Case report

Salmonella Sepsis and Osteomyelitis in Sickle Cell Disease

Abstract: We report a 19 months old boy with 3 days history of fever and left mid-arm pain and swelling. On examination his temperature was 39.5^0C, left mid-arm was swollen with tenderness, redness and hotness. Total white cell count was $15x10^9$/L with 75% neutrophils, erythrocyte sedimentation rate (ESR) was 109 mm/hour, and x-ray of the affected bone revealed periosteal elevations, irregular destructive lesions and sequestra formation. Cultures from the blood and from the bone biopsy revealed salmonella enteriditis group D. The patient was treated according to the results of the culture and sensitivity. Therefore, salmonella osteomyelitis should be considered as one of the differential diagnosis of soteomyelitis in children with sickle cell anemia. The choice, dosage, and duration of antibiotics therapy should be determined by causative organisms.
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Keywords: salmonella, osteomyelitis, sickle cell anemia, Saudi

Introduction

Bones and joints infections are one of the common sites for invasive bacterial infections in children leading to hospitalization and prolonged antibiotic administration. Patients with sickle cell anemia are more susceptible to osteomyelitis and septic arthritis than the population at large, especially osteomyelitis caused by Salmonella sp.

Most of the reported cases in Saudi Arabia are from the eastern province. In a previous study, the incidence of Salmonella infection in sickle cell disease (SCD) patients was 11.5% compared to only 0.65% in the general hospital population.[1]

The commonest sites of Salmonella infection were blood (42% of isolates), followed by gastrointestinal tract (23.5%) and the skeletal system (22.5%). Salmonella infection was commonly seen in patients less than 15 years of age[1]. Another study showed that the prevalence of osteomyelitis in children with SCD was 69 times higher than those with normal hemoglobin electrophoresis, and Salmonella organisms were significantly more frequently responsible for osteomyelitis in SCD.[2] In addition, there were similar reports from other countries which showed higher incidence of salmonella osteomyelitis in sickle cell diseased children.[3, 4]

The aim of this case report is to confirm that Salmonella sepsis and osteomyelitis is common in children with sickle cell anemia, and therefore, the empirical antibiotics should be considered to cover this type of organisms prior to the results of cultures and susceptibility to ensure better outcomes.

Keywords: salmonella, osteomyelitis, sickle cell anemia, Saudi.

Case report

A19 months old Saudi boy originally from the south of Saudi Arabia, presented with a 3 days history of fever and left upper extremity pain with inability to move his left arm. On examination his temperature was 39.5^0C, he was pale and ill looking. The left arm was tender with swelling extending from midarm down to the elbow, with redness and hotness at the site. Other systemic examination was unremarkable. Investigations showed a white blood cells (WBC) count of $15x10^6$/L, 75% neutrophils, heamoglobin was 7.7 g/dl (his baseline Hgb was 10 g/dl), and erythrocyte sedimentation rate (ESR) was 109 mm/hour. Hemoglobin electrophoresis results were as follows; Hgb A 4.6 %, Hgb F 10.3 %, Hgb S 82.2%, and Hgb A_2 2.9%. The patient was started empirically on ceftriaxone of 100 mg/kg/day divided every 12 hours and cloxacillin 150mg/kg/day divided every 6 hours as treatment of suspected osteomyelitis of the left humerous. Left forearm plain X- ray showed initially a soft tissue swelling. Repeated x-rays after 7 days from the start of the illness showed periosteal reaction, osteolysis, and formation of sequestra over the left humorous **(figure.1)**. MRI scan showed hyperintense signal in the marrow with periosteal collection in the left humerous suggesting osteomyelitis **(figure.2)**.

Open biopsy revealed skeletal, muscle, fibrous, and granulation tissues with heavy neutrophilic and variable mononuclear inflammatory cell infiltration. Microbiology revealed a blood culture growing Salmonella enteridis and this Gram-negative rod were cultured from the bone tissue, which were classified as Salmonella enteritidis group D1. The stool test did not reveal this pathogen. As the isolated pathogen was susceptible to ceftriaxone, the patient was continued on ceftriaxone and cloxacillin was discontinued.

Final diagnosis was Salmonella enteriditis group D1 sepsis and osteomyelitis of the left humerous. He completed 4 weeks of intravenous antibiotics as an inpatient. He was discharged on oral antibiotic which was completed for 2 weeks. The patient completed 6 weeks course of the above antibiotics with complete recovery of his disease. Three months later he was asymptomatic and ESR was 15 mm/hour.

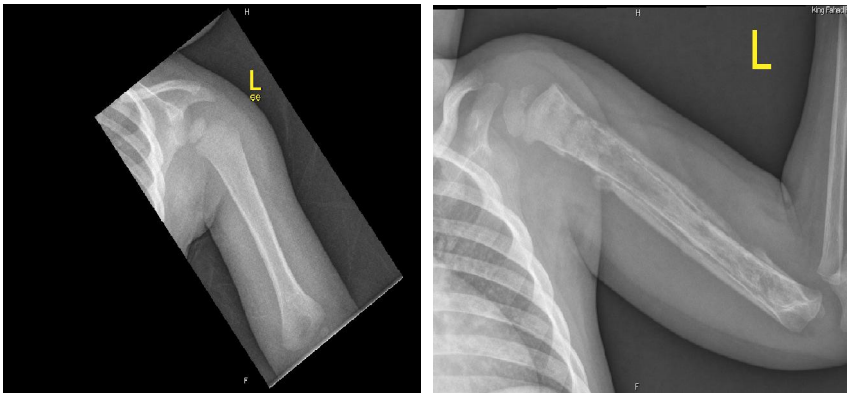

Figure 1- a)X-ray film of the left arm performed at the onset of illness revealed soft tissue swelling. **b)** X-Ray film performed 7 days after onset of illness shows bone within bone appearance.

