

Case Report

Candida Parapsilosis Total Hip Arthroplasty Infection: Case Report and Literature Review

全髖關節置換術併發近平滑假絲酵母菌真菌感染：案例報告及文獻回顧

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ABSTRACT

A 71 year-old male with a history of diabetes mellitus and right total hip arthroplasty (THA), received a revision surgery on the acetabulum cup of the THA because of loosening. The intraoperative culture yielded *Candida parapsilosis*. It was regarded as contamination initially. The patient had remained asymptomatic for 4 years after the revision surgery. The radiographs showed no evidence of loosening and the blood inflammatory markers were normal. The only abnormal finding was two subcutaneous swellings over the surgical scar. The patient then presented with right hip pain on walking and low-grade fever. A course of fluconazole had been given for 6 months, but the infection did not improve. Eventually, an excision arthroplasty of the right hip was performed. This case illustrates the rarity and the indolent pattern of presentation of fungal prosthetic infection. High index of suspicion and prompt treatment were needed. Literature on fungal prosthetic infection was also reviewed.

中文摘要

一位七十一歲有糖尿病史的男仕因右全髖關節鬆脫接受髖臼杯修複手術。手術中的培養栽植出近平滑假絲酵母菌。起初它被當作是污染。病人在修複手術後的四年間並沒有病徵，X光檢查顯示沒有鬆脫的証據及血液發炎標記亦正常。唯一的異常是在疤痕處有兩個皮下腫脹。及後病人走路時有右髖關節痛的徵狀，並有輕微發燒。使用了六個月療程的口服氟康唑，但病情並沒有好轉。最後進行了右髖關節切除造形術。這個案說明了假體真菌感染是罕有的及其表徵是非常不明顯，高警覺性與迅速的治療是十分需要。我們也回顧了假體真菌感染的文獻。

Introduction

Fungal infection in joint replacements is estimated to be < 1% of all joint prosthesis infections. However, it can lead to devastating consequences and significantly impair mobility if not treated timely.

We present a case of *Candida parapsilosis* right hip joint replacement infection in a 71-year-old male. The presentation was a notoriously indolent pattern. We adopted conservative management initially, but it failed eventually after 4 years.

We also reviewed the literature on the risk factors, clinical features and treatment options of fungal prosthetic joint infections.

Case Report

A 71-year-old male, with diabetes mellitus, received a revision surgery on the loosened acetabulum cup in 2005 (Figure 1). He received a primary right total hip replacement 15 years ago because of avascular necrosis of the right femoral head. The intra-operative culture in the revision surgery showed positive *Candida* species. It was regarded as contamination, as there was no clinical evidence of infection.

Two subcutaneous swellings were later noted over the right hip surgical scar in October 2006. Each of them was around 3 cm in diameter. There was no skin erythema. No sinus tract was observed. Both C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were normal. An ultrasound scan showed two subcutaneous swellings on the lateral aspect of the proximal thigh deep to the scar. The proximal one measured 39 mm long and 14 mm deep.

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The distal one measured 99.9mm long and 24mm deep. Both were aspirated with the aid of ultrasound using a 18G needle. Three mL of blood stained fluid was obtained from each of the swellings. The culture of the fluid found positive culture of *Candida parapsilosis*. The radiographs showed no evidence of prosthetic loosening. Because of the asymptomatic nature of these swellings, it was decided to continue close observation in the clinic. Despite repeated aspirations of these swellings, they recurred soon after aspirations.

A follow-up computer tomography of the right hip with contrast was performed in May 2008 (Figure 2). It showed the communication of the subcutaneous swellings with the hip joint. The patient remained asymptomatic and could walk unaided. There was no radiographic evidence of loosening or infection. The blood inflammatory markers were still normal. We decided to aspirate the collections (Figure 3) and to use fluconazole as an anti-fungal agent with the retention of right hip prosthesis. This was based on a sensitivity test on the fungal culture result from the aspirates. A 4-week course of oral fluconazole at 400 mg daily was prescribed after a discussion with the microbiologist.

