

Non-typhoidal Salmonella Osteomyelitis in the Midfoot of a Healthy Child and Review of the Literature

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Abstract

Background: Salmonella osteomyelitis in children is rare, and has mostly been described in children with sickle cell disease. The long bones of the extremities are most commonly affected.

Case Report: We present a unique case of Salmonella (non-typhoidal) osteomyelitis, affecting the tarsal bones of the foot of a previously healthy 4 year old child, likely contracted from a pet turtle.

Keywords: *Salmonella*; Osteomyelitis; Children

Introduction

Salmonella osteomyelitis is common among children with sickle cell disease. Most commonly, it occurs in the long bones of extremities and causes significant morbidity in this population. Salmonella osteomyelitis in healthy children is rare. Though in the developing nations, *S. typhi* and non-typhoidal *Salmonella* infections are common; osteomyelitis related to these organisms in healthy children is uncommon. Small bones are rarely affected by *Salmonella* species. We present a healthy child with osteomyelitis of his tarsal bones, caused by non-typhoidal *Salmonella* species.

Case Report

A 4 year old, previously healthy male, presented to the emergency department with a history of spraining his ankle 2 weeks prior to admission. At the time of the injury he had a history of diarrhea, vomiting and fever of 102°F. The diarrhea and vomiting resolved within 2-3 days, however, his fever persisted, and he stopped bearing weight on his left leg a few days prior to admission. His physical examination on admission was significant for left foot swelling and tenderness, especially around the entire midfoot, sparing his ankle joint. He was unable to bear weight on his left side. The rest of his physical examination was unremarkable. His initial white blood cell count was $13 \times 10^3/\text{UL}$, with 65% neutrophils and 9% bands, hemoglobin 12.7 mg/dl, Hematocrit 37, platelet count of $408 \times 10^3/\text{UL}$. His Erythrocyte Sedimentation Rate (ESR) and C Reactive Protein (CRP) were both elevated at 35 mm/hr and 2.3 mg/dl, respectively. Plain radiographs of his left foot displayed irregular contours of the proximal and distal aspects of his second to fifth metatarsal bones, as well as the navicular, cuneiform and calcaneal bones. A Magnetic Resonance Imaging (MRI) of his foot showed left cuboid osteomyelitis, with overriding cellulitis and small effusions of the tibiotalar and talonavicular joints. At that time, he underwent an incision and drainage of the left foot. Cultures for aerobic, anaerobic, fungi and acid fast bacilli were all negative. He was admitted to the hospital for one week, during which he received intravenous clindamycin. After he appeared to have been improving, he was sent home with a peripherally inserted central catheter, to complete a course of therapy. Blood culture and urine culture at this admission were negative, and he was afebrile at discharge.

He returned to the hospital after 5 days, with a new onset of fever and no further improvement of his left foot swelling and pain. On further questioning, it was discovered that he had a parrot and 3 turtles at home. One of the turtles "was sick" around the time of his initial presentation. He had handled the turtle extensively during that time.

At the time of his second admission, he had a temperature of 103°F and his left midfoot was warm, tender, erythematous and swollen. A complete blood count revealed a white cell count of $11.6 \times 10^3/\text{UL}$ with 57% neutrophils and 2.5 % bands, hemoglobin of 11.6 mg/dl, Hematocrit 34.6, and platelets of $404 \times 10^3/\text{UL}$. His ESR had increased to 63 mm/hr and CRP was 2.3 mg/dl. A repeat MRI of his left foot demonstrated progressive osteomyelitis of the navicular, cuboid and cuneiform bones, in addition to the cuboid bone, as well as new findings of plantar myositis, intertarsal joint synovitis and mid foot tendonitis. His central line blood culture was negative, and he was initially started on vancomycin, ceftazidime and gentamicin to cover for both Gram positive and Gram negative organisms. He underwent a repeat drainage in the operating room on hospital day 7 (of the second admission). This time his bone cultures grew *Salmonella* type B, which was susceptible to ampicillin. He was switched to ampicillin, but he remained febrile. He had a very indolent clinical course and had recurrent small abscessed around the small bones of his foot, which required four additional debridement procedures. He became afebrile by hospital day 15, after his third debridement. His blood, urine and stool cultures were all negative. An immune workup, including review of his peripheral blood smear, humoral immune panel, quantitative immunoglobulins, total complements, HIV ELISA and oxidative burst test were within normal limits. He was discharged home after 26 days on twice daily ceftriaxone intravenously, to complete 6 weeks of parenteral therapy. He was then switched to oral third generation cephalosporin for four months. At the follow up visit, he had full range of motion of his foot without any deformities.

Urine and stool samples of the baby turtle were obtained, but the cultures were negative. However, while he was in the hospital, one of the other turtles died due to unknown reasons. Samples from the third turtle were not cultured.

