Case of Sepsis and Probable Septic Arthritis with \textit{Plesiomonas Shigelloides} in a Patient with Sickle Cell Anemia

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\begin{abstract}
We present a case of sepsis with probable septic arthritis due to \textit{Plesiomonas shigelloides} in a 10 year old female with hemoglobin SC disease. There have been three other cases reported in pediatric sickle cell disease (SCD) patients. Awareness among clinicians regarding this Gram negative organism is important as it can cause serious invasive infection in SCD patients, including sepsis and involvement of joints, lungs and intraabdominal organs. Clinical suspicion with early microbiologic diagnosis and timely use of appropriate antibiotics are key to the management of this infection and prevention of associated mortality.

\textbf{Keywords}: Sickle cell anemia; Sepsis; \textit{Plesiomonas shigelloides}; Septic arthritis; Gram negative
\end{abstract}

\textbf{Background}

Sickle cell disease (SCD) patients are at increased risk for Gram negative and unusual bacterial infections. \textit{Plesiomonas shigelloides} is a Gram negative, facultative anaerobic rod, member of the family Enterobacteriaceae that has been isolated from environmental sources and a wide range of animals including mammals, birds, fish, water-dwelling reptiles and amphibians [1]. This report is the first to document a case of probable Plesiomonas septic arthritis in a pediatric SCD patient.

\textbf{Case Report}

A 10-year-old African American female known to have hemoglobin SC disease presented to the emergency department (ED) at Texas Children’s Hospital in late September with one day of fever, vomiting and leg pain. She had eaten sushi five days earlier, but she had no other identifiable risk factors for infection. In the ED she was found to have tachycardia, tachypnea, hypotension (108/50 mm of Hg) and a temperature of 103.3\degree F. On physical examination, she demonstrated diffuse bilateral lower extremity pain; the remainder of the examination was normal. Laboratory evaluation included a mildly elevated white blood cell (WBC) count and low hemoglobin. Three sets of appropriate volume peripheral blood cultures (aerobic and anaerobic) were obtained. She received one dose of ceftriaxone in addition to fluid resuscitation (total 40 cc/kg of normal saline) and medications for pain control. Her chest radiograph was unremarkable. She was admitted to continue empiric therapy with cefotaxime for presumed sepsis.

Her fever initially resolved after the first dose of antibiotics, but her WBC count increased from 16,560 cells/UL on admission to 64,000 cells/UL and hemoglobin dropped from 11.6 gm/dl to 9.6 gm/dl on hospital day 2. The C-reactive protein (CRP) was elevated at 14.3 mg/dL and erythrocyte sedimentation rate (ESR) was 48 mm/hr. Admission blood cultures became positive within 48 hours for a non-lactose fermenting Gram-negative rod and her antimicrobial therapy was changed to ceftazidime to broaden coverage for possible pseudomonas infection. Subsequently, all six of the admission blood culture bottles obtained in the ED was positive for \textit{Plesiomonas shigelloides}. The organism was susceptible to amoxicillin clavulanic acid, ceftriaxone, cepfime, levofloxacin, meropenem, piperacillin tazobactum and trimethoprim sulfamethoxazole. All blood cultures obtained after the initiation of antibiotics remained sterile. Infectious Diseases was consulted due to the unusual organism isolated in the blood and recurrence of fever after 48 hours (Figure 1).

On repeat examination on hospital day 2, she was found to have pain, swelling, warmth and limited range of motion of the right shoulder. Plain radiograph showed mild thickening and irregularity of the medial cortex of the right mid and distal humerus. Magnetic resonance imaging with contrast of the right shoulder showed moderate sized effusion with synovial enhancement and osteonecrosis of the right humeral diaphysis (Figure 2). Hence on day 3 of hospitalization, she underwent a right shoulder arthrotomy with exploration and drainage, and a drain was left in place which gave moderate sero-sanguinous discharge. Fluid from her shoulder joint was obtained, however no cell count was performed and cultures were sterile. The fever resolved after the 8th day of intravenous ceftazidime.

Upon clinical improvement and removal of the right shoulder joint drain, she was discharged after 11 days of hospitalization with instructions to continue treatment with amoxicillin-clavulanic acid to complete a total of 6 weeks of antimicrobial therapy for probable septic arthritis of the shoulder and possible osteomyelitis of the proximal humerus. At follow up after 4 weeks of therapy, she had remained afebrile and had improved range of motion of the right shoulder. A plain radiograph of her right shoulder was normal and her inflammatory markers had also normalized (CRP: 0.6 mg/dL; ESR: 17 mm/hr).

