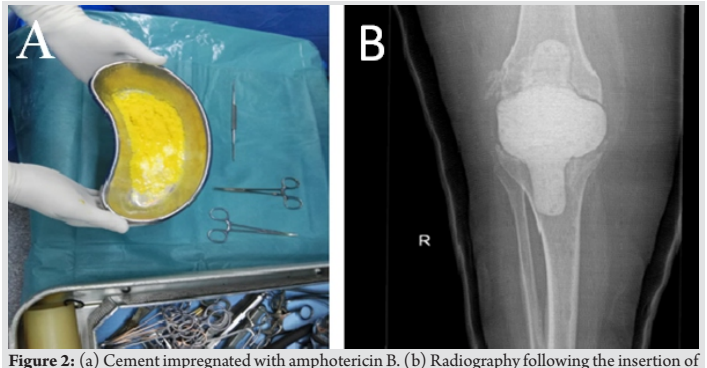


Figure 2: (a) Cement impregnated with amphotericin B. (b) Radiography following the insertion of cement spacer.

imipenem + cilastatin 500mg, amoxycillin 1g+ clavulanic 200mg, vancomycin 500mg, and cefuroxime 750mg. The patient was hospitalized for the next 42 days and discharged on amoxicillin 875mg and clavulanic acid 125mg [1*3]. Three months following the placement of cement spacer, the patient was admitted for the second stage of TKR with removal of the cement spacer and placement of the new prosthesis after confirming the sterility of the aspirated knee fluid. During the hospital stay, the patient was covered with imipenem + cilastatin 500mg, vancomycin 500mg, cefuroxime 750mg for prophylaxis, and discharged on amoxicillin 875mg+ clavulanic acid 125mg [1*2]. During the following period, the patient was improving and doing well.

However, 9 months following the two-stage revision TKR, the patient presented with the right knee pain, swelling, and hotness. The physical examination revealed redness, hotness, restricted range of movement, and tibial loosening which called for the admission of the patient. The patient’s complete blood count, kidney function tests, liver function tests, and chemistry were all sent for laboratory analysis refer to Table 1 and Fig. 1 which show the preoperative radiographs.

Right knee soft-tissue excision showed fibrofatty tissue with inflammatory infiltrate and fibrin. Necrotic bone periodic acid–Schiff (PAS) stain was negative for fungal spores and pseudohyphae. Right knee synovial fluid aspirate showed

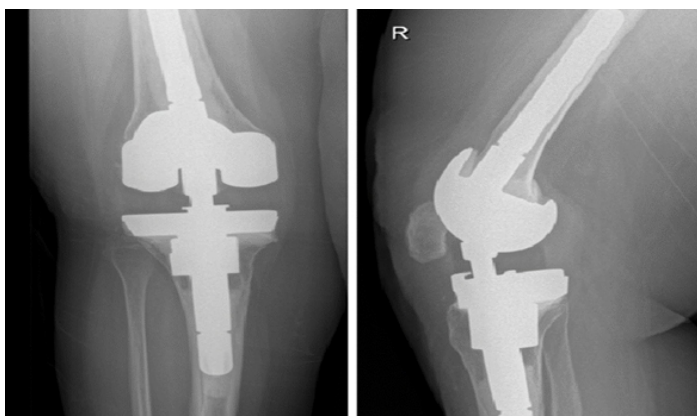


Table 1: Laboratory findings	
Laboratory test	Result
ESR	78
CRP	127.9
Hb/Ht	11.1/33.8
WBC	4.85
Platelets	302

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, Hb/Ht: Hemoglobin and hematocrit, WBC: White blood cells



sheets of neutrophils in hemorrhagic background. PAS stain is negative for fungal spores and pseudohyphae, but culture of the joint aspirate showed growth of "C.parapsilosis." A repeated culture confirmed the presence of the fungal infection. During this admission, the patient underwent the first stage revision of TKR with removal of the infected prosthesis and placement of amphotericin bimpregnated cement spacer (Fig. 2) and received capsosungin 50mg, fluconazole 200 mg, imipenam+cilastin 500mg, ceftriaxone 1g, levofloxacin 500mg, and vancomycin 500mg for 40 days and then was discharged on fluconazole 150 mg 1*1 for 6 weeks. Knee aspirate culture demonstrated no fungal presence 2 weeks post-anti-fungal treatment.