The patient, however, started to have pain over the right hip during walking. CRP and ESR levels were mildly elevated, up to 49.9 mg/L and 52 mm/hr, respectively. Computer tomography of the right hip showed an extension of the collection to the posterior proximal thigh. There was also osteolysis around the acetabulum. An acetabulum protrusio was also noted (Figure 4).

We offered to remove the prosthesis and to debride the right hip surrounding tissues. However, the patient was reluctant for surgical treatment. Oral fluconazole 400 mg daily was resumed in April 2009.

In October 2009, the patient developed fever with marked elevated CRP up to 102.8 mg/L. The patient could barely walk and he agreed for removal of the right hip prosthesis and surgical debridement. Fluconazole was continued after the operation. It was stopped in February 2010, as the patient suffered from the side effects of nausea and vomiting.

CRP and ESR levels returned to normal after the removal of prosthesis and debridement. The patient could walk with a frame without pain for more than 20 minutes. A raised shoe on the right side was used. No clinical evidence of recurrence of fungal infection was noted more than 2 years after the removal of prosthesis (Figure 5).

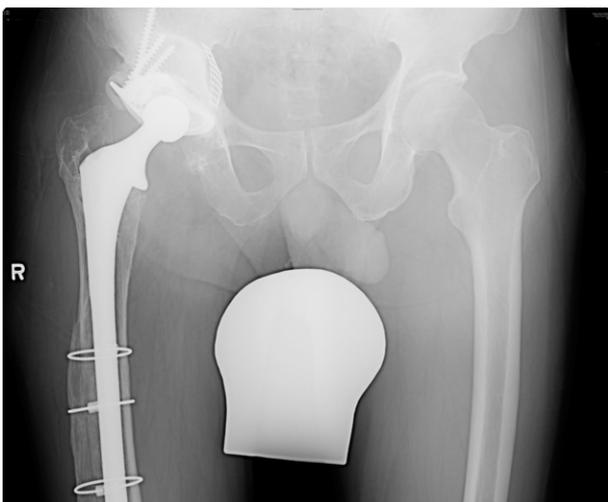


Figure 1. Radiograph showing the post revised right total hip arthroplasty in 2005.

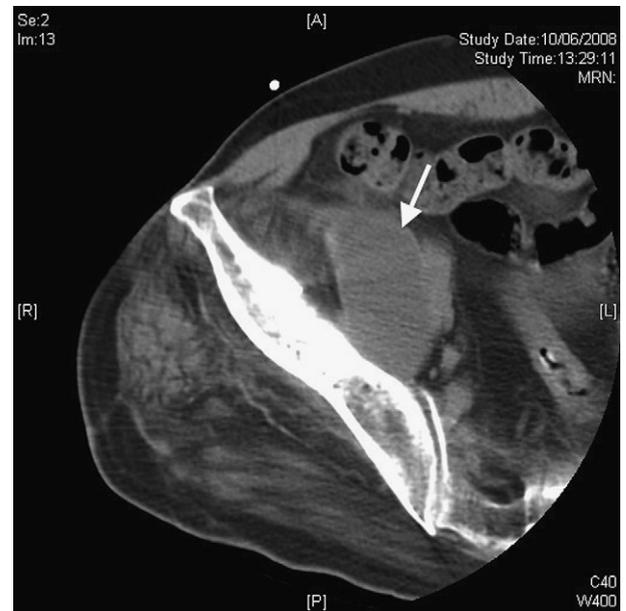


Figure 2. Computer tomography showing the iliacus muscle with a *Candida parapsilosis* collection in June 2008.

Discussion

(A) Pathogenesis: Fungal prosthetic joint infection is rare. The majority of these infections were caused by *Candida* species.

