

Bilateral septic arthritis of the knee in a seven-year old sickle cell disease patient: a case report

Shobowale E.O^{1*}, Akinmokun I²

¹Department of Medical Microbiology, Babcock University Teaching Hospital, Ogun State. ²Department of Surgery, Lagos University Teaching Hospital, Lagos State.

Corresponding author: shoekineh@gmail.com

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ABSTRACT

Background: Septic arthritis is an inflammatory process in the joints associated with isolation of pathogens or a positive Gram stain of the synovial fluid. It is a disease condition with significant complications such as joint destruction and immobility. Individual cases are difficult to manage and frequently necessitate prolonged courses of antibiotics. **Aim:** The aim of the study was to present our findings with the view towards improving treatment outcomes in similar clinical scenarios. **Findings:** Septic arthritis in the index patient developed insidiously and was diagnosed after multiple arthrocentesis were performed. It was bilateral and associated with recurrent bouts of fever, joint tenderness reduced mobility and swelling. The predisposing factor in the index patient, a seven year old male was sickle cell disease. Multiple antimicrobial regimens were instituted in the patient with unsatisfactory results. Initial treatment regimens did not appear to be based on bacteriological statistics which resulted in prolonged hospital stay. Culture of the synovial fluid was initially onto brain heart infusion both and subsequently sub-cultured onto chocolate and MacConkey agar. The isolate recovered was *Serratia rubideae* which was identified using the Microbact 12A kit. Susceptibility studies showed the isolate to be susceptible to only meropenem. The patient was subsequently placed on meropenem for forty two days and recovered with radiologic and clinical evidence of improvement and thereafter discharged home. **Conclusion:** Close collaboration between the orthopedic surgeon and microbiologist will help to improve treatment outcomes. The Microbact12A kit is recommended in the routine identification of gram negative pathogens.

Key words: Septic arthritis, sickle cell disease, meropenem, microbact, arthrocentesis, *Serratia rubideae*

INTRODUCTION

Septic arthritis, also known as infectious arthritis represents a direct invasion of joint space by various pathogens most commonly caused by a

variety of bacteria. However, viruses, mycobacteria, and fungi have been implicated.^[1] Septic arthritis is due to inflammation in the joint that is of an infectious etiology.^[2] With regards to the outcome of septic arthritis, early diagnosis and prompt



treatment are both essential in order to achieve good clinical results.

The most common bacterial isolates globally in native joints include gram-positive cocci, with *Staphylococcus aureus* found in 40% to 50% of reported cases.^[3] *Salmonella typhi* and *Klebsiella spp* are also implicated especially in sickle cell disease.^[3,4] Anaerobes such as *Bacteroides fragilis* have also been found in septic arthritis especially following bacteremia.^[3] Other pathogens include *Neisseria gonorrhoeae*, Streptococci, and Gram-negative cocci, each in about 10% to 20% of cases.^[4] Organisms less commonly isolated are mycobacteria and fungi. Gram-negative bacilli such as *Klebsiella spp* and *Enterobacter spp* are often present in neonates, the elderly, and patients with immune deficiency disorders.^[5] *Neisseria gonorrhoeae* is seen in sexually active young adults, usually with associated dermatitis and tenosynovitis.^[3,4,5] Mycobacterial infections should be suspected in patients from endemic areas, and fungal arthritis is seen in immunocompromised patients.^[3,4,5]

Haemophilus influenzae was a common cause of bacterial arthritis in young children, but the incidence has decreased almost 70% to 80% since the widespread use of *H. influenzae* type b conjugate vaccine.^[6] Organisms such as coagulase negative *Staphylococci* and *Propionibacterium spp* tend to contaminate surgical sites following repair of anterior cruciate ligaments.^[6,7]

The signs and symptoms of septic arthritis include joint pain, swelling and soreness with joint immobility; fever may also be present. Additional clinical features that are associated with arthritis are nausea, vomiting and diarrhea which represent a systemic upset.^[8]

Identified risk factors for septic arthritis are sickle cell disease, joint surgery, bacteremia, diabetes mellitus, malignancy, and rheumatoid arthritis. Others include sexually transmitted diseases such as gonorrhea, systemic lupus erythematosus, intravenous drug use, anemia, hemodialysis and the extremes of life.^[9]

Laboratory features that point towards joint infection include an elevated white cell count obtained from the synovial fluid with differentials for polymorphs, and crystal examination under a polarized microscope.^[10] A synovial fluid leukocyte count of greater than 50,000 with polymorphonuclear leukocyte predominance is usually seen in septic

arthritis.^[10] The gram stain is positive in about 11 to 80% of cases and as such can be a valuable tool in diagnosis. Synovial fluid culture is also positive in up to 90% of non-gonococcal septic arthritis.^[10]

As a result of the absence of a limiting membrane plate in synovial tissue, pathogens gain access via the haematogenous route into joint spaces in predisposed individuals. This also tends to follow bacteremia. Other routes include direct access following trauma or surgery particularly after prostheses have been implanted.

