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Case Report

Mixed bacterial-fungal infection following total hip arthroplasty: A case report

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ABSTRACT

Prosthetic infection is one of the severe postoperative complications of arthroplasty. Mixed bacterial-fungal prosthetic infection is rare but can be disastrous. This case was a 76-year-old female suffered from prosthetic infection following total hip replacement due to femoral neck fracture and underwent multiple debridements. The culture of periprosthetic tissue was bacteriologically sterile following the first debridement, while the *Staphylococcus hominis* was identified in the second debridement in the previous hospitalization where fungal infection had not been considered. Thus the pathogen spectrum of anti-infection therapy failed to contain fungus. Ultimately, the culture result of our sampled periprosthetic tissue during the third debridement was *Candida albicans* without bacterium in our hospital. The fungal prosthetic infection was successfully treated by a two-stage revision with antifungal drugs. Accurate diagnosis and standardized treatment is the key to the therapy of infection after hip arthroplasty, especially for mixed bacterial-fungal prosthetic infection.

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Introduction

For some serious hip diseases and fractures, total hip arthroplasty (THA) is a common option for joint reconstruction. Meanwhile prosthetic infection is a potentially disastrous postoperative complication.¹ The incidence of periprosthetic joint infection (PJI) is approximately 2%–3%.² To date, the most common pathogens for prosthetic infection are bacteria, especially *Streptococci* and *Staphylococci*, while fungal infection is rare,³ particularly *Candida albicans*. So far, we know little about the accurate diagnosis and effective treatment of fungal infection. Prosthetic fungal infection can easily be neglected, especially under the circumstance of mixed infection. Thus the treatment might be delayed and there are not specific guidelines for prosthetic fungal infection yet. The main reasons for the difficulty of surgical treatment of fungal infection of joint prosthesis are as follows: biomembrane against antifungal drug, insufficient application of antibiotics, and a lack of effective antifungal drugs used in cemented space. Combination of debridement and anti-infection drug may provide an efficient means to control prosthetic infection, especially for mixed bacterial-fungal infection.

We described here the case of mixed bacterial-fungal infections after THA surgery. This case might reveal the difficulty of accurate diagnosis and the effect of standardized two-stage exchange arthroplasty on periprosthetic joint infections.

Case report

A 76-year-old female was diagnosed as right femoral neck fracture after a sudden fall (Fig. 1A) with a history of hypertensive disease. There was no smoking and drinking history. The patient was treated with a THA surgery (Fig. 1B) and discharged from the hospital in a few days and returned to normal activities.

Dislocation due to a sprain occurred six months after the surgery, which was successfully treated by manipulative reduction in the same hospital (Fig. 2) with residual chronic hip pain. There was no X-ray evidence of loosening of the artificial joint component.

Three months later after the dislocation, the patient was admitted to the same hospital because of worsen hip pain accompanied by swelling and increased hip skin temperature. The blood test showed a normal white blood cell (WBC) level and increased erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Ultrasonography showed a plenty of liquid dark area in the hip. Emission computed tomography (ECT) scan showed abnormal enhanced imaging around the acetabulum. The involved hip was considered to be infected in that hospital. The patient underwent debridement with retention of the prosthesis and did not take any antibiotics before debridement. A large amount of fluid was found