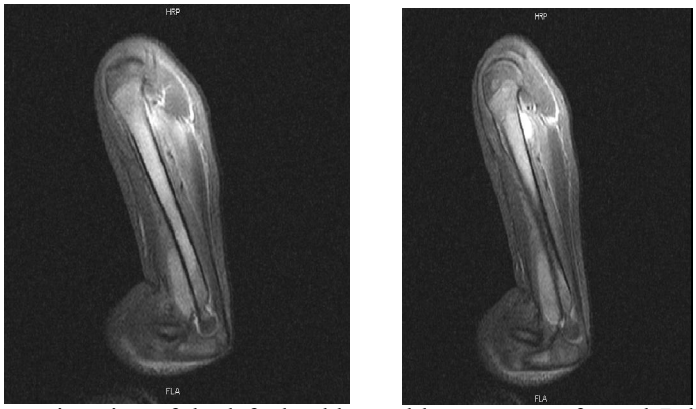

Figure 2- Magnetic resonance imaging of the left shoulder and humorous performed 7 days after onset of illness revealed hyperintense signal in the marrow with a small pocket pus elevating the periosteum and soft tissue swelling of the left humerous suggesting osteomyelitis.

Discussion

Bones and joints infections are serious complications of sickle cell disease and important causes of hospitalization. The most common cause of osteomyelitis among the general population is Staphylococcus aureus. However, it is well-known that in children with sickle cell disease who develop osteomyelitis**,** infection is often attributable to Salmonella**.** Al-Salem et al showed that salmonella was the commonest organism in osteomyelitis and septic arthritis in sickle cell patient, whereas Staphylococcus aeurus was commonest in normal patients and those with sickle cell trait.[5]

Three previous reports from the eastern province in Saudi Arabia showed that salmonella is the commonest organism and Staphylococcus aeurus is the second most common cause.[1, 2,6]

On the other hand, Staphylococcus aureus was found to be the most common causative organism in SCD patients with osteomyelitis and septic arthritis in two other reports from this province.[7, 8]

Various Salmonella species—in particular, nontypical serotypes such as S paratyphi B, S enteritidis, S typhimurium, and S choleraesuis— are the most common bacterial pathogens linked to bone and joint infection in sickle cell disease and are thought to be implicated in most cases of osteomyelitis.[9] Infection is commonly hematogenous in origin. Bacteremia due to Salmonella and other Gram-negative organisms is thought to result from sickling within mesenteric vessels and subsequent gastrointestinal infarction.[10] However, the direct spread of infection does occur, often from leg ulcers.

The most common sites for acute osteomyelitis are the growing ends of long bones, distal and proximal femur, distal humerous and distal radius.[11,12] These sites are the most common because of the sluggish circulation near the physis favoring deposition of bacteria and the lack of tissue-based macrophages.

The findings of x-ray, CAT scan and MRI of the bones are not specific for osteomyelitis, therefore, a definitive diagnosis of osteomyelitis in sickle cell disease still relies more upon clinical assessment together with positive cultures from blood or bone obtained by aspiration or biopsy, than upon any single imaging modality.

It is imperative to distinguish Salmonella osteomyelitis from bone infarctions. While clinical and hematologic data may be suggestive, radionuclide bone imaging studies, particularly combined technetium and gallium scintigraphy and technetium sulphur colloid bone marrow scans, and magnetic resonance imaging appear more sensitive and specific.[13-18]

Diagnosis of osteomyelitis in sickle cell disease can be one of the most common management dilemmas since failure to identify osteomyelitis may result in severe bone damage or life-threatening infection. In addition, an erroneous diagnosis subjects the patient to at least 6 weeks of unnecessary intravenous and oral antibiotics.

The treatment of invasive Salmonella disease such as osteomyelitis, abscess, meningitis or HIV with bacteremia should receive 4-6 weeks of therapy. Empiric antimicrobial therapy should include a broad-spectrum cephalosporin (cefotaxime or ceftriaxone). Once susceptibilities are available, narrow-spectrum therapy includes ampicillin, amoxicillin, cefotaxime, ceftriaxone, chloramphenicol, TMP-SMZ, or a fluoroquinolone.

Our patient was treated empirically with ceftriaxone and cloxacillin and after the results of culture and sensitivity the treatment was narrowed to ceftriaxone alone. The patient was seen in infectious clinic three months later, he was asymptomatic with normal vital signs and normal movement. The CBC, differentials and ESR were normal.

In conclusion, Salmonella organism is an important cause of osteomyelitis in children with sickle cell disease, therefore, empiric therapy should include coverage of this organism till the outcome of culture and sensitivity.

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