The optimal management of arthritis involves the use of agents that can penetrate sufficiently into bone tissue and these include antimicrobials such as third generation cephalosporins, vancomycin, ciprofloxacin and linezolid.^[11]

CASE REPORT

We present a seven-year old male patient who is a known sickle cell disease patient diagnosed since the age of one. The index patient presented with a month history of bilateral knee joint pain which were swollen and warm. There was no antecedent history of falls or trauma to the knees. In addition there were no known relieving factors for the pain, but it was aggravated by movement. There was also no prior history of surgery. Patient had been to a private health care facility and was on admission for twenty six days from where he was referred to LUTH on account of non-response to treatment.

While on admission, pain in the left leg resolved after ten days. There was also a history of fever which was low grade, persistent, and relieved by paracetamol though transiently. The paracetamol (450 mg) was administered as a slow infusion via a normal saline bag over six hours. While on admission, the patient was said to have had bronchopneumonia and congestive cardiac failure and was transfused with packed cells on four different occasions due to a concomitant low packed cell volume.

At the referral hospital he was placed on the following antibiotics in sequential order: Intravenous crystalline penicillin 1mU 12 hourly for 4 days, intravenous ciprofloxacin 200mg 12 hourly for two days, ampicillin-sulbactam and ceftazidime for 3 days intravenously. intravenous levofloxacin for three days, intravenous vancomycin for 8 days with anti-Koch's medication all with minimal improvement. The administration of anti-Koch's was a last gasp measure by the managing team due to

minimal response of the infection to several antimicrobials.

Laboratory investigations

No malaria parasite was seen on thick and thin films. Widal test for *Salmonella typhi* IgM was negative, while the PCV was 25% at admission.

Ultrasound scan of the right knee was indicative of soft tissue abscess collection in the right popliteal area indicative of osteomyelitis. X-ray of the right thigh showed a bone in bone appearance in the distal 3rd of the femur (osteomyelitis of distal 3rd of right femur). X-ray of the right leg area showed a collection in the proximal tibial metaphysis with an area of cortical discontinuity with slight angulations in the medial aspect of the proximal tibial metaphysis- green stick fracture of proximal 3rd of right tibia. The X-ray on the left knee joint revealed an area of translucency though of a much smaller size compared to the right knee joint which was much larger. Periarticular soft-tissue swelling of both right and left knee joints were seen on the X-rays.

A needle aspirate with repeating joint taps was frequently done to prevent significant re-accumulation of fluid. Aspirating the joint 2-3 times a day was performed. As a result of this open surgical drainage and large volume irrigation with normal saline, and immobilization was conducted.

Right hip joint aspirate was sent for microscopy culture and susceptibility, and a coliform was isolated and subsequently identified with Microbact12A kit as *Serratia rubideae* and was also sensitive to meropenem.

Medications on admission in LUTH sequentially were IV ceftriaxone 1g daily 12 hourly, meropenem 330mg 12hourly, IV amikacin 125mg 8 hourly, IV pentazocine 15mg for pain , oral ibuprofen 160mg 6 hourly (with foods alternating with paracetamol 160mg).

All intravenous antibiotics were discontinued when there was no symptom resolution and he was placed on intravenous vancomycin 10 mg/kg 12 hourly which was again discontinued based on the susceptibility results and accurate identification of the offending pathogen and re-introduction of meropenem which was administered for 42 days. There was steady improvement with consistent administration of meropenem and joint function was restored with resolution of tenderness and swelling. He was discharged home on cefepime and came

back to the clinic for follow up appointments symptom free.

DISCUSSION

This study documents the case of a seven-year old sickle cell disease patient who developed bone and joint pains (knee) of four weeks duration. The child at that point in time had a vaso-occlusive crisis necessitating blood transfusion at the referral hospital where he spent twenty six days. Due to non-improvement in the patient's condition he was referred to LUTH. Upon admission he was placed on the following drugs sequentially: IV ceftriaxone 1g 12hourly for 1 day, IV meropenem 330 mg 12 hourly and amikacin for 5 days, IV vancomycin 10 mg/kg 12 hourly for 8 days and finally IV meropenem 330 mg 12 hourly for 13 days (after *Serratia rubideae* was isolated and showed sensitivity to meropenem, bone pains subsided, minimal reduction in joint swelling).

Despite arthrocentesis, the clinical signs did not abate and this warranted prolonged therapy with meropenem for forty two days. The definitive diagnosis of joint fluid aspiration aided in isolating the offending pathogen, *Serratia marcescens*, via the use of the Microbact 12A kit. Treatment, irrigation and debridement of the joint still did not resolve the patient's clinical condition as the initial antimicrobial regimen was sub optimal; however this should be done till wound granulation is seen alongside appropriate antibiotics in order to achieve optimal results.