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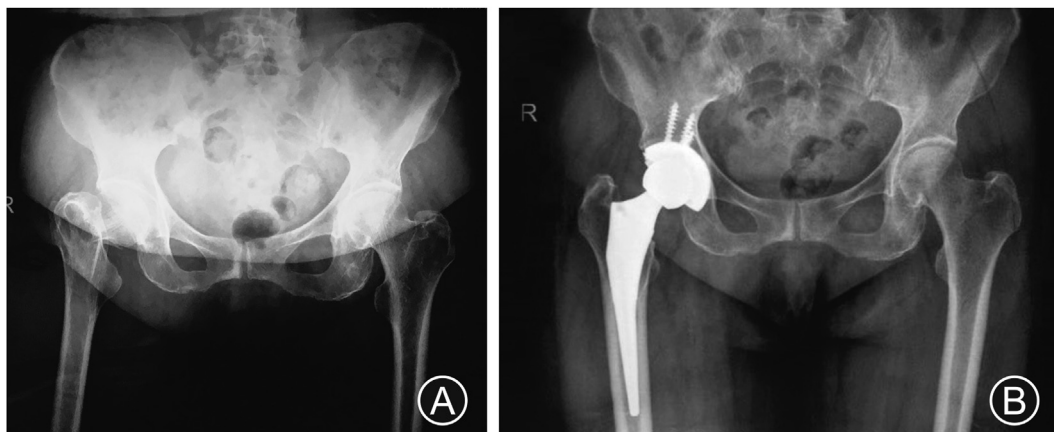


Fig. 1. (A) Right femoral neck fracture after a fall. (B) Radiography of the right hip total arthroplasty.

around the prosthesis intraoperatively. The culture of intraoperative joint fluid was bacteriologically sterile. No fungal culture was carried out. Pathological examination of the soft tissue around the prosthesis found fiber tissue hyperplasia, neutrophil infiltration and local abscess formation. She was treated with vancomycin 1 week after the surgery, but the local operative region remained painful, swelling and redness. Then a week later, the patient underwent the second debridement and the artificial femoral head was removed (Fig. 3A), replaced by the antibiotic-loaded cement spacer. The periprosthetic tissue samples around artificial femoral head were identified as *Staphylococcus hominis* sensitive in vitro to tigecycline, linezolid and vancomycin. No fungal culture was carried out. So she was eventually diagnosed as suffering from PJI.⁴ Thus vancomycin was used 2 months after the second debridement. The patient discharged from the hospital 2 months later and the infection was contained without pain and swelling. The patient did not take any antibiotic at home after discharge.

Three months after the last discharge, the hip pain and redness recurred. The patient was treated with vancomycin in the same hospital for 1 month. Unfortunately, the right hip joint pain got worse again.

The third debridement was performed and all of the hip prosthesis was removed (Fig. 3B), replaced by the conventional

antibiotic-loaded cement spacer (Fig. 4A). It was noted that some milky white stuff was floating in the periprosthetic fluid, which was clear. Necrotic and infected tissue was resected in the hip. For the spacer production, 60 g of bone cement was required and 6 g vancomycin was used in the bone cement. The tube in the hip can be removed when the amount of drainage was less than 25 mL for at least 3 consecutive days. Because the pathogen spectrum of vancomycin failed to contain fungus, a new anti-infective plan was used after the surgery (linezolid and levofloxacin). Five days later the culture of periprosthetic fluid sample of the hip showed no bacterium growth while *Candida albicans* was identified, which was sensitive in vitro to many antifungal drug, such as itraconazole, amphotericin B, and fluconazole. According to the opinion of pharmacy department of our hospital, fluconazole and linezolid were used intravenously for 6 weeks followed by fluconazole and levofloxacin for 6 weeks. Then fluconazole was used for 3 months. Minor adverse reaction to the drugs included nausea and vomiting. The adverse reactions were controlled through protecting gastric mucosa and acid suppression by gastroenterologist. The patient accepted 6-month course of antifungal treatment and did not experience any serious adverse reactions. The infection was finally inhibited. The index of infection level (ESR\|IL-6\|CRP\|procalcitonin) continued to decline since the second month after the third

