Case report

Diagnosis and treatment for primary *Candida parapsilosis* infection of the native knee joint: A case report

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**Abstract**

Introduction and importance: Candida arthritis is a very rare disease and *Candida parapsilosis* infection of the native knee joint is extremely rare. It is challenging to diagnose and treat because the clinical manifestations, laboratory and radiologic findings are not specific and not well defined. We report the rare case of *C. parapsilosis* infection of the native knee joint.

Case presentation: A 67-year-old man visit outpatient clinic for persistent right knee pain and effusion. Inflammatory markers were elevated and the biochemical studies of joint fluid showed elevated WBC counts. Under assumption of septic arthritis, arthroscopic irrigation and debridement were performed. *C. parapsilosis* was isolated on intraoperative knee joint culture. Fluconazole was used under diagnosis of Candida arthritis. Once there were no relapse of infection, total knee arthroplasty was implemented.

Clinical discussion: As Candida arthritis can be lead to poor prognosis, Candida arthritis should be considered in patients with untreated knee infections. Blood and radiographic examination, and fungus culture from the knee joint should be accompanied for early diagnosis. Total knee arthroplasty may be considered after treatment of Candida infection with fluconazole. Prognosis was similar compared with patients who underwent total knee arthroplasty for primary knee osteoarthritis.

Conclusion: If patients complaint persistent knee pain with or without effusion, surgeons should consider the possibility of Candida infection. After diagnosis of Candida arthritis, proper antifungal agents should be used for treatment of infection. After the infection has cleared up, total knee arthroplasty can be planned.

**Keywords:** Knee joint, Septic arthritis, Candida arthritis, Fluconazole, Total knee arthroplasty

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1. Introduction

Candida arthritis is a very rare disease and Candida infection of the native knee joint is extremely rare. And, most of the cases were associated with immunosuppressive conditions such as cancer, HIV, chronic steroid use, cancer, and recreational drugs [1,2]. It is challenging to diagnose and treat because the clinical manifestations, laboratory and radiologic findings are not specific and not well defined [3]. There are several studies about Candida infection after total knee arthroplasty [3], but studies of the native knee joint infections are rarely reported. We report on a case that showed good clinical results by performing total knee arthroplasty after treatment with an antifungal agent for *C. parapsilosis* of the native knee joint. The work has been reported in line with the SCARE criteria [4].

2. Case presentation

A 67-year-old man who had medical history of hypertension visited our outpatient clinic for right knee pain for over 2 months without any injury. He had no history of autoimmune disease, HIV, cancer, chronic steroid use, recreational drug use, smoking and drinking. In the initial X-ray, the patient showed early osteoarthritic change of the knee joint (Fig. 1A). The patient took medication under diagnosis for degenerative osteoarthritis of right knee. A year after first outpatient visit, he visited our hospital for acute right knee pain with knee joint effusion and erythema. He had no other symptoms of systemic infection or fever prior to the hospital visit. From the date of the first outpatient visit, the patient had no history of intra-articular injection or other procedure. Compared with the X-ray taken 1 year ago, osteoarthritic change was advanced (Fig. 1B). Blood tests and joint fluid analysis were performed to differentiate the knee joint infection. Blood tests showed elevated ESR (23 mm/h, reference range < 20 mm/h), CRP (2.85 mg/dl, reference range < 0.5 mg/dl).