\textbf{Discussion}

\textit{P shigelloides} belongs to the family Enterobacteriaceae [1]. These microbes are Gram-negative anaerobic rods that have been associated with diarrhea and dysentery [2]. The primary natural reservoirs for \textit{P shigelloides} are water and soil surfaces as well as fish and other marine animals, especially oysters. The organism is recovered from freshwater and estuaries in temperate and tropical regions and occasionally from seawater during the summer months [3].
Extra-intestinal *P. shigelloides* disease is less common than intestinal disease and it occurs in both immunocompromised and immunocompetent hosts [4,5]. Reported clinical manifestations include acute respiratory distress syndrome, disseminated intravascular coagulation, splenic abscess [6], ophthalmitis [7], neonatal meningitis [8,9], cellulitis [10,11] and orchi-epididymitis [12]. Though uncommon, *Plesiomonas* bacteremia has been associated with biliary tract disease, especially in older patients [13]. Invasive *P. shigelloides* infection has been associated with a mortality rate of 50% to 60% [14].

It is important to take notice of this organism in causing invasive disease in pediatric patients with sickle cell disease as it may lead to severe consequences. In addition to our case, three other cases of *P. shigelloides* sepsis have been reported in SCD patients (Table 1). Among them, two were associated with end organ disease (pneumonia and splenic abscess). There were no deaths reported. Similarly, our case illustrates the potential for *Plesiomonas* to cause serious infection in the context of bacteremia and sepsis in SCD patients and stresses the importance of having a high level of suspicion, and performing careful and repeated physical examinations to evaluate potential foci of infection such as a joint in patients with continuous or recurrent fever while on appropriate antimicrobial therapy. Development of joint pain in settings of high WBC count, MRI finding of moderate effusion, need for arthroscopy and drain placement are consistent with septic arthritis though synovial fluid culture remained negative. As osteonecrosis is a normal disease progression of underlying SCD, a joint infection could be missed. Moreover, the impaired reticulo-endothelial clearance associated with the disease has been shown to predispose patients with sickle cell anemia to bacterial infections [15].

*P. shigelloides* is inherently resistant to ampicillin, but amoxicillin or piperacillin in combination with beta-lactamase inhibitors (clavulanate and tazobactam) can be used as antimicrobial agents. Isolates generally are susceptible to cephalosporins, quinolones and carbapenems [9,16-18].

Aminoglycosides are generally ineffective. Duration of therapy depends on the type of infection. No definitive source of infection was identified in our patient.

Early diagnosis with blood cultures and timely use of appropriate antibiotics were key to the management of this infection and daily evaluation to identify additional foci of infection resulted in a prompt diagnosis of probable septic arthritis, which required surgical drainage in addition to prolonged antibiotic therapy to resolve.

**Conclusion**

Ours is the first case of P. shigelloides bacteremia in a pediatric SCD patient with probable joint infection in a pediatric SCD patient. An increased awareness among clinicians regarding this Gram negative organism is necessary as Plesiomonas has been associated with sepsis and bacteremia, and has the potential to involve other organs like joints, spleen and lungs in vulnerable populations such as patients with SCD.

**References**


**Table 1: Reported cases of sickle cell pediatrian patients with Plesiomonas infection**

<table>
<thead>
<tr>
<th>Year</th>
<th>Age</th>
<th>Location</th>
<th>Diagnosis</th>
<th>Susceptibility pattern</th>
<th>Complications</th>
<th>Antibiotics</th>
<th>Discharge home</th>
</tr>
</thead>
<tbody>
<tr>
<td>1984</td>
<td>10/F</td>
<td>Los Angeles, US</td>
<td>Sepsis and pneumonia with effusion</td>
<td>Blood culture</td>
<td>Thoracentesis</td>
<td>Ampicillin, gentamicin, chloramphenicol, cefazolin, moxalactam</td>
<td>Day 14</td>
</tr>
<tr>
<td>2001</td>
<td>13/F</td>
<td>New York, US</td>
<td>Sepsis and splenic abscess</td>
<td>Blood culture grew Gram-negative rods in 5 hours; identified on day 2</td>
<td>Not mentioned</td>
<td>Cefotaxime, gentamicin; followed by ciprofloxacin orally for 14 days</td>
<td>Day 57</td>
</tr>
<tr>
<td>2010</td>
<td>16/F</td>
<td>Sao Paulo, Brazil</td>
<td>Septic shock</td>
<td>Blood culture positive and organism identified on day 2</td>
<td>Resistant to ampicillin, susceptible to amikacin, gentamicin, trimethoprim-sulfamethoxazole, imipenem, ciprofloxacin, ceftizoxime</td>
<td>ICU stay 14 days; required intubation, chest tubes, exploratory laparotomy, SuperInfection with MRSA (vancomycin susceptible)</td>
<td>Day 24</td>
</tr>
<tr>
<td>2014</td>
<td>10/F</td>
<td>Houston, US</td>
<td>Sepsis and septic arthritis</td>
<td>Blood culture positive and organism identified on day 2</td>
<td>Susceptible to amoxicillin-clavulanic acid, ceftriaxone, ceftizoxime, levofloxacin, meropenem, piperacillin, tazobactam, trimethoprim-sulfamethoxazole</td>
<td>No ICU stay. Required arthrotomy and drainage of the right shoulder joint, drain left in place for 3 days</td>
<td>Day 11</td>
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†MRSA, methicillin-resistant Staphylococcus aureus.


