

## Pediatric Pyogenic Knee Arthritis Difficult to Treat Due to Drug Allergy

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#### Abstract

**Background:** In pediatric pyogenic knee arthritis, surgical drainage and antibiotic therapy are required early after diagnosis. The antibiotic is initially selected on an empirical basis to cover the most common pathogens responsible for pediatric pyogenic knee arthritis. However, pyogenic knee arthritis is difficult to treat if the patient has drug allergy to antibiotics. In addition, it is necessary to consider whether acute pyogenic arthritis and osteomyelitis in the knee are combined.

**Case presentation:** A 9-year-old boy was injured by contaminated tweezers stabbed in his left knee. He was referred to our hospital for treatment of pyogenic knee arthritis. Bacterial culture of the aspirated synovial fluid was negative. He was allergic to cefazolin and meropenem. Also, he had acute pyogenic knee arthritis and osteomyelitis in the femoral condyle. Clindamycin and hyperbaric oxygen therapy were used in consideration of the possibility of anaerobic bacteria and therapeutic efficacy was confirmed.

**Conclusion:** Knowledge of the epidemiology reported for different age groups is important to help select an appropriate empirical treatment. The duration of antibiotic treatment should be based on clinical judgment, objective diagnostic data, and MRI findings.

Keywords: Pediatric Pyogenic Arthritis; Knee; Antibiotic Therapy; Magnetic Resonance Imaging

#### Abbreviations

WBC: CRP: CEZ: Cefazolin; MSSA: Methicillin-Sensitive Strain S. Aureus; MEPM: Meropenem; LZD: Linezolid; HBO: Hyperbaric Oxygen Therapy; MRSA: Methicillin-Resistant Strains Of S. Aureus; CLDM: Clindamycin; MRI: Magnetic Resonance Imaging; VCM: Vancomycin; BML: Bone Marrow Lesions

#### Introduction

Pediatric pyogenic arthritis is a serious disease that can lead to joint destruction and deformity due to delayed diagnosis and insufficient treatment, resulting in serious sequelae. It is important to administer appropriate antimicrobials and surgical drainage as early as possible to prevent sequelae. Initial therapeutic antimicrobial agents are empirically selected based on the results of Gram staining, the assumed age-dependent proinflammatory bacteria, and the drug susceptibility of the assumed proinflammatory bacteria [1-4]. However, pediatric pyogenic knee arthritis is difficult to treat if the patient has drug allergy to antibiotics. We report a pediatric case of pyogenic knee arthritis that was difficult to treat due to drug allergy at our hospital.

#### **Case presentation**

A 9-year-old boy had left knee pain and gait disturbance. He was injured by contaminated tweezers stabbed in his left knee at home. He underwent wound treatment and antibiotic treatment (Cefdinir). On the next day, he developed high fever, swelling, and pain in the left knee joint, and was referred to our hospital. His past history and family history were unremarkable. On the initial examination, swelling, effusion, redness, and localized heat of the left knee joint were noted. The range of motion was between 30° and 120°, and there were no signs of damage to the menisci or ligaments.

Laboratory tests revealed an Hb level of 13.1 g/dl, WBC of 7400, and CRP of 2.5 mg/dl. The aspirated synovial fluid was yellowish and slightly turbid. Bacterial culture was negative.

#### X-ray demonstrated no osteolysis or periosteal reaction of the right knee

Arthroscopic examination was conducted under general anesthesia (Figure1). The menisci and articular cartilage were intact, but synovial hypercellularity was noted (Figure 2). These findings were highly suggestive of purulent knee arthritis. The patient received intravenous cefazolin (CEZ) from the first day of hospitalization. However, a generalized skin eruption appeared on the second day. Administration of CEZ was discontinued. Although side effects due to having a similar structure to cefazolin were unable to be excluded, we consulted with his family and changed to meropenem (MEPM). However, the generalized skin eruption worsened after administration of MEPM and the drug was discontinued. Change to linezolid (LZD) and hyperbaric oxygen therapy (HBO) were initiated considering methicillin-resistant strains of S. aureus (MRSA) involvement, and clindamycin (CLDM) was added to cover anaerobes. As it was less likely that MRSA was the cause, we changed to CLDM alone. The patient gradually recovered from fever and his CRP normalized, the administration method of clindamycin was changed from intravenous to oral, and the patient was discharged. Upon discharge, he had mild swelling in his left knee, but had no feeling of heat or pain, and the range of motion was normal. Two weeks after discharge, there was slight pain in the left knee at night, and when he moved often, he felt a heavy sensation in the left knee. The physical findings of the left knee were mild localized heat, but no swelling or tenderness. His CRP was mildly increased to 0.24 mg/dl. Magnetic resonance imaging (MRI) revealed a high-intensity region in the medial femoral condyle with T2-weighting (Figure3A). We diagnosed acute osteomyelitis in the femoral condyle accompanying purulent knee arthritis. Oral administration of clindamycin and HBO were resumed, and CRP normalized 13 days after the treatment. On MRI, the high-intensity area was reduced compared with the previous examination (Figure3B), and the symptoms and findings of the left knee disappeared. One month later, he was able to resume daily activities.