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<0.0–0.5 mg/dl). About 70 cc of right knee joint aspiration was done and joint fluid was yellowish and turbid. The biochemical studies of joint fluid were as follows: WBC 247200 (neutrophil 90% mononuclear cell 10%). The gram stain, AFB stain and fungus culture of the joint fluid showed negative results. Knee joint infection could be diagnosed by considering blood test and the biochemical studies of joint fluid. Under the assumption of knee joint infection, arthroscopic irrigation and synovectomy were performed by knee surgeon with over 10 years of experience. *C. parapsilosis* was isolated on intraoperative knee joint culture (Fig. 1C). Intravenous fluconazole 400 mg was injected daily for 4 weeks and then usage of oral fluconazole 400 mg was planned for 6 months. After arthroscopy, joint aspiration was performed once a month for 4 months. In fungus culture of right knee joint, *C. parapsilosis* was cultured in the first 2 months but in the next 2 months, *C. parapsilosis* was no longer cultured. 6 months after arthroscopy, the patient visited outpatient clinic with persistent right knee pain. MRI study showed synovial enhancement with bone destruction of right proximal tibia that could suggest osteomyelitis (Fig. 1D). On suspicion of osteomyelitis, oral fluconazole was taken for additional 6 months. A year after discontinuation of fluconazole, the patient continued to complain of right knee pain, but there were no signs of infection considering the blood test including inflammatory marker such as ESR, CRP and negative results of fungus culture of the knee joint. Compared with the previous X-ray, osteoarthritic change was significantly advanced so total knee arthroplasty was planned (Fig. 1E). Total knee arthroplasty progressed similarly to patients who underwent total knee arthroplasty for primary osteoarthritis and intraoperative fungus culture came out negative. 43 months after total knee arthroplasty the patient had no evidence of infection and Oxford knee score was 42, which showed good clinical outcome [5]. Prognosis was similar compared with patients who underwent total knee arthroplasty for primary knee osteoarthritis (Fig. 1F).

3. Discussion

Candidiasis is uncommon in immunocompetent patients. Previously, many lines of evidence have indicated that most patients with fungal infection are immunosuppressed with predisposing factors. For example, candidiasis is associated with autoimmune disease, HIV, chronic steroid use, cancer cachexia, and recreational drugs [1,2]. Healthy hosts can also develop fungal musculoskeletal infections from

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![Fig. 1.](image-url)

A Initial X-ray of right knee showed early osteoarthritic change.
B X-ray of the right knee on a year follow up showed progression of degenerative osteoarthritis without bone destruction.
C Under arthroscopy, inflammatory synovium was observed.
D MRI T2-weighted image 6 months after arthroscopy demonstrated progressed osteoarthritic change and bone destruction of right proximal tibia that could suggest osteomyelitis.
E X-ray after 22 months after arthroscopy showed progressed osteoarthritic change and bone destruction.
F X-ray of right knee joint 43 months after total knee arthroplasty.
were bone destruction and joint effusion, followed by extension into soft tissues. Arthroscopy is warranted for the definitive diagnosis [13,14]. Markers are not specific for Candida arthritis, arthrocentesis or fungal antigen. As the clinical manifestations and inflammatory markers continued to be normal, and the culture result was negative, therefore a total knee arthroplasty was implemented.

4. Conclusion

We report the case of Candida arthritis developing in native knee joint without predisposing factors. If patients complain persistent knee pain with or without effusion, surgeons also should consider the possibility of Candida infection in the differential diagnosis. In addition to detailed blood examination and radiographic examination, it is worth to consider fungus culture under assumption of Candida infection. After the diagnosis of Candida arthritis, proper antifungal agents should be used for treatment of infection. Arthroscopic irrigation and debridement are helpful in the treatment of infection. After there is no relapse of infection, total knee arthroplasty can be implemented and good clinical results can be expected. Although clinically good result was obtained in this case, it is considered that further studies are needed due to the limitations of the short follow-up period and insufficient cases.

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None.

Ethical approval

This is a case report study, no ethical approval was needed. On the other hand, the patient had been informed and gave their consent regarding this publication.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Registration of research studies

This manuscript is not a human study, but a case report.

Guarantor

Jae Hwi Han

CRediT authorship contribution statement

JH Han performed the operation and periooperative management of procedure.

impairments, type of joint, and adequacy of debridement. The patient in this case complained of continuous effusion and bone destruction was progressing on MRI and X-ray findings taken 6 months after administration. Accordingly, fluconazole was used for 12 months under the diagnosis of Candida osteomyelitis.