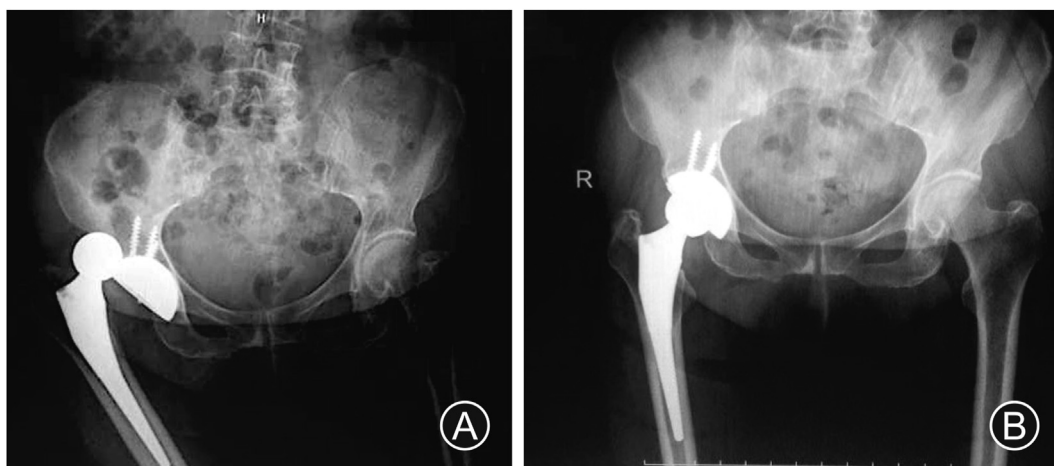


Fig. 2. Dislocation occurred six months after total hip replacement (A), which was successfully treated by manipulative reduction (B).

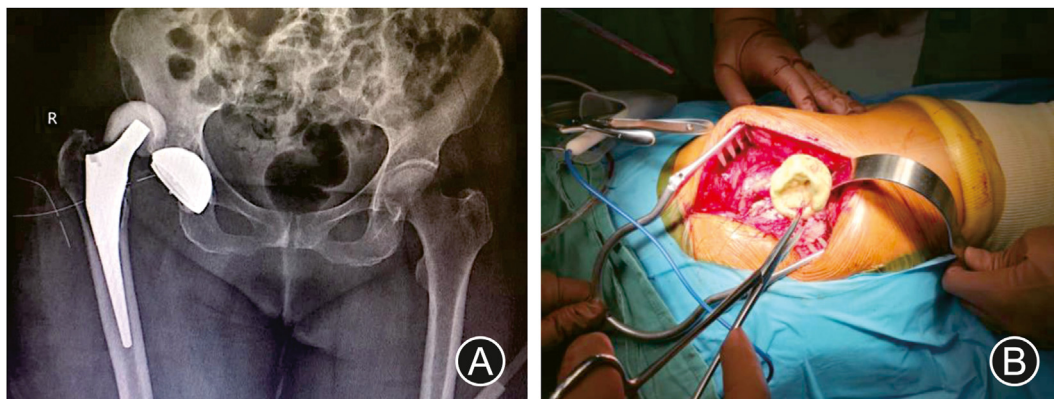


Fig. 3. (A) Dislocation after the second debridement and the part of prosthetic components (artificial femoral head) was removed. The artificial femoral head was made from cement. (B) The antibiotic-loaded cement spacer was removed at the third debridement.