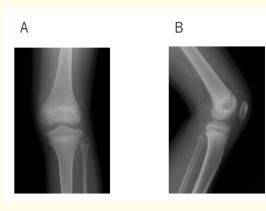


Figure 1



Figure 2

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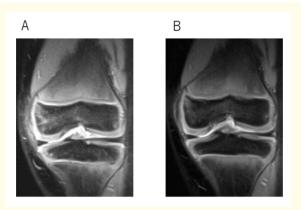


Figure 3

#### Discussion

The yearly incidence of septic arthritis varies from 2 to 10 per 100,000 patients in the general population [5]. In adults, the knee is the most affected site. On the other hand, the incidence of acute septic arthritis and osteomyelitis is approximately 8 per 100,000 children per year. In recent years, an increase in their incidence has been observed [6-8]. Hips, knees, and ankles are the most frequently involved joints [9-11]. Inflammatory diseases may be associated with sepsis and sequelae, such as joint destruction, growth failure, and death, if they are not sufficiently treated. In this case, we initially diagnosed pyogenic knee arthritis after penetration of the infectious agent, as in adults. However, he had acute pyogenic knee arthritis and osteomyelitis in the femoral condyle. Castellazzi reported that acute pyogenic knee arthritis and osteomyelitis can develop alone or in combination in pediatric patients. These diseases need to be carefully assessed, diagnosed, and treated to avoid serious sequelae [1]. We should have performed MRI initially as he had acute pyogenic arthritis and osteomyelitis in the knee. In general, surgical drainage and antibiotic therapy are required early after diagnosis for pediatric pyogenic knee arthritis and osteomyelitis. However, there is no consensus regarding the best antibiotic therapy to be administered, the mode of administration, or the duration of therapy. The antibiotic is initially selected on an empirical basis to cover the most common pathogens responsible for these conditions based on the age of the child, and then on the basis of the antibiograms obtained from cultures performed before starting antimicrobial therapy [2,3]. However, the bacterial culture test can be negative in some cases. Therefore, it is important to know the epidemiology reported for different age groups to help select an appropriate empirical treatment. Afghani reported that in children older than three months, to cover methicillin-sensitive strain S. aureus (MSSA), S. pyogenes, and K. kingae, ant staphylococcal penicillin, such as nafcillin or oxacillin, or a first-generation cephalosporin, such as cefazolin, should be used [12]. In this case, the bacterial culture test was negative. Therefore, we chose CEZ, considering MSSA to be the most common bacterium causing pediatric pyogenic arthritis. However, the patient was allergic to CEZ and its administration was discontinued, although it was not sufficiently effective. As the antibiograms may have been gram-negative bacteria, administration of MEPM was started. However, the generalized skin eruption worsened, and the drug was discontinued. If MEPM had been available, there may have been no treatment difficulties. According to the Sanford Guide to the Treatment of Infectious Diseases in the United States, VCM and cefotaxime (or ceftriaxone) are the first-line agents for pyogenic arthritis in children 3 months to 14 years of age, reflecting the high frequency of community-acquired MRSA in the United States [4]. Peltola reported that if MRSA infection is highly suspected, the first choice may be clindamycin (CLDM), an antibiotic belonging to the class of lincosamides, the effectiveness of which has been demonstrated. If the percentage of local resistance to CLDM is greater than 10%, the first-choice drug is vancomycin (VCM) [13]. As the MRSA detection rate at our hospital is 10 - 15% or higher, and the source of infection was a puncture wound, we considered the antibiogram to possibly be MRSA, and used LZD, which has better bone and joint tissue transitivity than VCM. As the clinical symptoms were not sufficiently improved by LZD, CLDM was used in consideration of the possibility of anaerobic bacteria and therapeutic efficacy was confirmed.

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There is no consensus regarding the duration of antibiotics or when to change to oral treatment. Castellazzi reported that a short course of intravenous antibiotic treatment, followed by oral antimicrobial therapy for two to three weeks for septic arthritis and three weeks for osteomyelitis may be safe and effective in cases of uncomplicated osteoarticular infection [1]. In other cases, intravenous therapy should be prolonged for at least three weeks for septic arthritis and four to six weeks for osteomyelitis. However, the duration of antibiotic treatment should always be based on clinical judgment, objective diagnostic data, and oral bioavailability of the different antibiotics. It is necessary to consider the combination of osteomyelitis in children with purulent knee arthritis. MRI should be performed considering the combination of acute pyogenic arthritis and osteomyelitis in the knee. We think that the duration of antibiotic treatment should always be based on clinical judgmostic data, and MRI findings.

#### Conclusion

For pediatric pyogenic knee arthritis, the administration of clindamycin should be prioritized even if the patient is allergic to cephem. It is necessary to consider the combination of osteomyelitis in pediatric purulent knee arthritis. If appropriate antibiotic treatment is not administered for acute pyogenic arthritis and osteomyelitis in the knee, it may lead to sequelae.

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