There are three possible modes of infection described: (1) haematogenous route; (2) direct inoculation during implantation or arthrocentesis;¹ (3) extension of infection from infected adjacent bones into the synovial space.¹ It was postulated that direct inoculation was the most likely cause of infection in prosthetic joint fungal infection while haematogenous spread was more likely in natural joint fungal infection.

There are a number of risk factors for fungal prosthetic joint infection: (1) previous antibiotics or antifungal treatment;

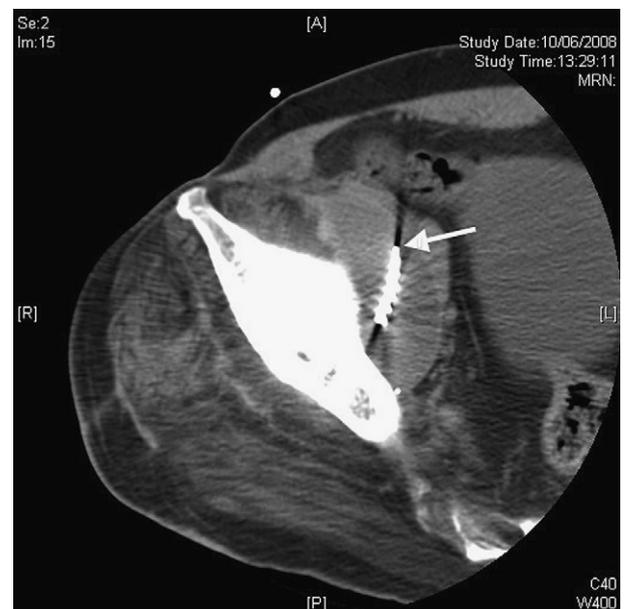


Figure 3. Computer tomography guided aspiration of the iliacus collection in June 2008 (white arrow).

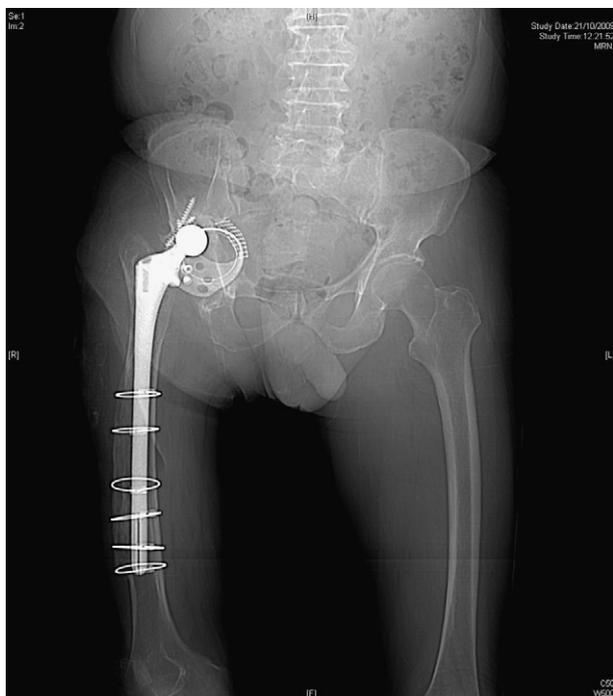


Figure 4. Radiograph showing the acetabulum osteolysis and protrusion of the acetabulum cup in October 2009.

(2) history of surgical revision of implants, (3) age > 65 years, (4) immunodeficiency, (5) diabetes.¹

It was also mentioned that preceding bacterial infection of the prosthesis was also a risk factor for subsequent fungal infection.¹ Some of these risks factors were observed in our case, such as multiple revision surgeries, old age and history of diabetes.

