Severity of Salmonella infection among sickle cell disease pediatric patients: Description of the infection pattern

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ABSTRACT

Introduction: Sickle cell disease (SCD) affects millions worldwide. It has a spectrum of clinical manifestations. However, SCD is more prone to have invasive infection compared with normal individual, and one of the main pathogen of concern is salmonella, where the individual with SCD is more susceptible to salmonella infection. Furthermore, several distinct clinical syndromes can develop in children infected with salmonella, depending on both host factors and the specific serotype involved

Objectives: We aim to describe the infection patterns and whole range of potential complications in children with SCD exposed to invasive salmonella infection.

Method: This is a retrospective observational cohort study which was conducted at King Fahad Medical City (KFMC), Riyadh, Saudi Arabia between 2012 and 2018. All sickle cell patients who are exposed to invasive salmonella infections and treated in our hospital over the last 6 years were included in our study.

Results: Six patients were enrolled in the study, five males and one female with ratio of (M: F) 5:1, age range from 20 months—14 years, and the diagnosis at admission were as follows: (three as vasooclusive crisis, three as infection) with different kind of infections (three sepsis, three septic arthritis, four osteomyelitis, one meningitis, one myositis, one periorbital cellulitis, one diskitis), where three (50%) suffered multiple sites of infections and the other three (50%) with one site of infection, two (50%) of osteomyelitis patients suffered multifocal infection. Species identification is as follows: (three group D, one group C, and two were not specified), only two occasions where resistant to ciprofloxacin while all others were pan sensitive. Fever was prolonged (take more than seven days to subside even with appropriate therapy and intervention) in five out of six.

Conclusions: Multiple site of infection, sever osteomyelitis, and delay in fever response consolidated the fact of high virulence of salmonella in SCD patients. We did not encounter significant resistant rate to both quinolone and cephalosporin.

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1. Introduction

Sickle cell disease (SCD) affects millions worldwide[1], particularly those of black African and Afro-Caribbean descent and also those from the Mediterranean, Middle East, and parts of India [2]. It has a wide range of clinical manifestations. However, SCD is more prone to have invasive infection compared with normal individual, and many reasons were encountered [3]. One of the main pathogens of concern is salmonella, where the individual with SCD is more susceptible to salmonella infection due to recurrent vaso-occlusion with intestinal infarction leads to necrosis and increased gut permeability in addition to decreased neutrophil killing [3]. Furthermore, children infected with salmonella are prone to developing multisystem infection such as osteomyelitis, liver and splenic abscesses, and overwhelming sepsis, sometimes with fatal consequences [4].

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2. Objectives

Using a case series, we aim to highlight the invasive and virulent nature of salmonella and demonstrate the infection patterns and whole range of potential complications.

3. Method

This is a retrospective observational cohort study which was conducted at King Fahad Medical City (KFMC), Riyadh, Saudi Arabia between 2012 and 2018. All sickle cell patients who are exposed to invasive salmonella infections and treated in our hospital over the last 6 years were included in our study.

Structured data sheet were prepared, and electronic file were reviewed for all included patients.

Ethical approval was obtained from the Institutional Review Board at KFMC.

4. Results

Six patients were enrolled in the study, five males and one female with ratio of (M: F) 5:1, age range from 20 months—12 years, and the diagnosis at admission were as follows: (three as vaso-occlusive crisis, three as infection), patients suffered different kind of infections (three sepsis, three septic arthritis, five osteomyelitis, one meningitis, one myositis, one spondylodiskitis) diagnosed by direct culture or by supported imaging with positive culture at other sites. Four patients (66.7%) suffered multiple site of infections and two (33.3%) with one site of infection, two (40%) of osteomyelitis patients suffered of disseminated osteomyelitis, with most common bone affected is femur (44.4%) (Table 1). In general, pre- ceded illnesses were fever and body pain.

None of our patients was found with apparent immunodeficiency, while two of them were on hydroxyurea. Maximum ESR reported on admission was 120 mm/h while the lowest was 29 mm/h, and maximum WBC was reported is 17.6 (10e/L), five out of six patients (83.3%) ended with surgical intervention with incision and drainage. Salmonella species were isolated from different sites as follow (blood, CSF, joints, bone, Para spinal abscess), and species identification as follows: (three group D, one group C, and two were not specified only non typhi), only two occasions where resistant to ciprofloxacin while all others were pan sensitive. Fever was prolonged (take more than seven days to subside even with appropriate therapy and intervention) in five out of six (83%). However, four (80%) of osteomyelitis patients ended with chronic osteomyelitis, where three (75%) cured with disabilities which include either limb deformity or vertebral destruction while two (40%) cured with neither complications nor disabilities (Table 1).

5. Discussion

Patients with SCD are known to have an increased susceptibility to severe bacterial infections compared with the population at large [5,6]. Also SCD patients are at higher risk for invasive salmonella disease at both pediatric and adult population [7,8]. In a previous Saudi study, [4] the incidence of Salmonella infections was 11.5% compared to only 0.64% during the same period in the general hospital population. In London, 52.3% of all bacteremia over a 15-year period in SCD patients were found to be due to Salmonella, compared to 0.4% in non-SCD individuals. Most of these infections were Salmonella typhimurium, a common food-borne pathogen [9].