Three months following the placement of amphotericin B impregnated cement spacer, the patient was admitted for the second stage TKR with removal of the cement spacer and placement of the new knee prosthesis after confirming the sterility of the aspired knee culture during the hospital stay, the patient was on imipenem + cilastatin 500mg, amphotericin B 50mg, fluconazole 150 mg capsules, vancomycin 500mg, and cefuroxime 750mg. The patient was discharged on fluconazole 150 mg 1*2 for at least 12 months.

During the subsequent period, the patient was improving and gradually regaining the range of motion and her X-ray at 8th months post-operative is presented in Fig. 3. The patient was seen in the clinic for regular checkup and serial laboratory testing every 4 weeks.. However, after completion a period of 9 months out of the planned 12 months of oral Fluconazole, the patient developed skin rash and stopped the medication.

Discussion

Fungal PJI is a rare complication of TKR, and primary candida infection is extremely rare. Yet, this infection requires a careful evaluation of the patient condition and extensive workup to detect the underlying micro-organism. Several factors are implicated in the development of fungal PJI. These factors can be categorized into patient-specific characteristics, including patient's age, immunocompromised status, and comorbidities such as diabetes mellitus and obesity.

The procedure-related risk factors include; prolonged operation time, previous joint surgery and the presence of remote infection or bacteremia.[4, 5]. In spite of that, almost half of the cases occur in patients without identifiable risk factor [6].

The diagnostic process of fungal prosthetic infection represents a challenging task for the treating physician, as fungal PJI presents with vague infection signs such as swelling, skin erythema, hyperthermia, and drainage of the fluid that closely resemble that of the bacterial PJI, the biological marker (C-

reactive protein, leukocytes, and sedimentation rate) provides limited information about prosthetic infection, and routine culture may show negative results, the diagnosis of fungal PJI needs a high index of suspicion. Culture of multiple samples obtained from joint aspiration or perioperative samples, consider the gold standard to diagnose fungal PJI [2]. The findings of the radiological evaluation, in most of the cases, showed loosening of the implant, osteolysis, or local bone destruction [7]. In the light of high clinical suspicion and the presence of confirmatory culture-based and radiographic evidence, the patient should undergo a revision surgery preferably two-stage revision arthroplasty.

The other modalities of treatment as debridement with prosthesis retention or resection arthroplasty had shown high failure and revision rates [8,9].

Given the rarity of fungal PJI and the paucity of the literature about this condition, there is no standard management guideline to follow. However, most of the literature recommend a two stages revision surgery with antifungal-loaded cement spacer and antifungal therapy. After the first operation, the majority of the patients have at least 6 weeks of systemic antifungal therapy. Following the second stage, the antifungal therapy was continued for further 2 weeks to 6 months, with fluconazole being the most frequently used agent. Other treatment options include debridement, antibiotics and implant retention, or one-stage exchange arthroplasty [10].

Between the different kind of systemic antifungal , there is still no consensus about the drug of choice in the cases of PJI

. Amphotericin B considers the gold standard, but a side effect, especially nephrotoxicity, may limit its use, particularly for the long term. Fluconazole is an alternative with fewer side effects [6].

Despite the aforementioned therapeutic strategies, the failure rate remains high. The suboptimal treatment outcomes may be attributed to the complexity of the fungal biofilm and the associated immune suppressive diseases; the patients usually suffer from [10]. To the best of our knowledge, this is the first fungal PJI following total knee arthroplasty reported in Jordan.

Conclusion

Fungal PJI is a rare complication of TKR, yet it results in severe debilitating symptoms and impairment of the patient functional capacity. Careful evaluation of the patient followed by detailed workup is necessary for the identification of the underlying causative microorganism. Two-stage revision surgery with antifungal-loaded cement spacer and antifungal therapy currently is the standard of management.

Clinical Message

Although rare, the fungi can be the causative agents of PJI, which needs clinical suspicion. The delay re-implantation as two-stage revision with the usage of systemic antifungal and cement impregnated with amphotericin B shows good result in the treatment of fungal PJI, considering the regular laboratory evaluation for their side effects.

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