Adequate and/or repeated drainage is often critical to successful therapy. Involvement of a prosthetic joint with Candida arthritis requires resection arthroplasty [18]. Some authors strongly recommend surgical drainage in all cases of Candida septic arthritis [8]. The rationale for medical therapy alone versus combined medical and surgical intervention in individual cases was not apparent in most reports. There are few reports that good results were obtained only with medical treatment [15]. Therefore, more research will be required on which patients can be administered medical therapy without surgical treatment.

A new prosthesis may be inserted after successful clearance of the local infection as defined by lack of return of symptoms after cessation of therapy [19]. In our clinical experience, there was no recurrence or specific symptoms for 1 year after discontinuation of fluconazole and the inflammatory marker continued to be normal, and the culture result was negative, therefore a total knee arthroplasty was implemented.

C. parapsilosis is an opportunistic human pathogenic fungal species and also an uncommon cause of septic arthritis [3]. The most common fungal group causing osteoarticular infection, the Candida, comprises at least 15 distinct species, of which C. albicans is by far the most common. As immunosuppression and antifungal exposure increase, the incidence of infections caused by non-albicans Candida species increases [9]. In recent years, there has been an increasing number of C. parapsilosis infections reported, with their pathogenesis associated with many factors, including adhesion, biofilm formation, and hydrolytic enzymes [10,11]. However, reports of primary C. parapsilosis infection in native knee joints are very rare [12].

Septic arthritis or tuberculosis was initially suspected, and Candida was not considered as a cause because it is rarely reported in an immunocompetent patient; however, postoperative infectious arthritis caused by bacteria or tuberculosis is not rare in an immunocompetent patient [2]. The data suggested that local pain and swelling were the most common clinical manifestations of C. parapsilosis infection, while fever and erythema occurred infrequently. Since the symptoms are always mild and unspecific, the diagnosis can often be delayed.

Owing to their rarity and generally subacute presentation, the most important aspect of the diagnosis of these infections is their inclusion in the differential diagnosis, particularly in immunocompetent patients. We initially suspected septic arthritis, and arthroscopic irrigation and debridement were planned and implemented. Fortunately, we were routinely performing intraoperative fungus culture, and the results of intraoperative culture showed C. parapsilosis and we were able to start antifungal agent. As the clinical manifestations and inflammatory markers are not specific for Candida arthritis, arthrocentesis or arthroscopy is warranted for the definitive diagnosis [13,14].

The most common radiological abnormalities in Candida arthritis were bone destruction and joint effusion, followed by extension into soft tissues, decrease of articular space, osteoarthritis and periosteal reaction, and/or synovitis [15]. However, these findings are not exclusive to Candida arthritis.

Recent literature favors the use of fluconazole or an echinocandin over Amphotericin B [16]. Peter et al. strongly recommended Fluconazole, 400 mg (6 mg/kg) daily, for 6–12 months or an echinocandin (caspofungin 50–70 mg daily, micafungin 100 mg daily, or anidulafungin 100 mg daily) for at least 2 weeks followed by fluconazole, 400 mg (6 mg/kg) daily, for 6–12 months. In the case of Candida septic arthritis, they recommend using fluconazole alone or echinocandin for 2 weeks followed by fluconazole for 4 weeks [8]. Recently, fluconazole is supposed to be superior to echinocandin for the treatment of C. parapsilosis arthritis on the basis of the decreased in vitro activity of echinocandin against C. parapsilosis and reports of echinocandin resistance among selected isolates [17]. The optimal duration of antifungal therapy remains to be defined with individual considerations of immune
the patient. J.H. Han also acquired and collected the data and drafted the manuscript. J.H. Yoo participated in the operation, perioperative management of the patient. S Choi revision of the manuscript.

Declaration of competing interest

None.

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