In our review, Salmonella can affect all childhood age with diversity of clinical presentation in addition to a variety of clinical diseases predominantly (15 out of 19 episodes = 79%) of musculoskeletal diseases where osteomyelitis consists of 60%.

In SCD, Salmonella is the most common agent causing osteomyelitis, followed by S. aureus, then Gram-negative enteric bacteria [10]. In long-term retrospective reviews from the USA [11] and Saudi Arabia [12]. Salmonella accounted for 57% and 41.7% of cases of acute osteomyelitis, respectively. In our study, osteomyelitis encountered significant number (47.3%) of invasive salmonella episodes in SCD, corresponding with what have been reported in the previous studies [4,9] which were 42% and one third respectively, nevertheless; the difference in population age and number of cases should be considered. However, in our study, osteomyelitis was much severe than other series where 40% of osteomyelitis patients suffered of disseminated osteomyelitis, and the majority underwent multiple interventions and required prolonged therapy, and the majority ended with chronic osteomyelitis. However, B. L Atkins et al., described such severity [13].

The extraordinary susceptibility of patients with SCD to Salmonella osteomyelitis was first described fully in 1951 by Hodges and Holt [14] and has since been confirmed in several studies [15,16]. However, the susceptibility of SCD patients to Salmonella

| Table 1 | Patients description. |
|---------|----------------------|
| Age     | Sex | Diagnosis                  | Fever | Complication             | Species Treatment                        | Duration | Outcome |
| Case 1  | M   | Femur Osteomyelitis        | Short | Chronic Osteomyelitis    | Group D Ceftriazone I.V. Cefdinir P.O.  | Four     | Cure    |
| Case 2  | M   | Sepsis                     | Prolonged | None                  | Group D Ceftriazone 4 weeks/Cipro 2 weeks | Four     | Cured (Fever continued 3 weeks) |
| Case 3  | M   | Knee septic arthritis, Femur Osteomyelitis | Prolonged | Chronic osteomyelitis | Group D Ceftriazone I.V. + Cefdinir P.O.  | Four     | Cure with disabilities* |
| Case 4  | M   | Sepsis, Meningitis, Knee septic arthritis, Femur, Humerus: Disseminated osteomyelitis, | Prolonged | Disseminated infection, Disseminated osteomyelitis, chronic osteomyelitis | Non-Typhi Ceftriazone I.V.+ Ciprofloxacin I.V., then Ciprofloxacin P.O.  | Four     | Cure with disabilities* |
| Case 5  | F   | Psosas myositis, Hip septic arthritis, Femur osteomyelitis | Prolonged | None                  | Group C Ceftriazone I.V. (Cipro R)*  | Six      | Cure    |
| Case 6  | M   | Sepsis, shoulder, Mandible, Lumbar osteomyelitis, Spondylodiskitis, Para spinal abscess | Prolonged | Disseminated infection, Disseminated osteomyelitis, intervertebral destruction, | Non-Typhi Ceftriazone I.V. Bactrim I.V. 6 weeks, then Cefdinir P.O., Bactrim P.O. (4 months). (Cipro R)*  | Six      | Cure with disabilities* |

*R—Resistant.
*Disabilities — Limb deformity — Vertebral destruction.
osteomyelitis has not been fully explained, but certain factors deserve emphasis. It has been proposed that repeated intravascular sickling and vaso-occlusive episodes devitalize the gut wall, leading to frequent seeding of Salmonella organisms from the bowel into the blood stream [16]. The presence of repeated marrow thrombosis, infarction and necrosis would make the bone a favored site of localization, leading to osteomyelitis and septic arthritis.

Interestingly, non-SCD patients usually became afebrile within 2–3 days after initiation of adequate antimicrobial treatment for salmonellosis [17], unlike in SCD patients where fever persists more which could be explained by prolongation of apoptotic cell death that allows the bacteria to persist in the host cells for a longer period [18], or due to high initial immune response triggered by bacteremia [19].

In our series, we do not encounter multi resistant salmonella species. However, the emergence of Salmonella serotypes resistant to quinolones which increasing through the time in multiple area over world [20–22], and to less extent to cephalosporin where both poses a new challenge in treating infected patients. In our series, we encountered only two isolates (33%) of salmonella were resistant to quinolone which consider relatively low in comparison with encountered only two isolates (33%) of salmonella were resistant to quinolone which consider relatively low in comparison with

6. Conclusions

Invasive Salmonella infection can have catastrophic consequences in pediatric patients with sickle cell disease. There is an emphasis for early recognition and therapeutic intervention in all cases. Multiple site of infection and severe bone destructions in addition to delay in fever response consolidated the fact of high virulence of salmonella in SCD patients. Presently, aggressive treatment with antibiotics and early recognition of complications are the mainstay of management. We encountered relatively low resistant rate to quinolone and no resistant to cephalosporin. Additionally, health promotion strategies to prevent infection play an important role.

We are Tariq AlFawaz, Omar Alzumar, Dayel AlShahrani, Mohammed Alshehri; authors of paper: Severity of Salmonella infection among sickle cell diseases pediatric patients: description of the infection pattern:

Agreed to submit our paper to international journal of pediatric and adolescent

And our work was approved by the Institutional Review Board at KFMC.

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