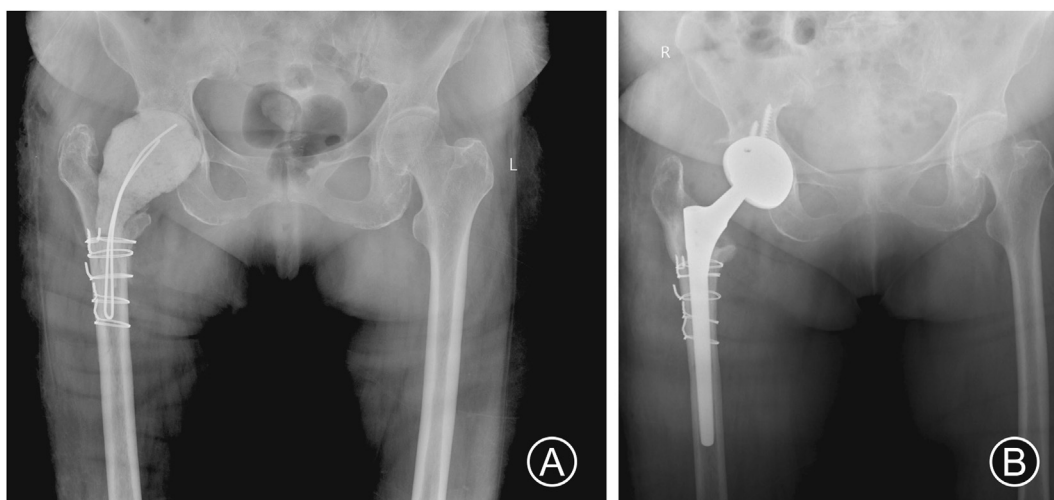


Fig. 4. (A) Postoperative AP X-ray shows an antibiotic-loaded, articulating hip spacer in situ after the third debridement for periprosthetic joint infection. (B) The revision was performed using a cementless femoral stem and a porous tantalum acetabular cup.

debridement. CRP, ESR and WBC returned to almost a normal level within 3 months. During this period, the revision was performed using a Wagner SL revision stem (Zimmer, Warsaw, IN, USA) and a porous tantalum acetabular cup (Fig. 4B). Then the antibiotics (fluconazole and levofloxacin) were administered for 6 weeks until the CRP, ESR and WBC returned to an acceptable range after revision operation. Antibiotics and principal laboratory findings for the patient are shown in Table 1.

In one-year's follow-up, the patient had no evidence of recurring infection and remained pain-free. The results of CRP, ESR and WBC were normal. The total Harris hip score was 75 points.

Discussion

With the development of joint replacement surgery, prosthetic joint infections become a major complication as various relevant studies have been reported. Infection after THA is complicated and intractable. The management of infection after THA is complex and challenging.¹ This case showed that the procedure of repeated debridement was a great challenge for postoperative infection, especially for *Candida albicans*. On the one hand, results of culture of the periprosthetic tissue taken during 3 debridements were not consistent, so it was extremely difficult for us to identify the key

Table 1
Antibiotics and principles laboratory findings for the patient.

Variables	WBC	ESR	CRP	Antibiotics
Before the first debridement	7.71	117	24.3	
Before the second debridement	6.38	65	6.1	Vancomycin
At the end of treatment after the second debridement (in the previous hospital)	6.46	38	19.6	Vancomycin
Before the third debridement	7.22	70	10.8	
At the end of treatment after the third debridement (in our hospital)	4.93	21	6.8	Fluconazole and linezolid
Before the revision	6.51	35	5.6	
At the end of treatment after the revision	5.82	41	4.6	Fluconazole and levofloxacin

WBC: white blood cells; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.
Note: WBC reference value: (4.0-10.0)×10⁹/L; ESR reference value: 0–20 mm/h; CRP reference value: 0.0–8 mg/L.

pathogenic microorganism and provide a proper therapy. On the other hand, to our knowledge, reports about fungal prosthetic infection were rare and there existed no established guidelines for the therapy of this kind of periprosthetic infection.^{5,6} Therefore it is formidable to diagnose fungal prosthetic infection and provide a proper antifungal therapy. Kim et al.⁷ thought that the diagnosis of *Candida albicans* infection was rare and no standard guidelines existed on the therapy of *Candida* species. In this case, fungal infection had not been considered in previous hospitalization, thus accurate diagnosis might be missed at first time. Bacterial infection might be not only one of the pathogens in the PJI.

Candida albicans is an opportunistic pathogen and could be symptom-free in the healthy individuals.⁸ According to relevant researches, risk factors for patients with fungal infection include diabetes, immunocompromised status, tuberculosis, drug abuse, misuse of antibiotics or prosthetic devices.^{1,9} Sometimes it is hard to establish the precise causes of fungal infection. This patient did not suffer from diabetes and tuberculosis and was non-immunocompromised host without drug abuse. In this case, *Staphylococcus hominis* and *Candida albicans* were cultured from the hip joint, so the patient suffered from rare mixed bacterial-fungal infections following THA. Periprosthetic joint infection occurred 3 months after dislocation of THA in this case, which was not considered as the cause of PJI.