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Discussion

Though common in the developing nations, *S. typhi* and *S. paratyphi* account for less than 1% of *Salmonella* infections in the United States [1]. Non-typhoidal *Salmonella* was causing approximately 1.4 million illnesses in the United States each year, resulting in about 15,000 hospitalizations, and more than 400 deaths [2]. In the late 1990s, *S. typhimurium* serogroup B and *S. enteritidis* serogroup D were the most common serotypes, accounting for 50% of the isolates from patients in the United States [3]. The reported incidence of Salmonella osteomyelitis prior to the antibiotic era was 0.76%-0.84% [4,5]. According to the study by Jones et al. [6], among 51,964 cases of non-typhi *Salmonella* infections in the United States, 0.04% was associated with bone and joint infections. Salmonella osteomyelitis is more common in children with sickle cell disease, accounting for about 60%-80% of cases [7,8]. It has also been associated with other conditions, including previous trauma, connective tissue disorders and immunosuppressive states including malignancies. However, there is no data available to elucidate the actual incidence of Salmonella osteomyelitis in healthy children.

To our knowledge, there has been only one reported case of osteomyelitis due to non-typhoidal *Salmonella spp.*, involving the

navicular bone in a 4 year old healthy child [9]. This is the first reported case of Salmonella osteomyelitis and septic arthritis of multiple tarsal bones in a healthy child. Osteomyelitis with *Salmonella spp.* in the tarsal bones has been reported in children with sickle cell disease. In one study, about 19% of the patients with sickle cell disease had osteomyelitis of the bones of the foot, and were more frequently seen in children younger than 2 years of age [10]. In another review of 37 bone infections by non-typhoidal *Salmonella*, only 3 patients had tarsal bone involvement. All of these 3 patients had sickle cell disease, and only one of them was a child [11]. *S. typhimurium* and *S. enteritidis* were the most frequently isolated organisms in this study. The reported incidence of Salmonella osteomyelitis according to sites include femur (26%), tibia (23%), humerus (21%), lumbar vertebra (17%), radius (10%), ulna (7%) [12]. The infection is confined to a single bone in 69% of cases. Though multifocal involvement is common in the developing nations, the incidence is low in the United States [8].

We reviewed published reports of non-typhoidal Salmonella osteomyelitis in healthy children in the English literature from 1978 to 2012. To our knowledge, there are 21 reported cases of Salmonella osteomyelitis in healthy children (Table 1), of which one report could

| Reference Study | Year | Age /Sex | Presentation | Organism | Bones involved | Animal Exposures | Blood Cx | Tissue Cx | Stool Cx | Outcome |
|-----------------|------|-------------|--|-------------------------------|-----------------------------|--|------------|-----------|------------|---|
| 9 | 2009 | 4 years /M | Limp/pain on foot/ diarrhea/ vomiting | <i>Salmonella enteritidis</i> | Navicular bone | None | - | + | - | 1 Surgical debridement, full recovery |
| 20 | 2007 | 17 months/M | Unable to bear weight, fever | <i>Salmonella</i> type B | Epiphysis of distal femur | Not listed | - | + | Not listed | Required 4 debridements during the same hospitalization but no chronic sequelae |
| 21 | 2007 | Not listed | Not listed | <i>Salmonella</i> | Pelvis | Not listed | - | + | Not listed | Full recovery |
| 16 | 2003 | 4 months/F | Fever and swelling of both hands | <i>Salmonella</i> Group C1 | Short tubular bones of hand | Not listed | Not listed | + | Not listed | Recurrences till 19 years of age, multiple debridements |
| 22 | 2003 | 13 years/M | Fever, pain in knee joint, limping | <i>Salmonella</i> | Metaphysis of tibia | Not listed | - | + | Not listed | Full recovery |
| 23 | 2001 | 8 years/M | Back pain/fever | <i>Salmonella oranienburg</i> | Thoracic spine | Dried squid | - | + | Not listed | Full recovery |
| 24 | 2000 | 7 months/F | Refusal to move arm, fever | <i>Salmonella arizonae</i> | Humerus | Iguana | - | + | - | Full recovery, 2 debridements |
| 25 | 1997 | 16 years/M | Left hip pain/fever | <i>Salmonella</i> group C | Left ASIS | Not listed | - | + | Not listed | Full recovery |
| | | 12 years/M | Right hip pain/URI symptoms, vomiting/ headache | <i>Salmonella</i> Group B | Acetabulum | Not listed | - | + | Not listed | Full recovery |
| 26 | 1996 | 17 years/ F | L postauricular discomfort, sore throat, URI symptoms | <i>Salmonella typhimurium</i> | Mastoid | Not listed | - | + | Not listed | Full recovery |
| 27 | 1994 | 7 years/F | Pain/swelling of Right elbow s/p fracture, vomiting/diarrhea/fever | <i>Salmonella enteritidis</i> | Ulna | Undercooked chicken | - | + | - | Full recovery |
| 28 | 1992 | 8 years /F | Back pain/ chills/ fever | <i>Salmonella panama</i> | Left iliac crest | Visit to El-Salvador-diarrhea in recent past | + | NA | Not listed | Full recovery |
| 29 | 1988 | 12 years/F | Back pain | <i>Salmonella</i> Group B | Vertebra | Not listed | - | + | Not listed | Full recovery |
| 30 | 1988 | 5 years/ F | Fracture of distal radius | <i>Salmonella newport</i> | Radius | Not listed | - | + | - | Reduction in bone length |
| 31 | 1988 | 12 years/F | Back pain | <i>Salmonella virchow</i> | Vertebra | Diarrheal illness in family | - | + | + | Full recovery |
| 32 | 1982 | 15 years /F | Back pain | <i>Salmonella cerro</i> | Vertebra | Diarrheal illness in the recent past | + | - | Not listed | Chronic |