(B) Clinical features: In the published literatures, the clinical presentation of prosthetic fungal infection was often indolent.^{1–3} The interval from the index surgery to the diagnosis could be as long as 12 years with an average of 25 months.² The long history (15 years) of our reported case could confirm this point. Chronic pain and swelling were the most common complaints.^{1–3} The presence of fever or fistula was relatively uncommon in fungal prosthetic infections compared with bacterial ones.^{3,4}

(C) Diagnosis: In contrary to bacterial prosthetic infections, routine biological markers such as white cell count, ESR and CRP are not necessarily elevated in fungal prosthetic infections.^{2,3} Another hindrance in making the diagnosis is the misinterpretation of positive cultures as contaminants.^{4,5} We had the same problem in our patient as well. This could lead to a delay in making a correct diagnosis. It was suggested that when one suspected a prosthetic infection, positive fungus culture should be considered as a pathogen.³ By contrast, some authors suggested repeating fluid cultures and obtaining multiple positive tissue cultures before making a diagnosis of fungal peri-prosthetic joint infection.⁵ It was also reported that radiological findings in the cases of fungal prosthetic infections looked very much similar to bacterial ones.³

(D) Treatment: Despite the limited number of cases, the mainstay of treatment reported in the literature was resection arthroplasty, with or without delayed reimplantation.^{2,3,5} This was also the recommendation from the Infectious Diseases Society of America.⁶ The decision for reimplantation should be based