The patient underwent a routine debridement, and the therapy turned out to be ineffective. The review of literature illustrated that debridement alone with prosthesis retention fail to control infection.⁹ A large series of cases demonstrated that debridement with retention of the prostheses was unable to control the infection.¹⁰ Even though the part of prosthetic components was removed and a temporary antibiotic spacer was implanted, the pathogen still can not be suppressed. As the standard therapy for chronic periprosthetic joint infections, two-stage exchange arthroplasty has been reported with a high successful rates of 65%–98%.¹¹ In addition, prosthetic joints are ideal for microbes to adhere to and to form extracellular polymers, providing a matrix that allows further adhesion. Pathogenic microorganism tended to adhere to the surface of prostheses. The biofilms of organisms can resist antimicrobial therapy.¹² *Candida albicans* biofilm could be in response to environmental conditions.¹³ The implant retention for fungal PJI with irrigation and debridement demonstrated poor long-term outcomes.¹⁴ All of the prostheses should be removed in debridement. Fungal PJI had high recurrence rate,¹⁵ so two-stage exchange arthroplasty for fungal PJIs should be recommended for reducing the relapse rate. Gebauer et al.¹⁶ reviewed the previous literature on fungal PJIs and hold that two-stage exchange arthroplasty for fungal PJIs had the consistent outcome. Before we knew the result of fungal culture, vancomycin was used in the cement spacer during the third debridement. Kim et al.¹⁷ thought that antifungal-impregnated cement spacer was an efficient method for fungal PJI after total knee arthroplasty (TKA). For the therapy of fungal PJIs, there was no consensus on the type and dosage of antibiotics mixed with bone cement. Currently, the effectiveness of the antibiotic-loaded cement spacer in reducing the risk of recurred infection was no documented by clinical studies.¹⁸

The antifungal drug is vital for the treatment of fungal prosthetic infection. Goodman et al.¹⁹ reported the fungal prosthetic infection cases without systemic antifungal therapy and only local irrigation with amphotericin B and removal of the prosthesis. The prosthetic hips were not reimplanted. For any periprosthetic fungal infection, culture is needed to identify the species of pathogenic microorganism and provide a proper antifungal treatment.¹¹ Some guidelines recommend using antifungal drug for 6 weeks for *Candida* specie,²⁰ but no guideline for periprosthetic fungal infection. In the literature, length of antifungal therapy is from 6 weeks to 25

weeks.⁴ Some literature reported that treatment with antifungals for a mean of 8 months (range 3–18 months) is associated with greater successful rate.²¹ According to previous review literature, the most common choice was fluconazole in combination with flucytosine and amphotericin B.²² Prolonged antibiotic drug is a viable option for PJI and no high incidence of complications has been reported.²³ In the previous report, 33% of patients had the combined infection (fungal and bacterial) in the cases of PJI.²⁴ Theil et al.²⁵ reported bacterial co-infection was 44% in patients with fungal infection after THA. Thus, the therapy of PJI frequently requires multiple antibiotics covering the microorganisms. So in this case, fluconazole and linezolid were used in combination for anti-infection therapy. It should be noted that combined usage of anti-infection drug may increase the risk of systemic toxicity of the patient, especially elderly patients.

This case shows the importance of accurate diagnosis for mixed fungal prosthetic infection. Fungal infection should be routinely considered in the PJIs. All of the hip prosthesis should be removed in the debridement for PJI in most cases. Standardized two-stage exchange arthroplasty is strongly recommended for fungal prosthetic infection.

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Ethical statement

The patient's consent has been obtained.

Declaration of competing interest

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

Author contributions

Yang-Jing Lin made investigation and data collection, wrote the original draft. Tiao Su conducted the data analysis and validation. Liu Yang provided resources and supervision. Guang-Xing Chen preformed the surgery and edited the text.

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