| | | | | | | | | | | |
|----|------|-------------|----------------------|-------------------------------|--------------------------|------------|---|---|------------|---------------------------------|
| 10 | 1980 | 10 years/ M | Pain/swelling | <i>Salmonella</i> species | Radius/ulna/tibia/fibula | Not listed | - | + | - | Chronic |
| | | 6 months/ F | Meningitis | <i>Salmonella</i> species | Humerus | Not listed | - | + | Not listed | Defaulted, CSF culture negative |
| 11 | 1978 | 6 months/M | Fever/ pain/swelling | <i>Salmonella typhimurium</i> | Humerus | - | + | - | - | Chronic |
| | | 1 year/ M | Fever/ pain/swelling | <i>Salmonella enteritidis</i> | Tibia | - | - | + | + | Full recovery |

M: Male; F: Female; -: Negative; + Positive; NA: Not Applicable; URI: Upper Respiratory Tract; ASIS: Anterior Superior Iliac Spine

Table 1: Clinical features, etiological agent and outcome of non-typhoidal Salmonella osteomyelitis in healthy children from review of the literature.

not be fully reviewed. Of the 20 patients, 45% (n=9) of the patients had involvement of the long bones, followed by pelvic bones and vertebrae. The age of the patients ranged between 4 months to 17 yrs. There was no gender predilection. About 55% (n=11) of the patients had fever at the onset of illness, while almost all of them had local pain, swelling, or both at presentation. About one fourth of the patients had diarrhea or vomiting, either at presentation or prior to their joint symptoms. Interestingly only 15% (n=3) of the patients had positive blood cultures for *Salmonella spp.* The diagnosis was made mostly by surgical bone cultures. Only one patient had a history of pet animal exposure (iguana). Multifocal involvement was seen in only 10% (n=2). Initial radiographs were reportedly negative or not done in 50% of the patients (n=9, 1=unknown). Bone scans were done in 30% (n=6) of the patients, of which 28% were negative at presentation. MRI or a Computed Tomogram (CT) scan were done in about 50% of the patients (n=10), which had a higher diagnostic yield. Ampicillin or third generation cephalosporins were used in almost all of these patients. Two patients received chloramphenicol. All except one child had surgical drainage, and 15% (n=3) of the patients had multiple surgical debridements. Most of the patients received 4-6 weeks of antibiotics, but those with an indolent course received an additional 2-6 weeks. The majority of the patients had acute presentations, and most children recovered completely without chronic sequelae. However, 2 children developed shortening of their affected extremity, while 3 others had chronic or recurrent osteomyelitis.

Chronic relapsing osteomyelitis with *Salmonella spp* has been described in the literature [13-16], but there is limited data in children. Moreover, there is no consensus regarding the best treatment modalities to prevent chronic Salmonella osteomyelitis. However, higher failure rates have been associated with patients treated with antibiotics, when compared to a combination of antibiotics and surgery [17].

Though the majority of *Salmonella* infections are thought to be food or water borne, human disease from exposure to pets (reptiles, turtles) is not uncommon in the United States [18]. The association of Salmonellosis with baby turtles led to federal legislation in 1975, prohibiting the sale or distribution of small turtles (carapace less than 4 inches) in the United States. The Center for Disease Control (CDC) reports only one case of non-typhoidal *Salmonella* osteoarticular infection (following iguana exposure) presenting as septic arthritis in a 4 month old child [19]. The other cases of pet associated Salmonellosis reported by the CDC included patients presenting mostly with gastroenteritis, and/or bacteremia [18,19]. None of the CDC reported cases of turtle associated *Salmonella* infections presented with osteomyelitis.

In summary, this is the first reported case of Salmonella non-typhoidal osteomyelitis and septic arthritis of multiple tarsal bones of the foot in a healthy child, most likely contracted from his pet turtle.

Since blood cultures are not reliable in focal infections with *Salmonella*, surgical cultures of the bone typically are required for diagnosis. MRI are superior to plain radiographs, CT scan, gallium scan or bone scans in identifying the osteomyelitic lesions, and surgical debridement should be undertaken for both diagnostic and therapeutic purposes. For acute osteomyelitis with *Salmonella*, 4-6 weeks of antibiotic therapy should be sufficient. For those with a protracted course, the treatment duration could be extended to an additional 2-8 weeks or longer.

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