Septic arthritis still remains an important and serious disease of the young because of its high potential to cause permanent sequelae, therefore aggressive therapy with the appropriate antimicrobial is essential.^[12,13] It is a challenging clinical problem because signs and symptoms may be subtle and overlap with those found in other conditions, screening laboratory studies and synovial fluid cultures are relatively insensitive and optimal management, including duration of antibiotics and surgical approach is not always evidence based.^[14]

The treatment of septic arthritis involves urgent surgical drainage and lavage of the joint. This can be performed arthroscopically or via an open arthrotomy.^[1] In the paediatric setting, the knee and shoulder joints are often approached arthroscopically, whereas the hip and ankle joints are generally approached via an arthrotomy.^[1] In very young children, standard arthroscopic

instruments are too large and, therefore, arthrotomy is generally performed.^[1]

Acute septic arthritis may develop as a result of hematogenous seeding, direct introduction, or extension from a contiguous focus of infection. The pathogenesis of acute septic arthritis is multifactorial and depends on the interaction of the host immune response and the adherence factors of different pathogens, the toxins they elaborate and immunoavoidance strategies of the invading pathogen.^[15]

While diagnosis rests on isolation of the bacterial species from synovial fluid samples, patient history, clinical presentation, laboratory findings, and imaging studies are also important. Acute septic arthritis is a medical emergency that can lead to significant morbidity and mortality. Therefore, prompt recognition, rapid and aggressive antimicrobial therapy, and surgical treatment are critical to ensuring a good prognosis. Even with prompt diagnosis and treatment, high mortality and morbidity rates still occur.^[15]

Table 1: Susceptibility results performed with oxoid discs

CAZ	TZP	CRO	CEF	AMX	CIP	AMC	CN	MEM	CFX
R	R	R	R	R	R	R	R	S	S

Key: CAZ – Ceftazidime, TZP – Piperacillin Tazobactam, CEF – Cefuroxime, AMX – Amoxicillin, CIP – Ciprofloxacin, CN – Gentamicin, MEM – Meropenem, CFX – Cefixime
S = Susceptible, R = Resistant.

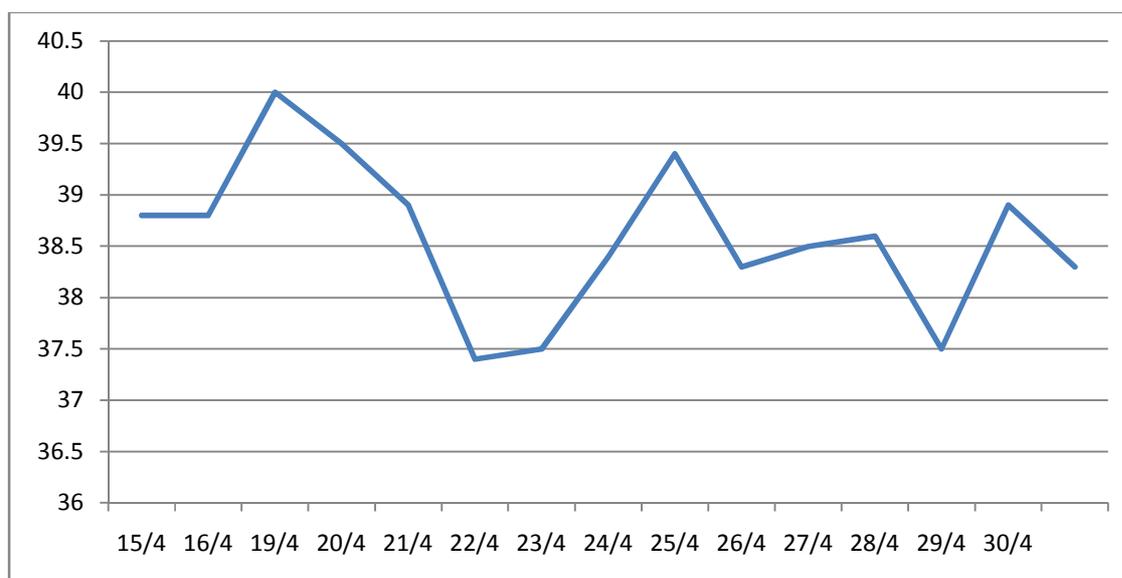


Figure 1: Temperature chart despite cocktail of antibiotics

CONCLUSION

In the index case, sickle cell disease was the risk factor for septic arthritis. Concerted efforts must be made to rapidly identify septic arthritis in this at risk group. In septic arthritis, early diagnosis and treatment is quite important. In this study, we presented a case with both knee joints involved in

septic arthritis. The patient, a seven year old male with underlying sickle cell disease had a protracted course with several antimicrobial regimens. Close collaboration between the orthopedic surgeon and microbiologist ultimately helped to improve the outcome. The Microbact12A kit is recommended as a valuable tool in the routine identification of gram negative pathogens.

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