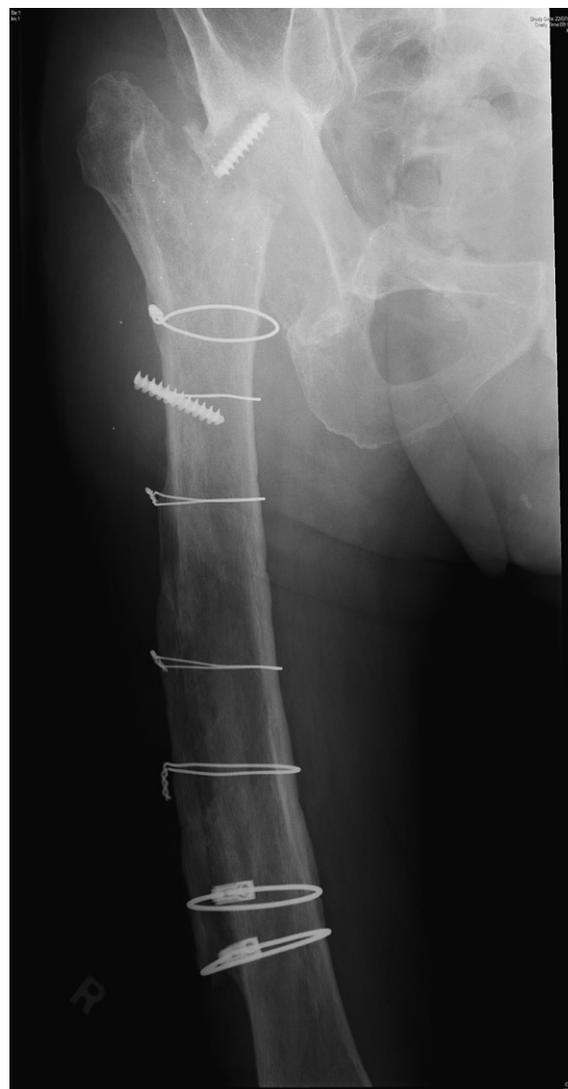


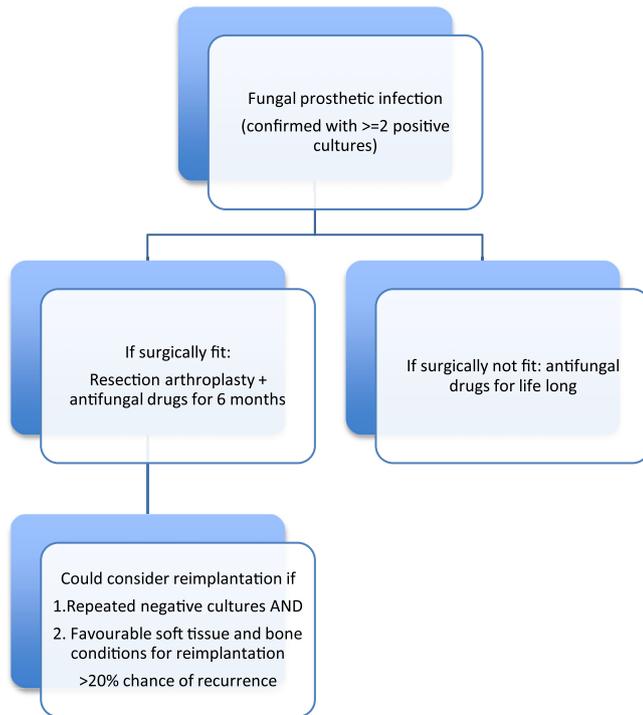
Figure 5. Radiograph showing the right hip after the excisional arthroplasty in July 2011.

on negative cultures and a favourable clinical condition after a long follow-up period. This should be performed in two stages. A recurrence rate of 20% after two stage reimplantation for fungal prosthetic joints infection was reported.⁷ There was only one report showing success in one stage exchange arthroplasty for fungal prosthetic infection.⁸

There were 5 cases of successful treatment of fungal prosthetic infections with antifungals without surgery. However four out of the five cases had a follow-up < 2 years.^{1,9} *In vitro* experiments also showed the failure of fluconazole to eradicate fungal species from an established biofilm or to prevent biofilm formation.¹⁰ In particular, *Candida albicans* produces larger and more complex biofilms than other *Candida* species do. This provides resistance to antifungal agents. Therefore, this conservative approach should be limited to debilitated patients with unacceptable high surgical risk or patients who refuse surgery.

Patients should also be given antifungal drugs such as fluconazole and amphotericin B during the perioperative and post-operative periods.⁶ The use of the antifungal agent should be based on susceptibility testing. The length and dosage of antifungal

Algorithm for treatment of fungal prosthetic infection



drugs were much varied among the cases published in the literature. A minimum of 6 months of anti-fungal drugs for most cases of fungal prosthetic infections was recommended.^{3,6}

There were several reports successfully using spacers and cements impregnated with antifungal drugs. There were few reports using debridement alone to treat fungal prosthetic infection.¹⁰ The formation of biofilm, the chronic nature of the infection and the compromised immunity of hosts were recognized causes of failure of debridement alone. Debridement and retention of components should be applied only to those patients with good soft tissue and acute infections.

It is, however, important to keep in mind that these patients should be monitored regularly for life. These infections have a notoriously indolent pattern of development and recurrence.

Conclusion

Candida total joint replacement infections remain very rare, despite the rising incidence of prosthetic joint infections. Despite

the indolent presentation of these infections, they would lead to detrimental consequences and significant impaired mobility if they were not treated promptly.

Our case demonstrated a failure in early recognition and treatment of the infection. It also illustrated an unsuccessful attempt to treat the infection with antifungal drug alone without the removal of prosthesis. There was progression of Candida infection in the years following the initial positive culture. This required the removal of implants eventually to eradicate the infection. It also showed the common misinterpretation of a positive fungal culture as a contamination.

We propose a treatment algorithm for cases of fungal prosthetic infections. Cases with two or more positive fungal cultures should be regarded as confirmed cases. Prosthesis removal and debridement should be performed if the patient is medically fit. Treating infections with antifungal agents should be reserved in patients who are medically unfit or reluctant for surgery. Reimplantation should be considered only if negative fungal cultures are obtained repeatedly with good soft tissue and bone stock.

There are two aspects in the treatment of fungal prosthetic infections which remain unanswered. One is the optimal duration and the choice of antifungal agents. The other is the timing of reimplantation. Further studies in these two aspects are necessary.

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