

Case Report

Sacroiliitis caused by *Salmonella typhi*

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Abstract

Although the commonest manifestation of *Salmonella* infection is acute gastroenteritis, infection may spread to the blood-stream and the illness can present with focal lesions in almost any organ with or without septicemia. We describe here a case of *Salmonella typhi* infection of a sacroiliac joint that was cured with ciprofloxacin therapy for six weeks. The patient was immunologically normal. *Salmonella* etiology was not suspected in this case, and the diagnosis was made only after bacterial isolation. Physicians should be aware of this rare manifestation of *Salmonella* infection, especially in endemic areas.

Key words: sacroiliitis, *Salmonella typhi*, Turkey, medical treatment

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Introduction

Salmonella consists of a large heterogeneous group of motile gram-negative bacilli that affect animals and humans. As a group, they are enteroinvasive and enteropathogenic organisms. Humans are infected with *Salmonella* almost solely by ingestion of contaminated food or drink, although under quite unusual circumstances, transmission has occurred by direct contact or inhalation [1].

Salmonellosis is a global health problem that can have a devastating impact on resource-poor countries. Regions with contaminated water supplies and inadequate waste disposal have a high incidence of salmonellosis [2]. Approximately 10,000 patients are hospitalized annually for this infection in Turkey, and more than 60 percent of these cases are reported from the southeast region. The incidence of salmonellosis in southeastern Turkey ranges from 210 to 320 cases per 100,000 populations [3].

Salmonella infections present in multiple ways: gastroenteritis most commonly; enteric fever; bacteremia with or without endovascular infections such as aortitis and endocarditis; and focal metastatic infections such as sacroiliitis (SI), osteomyelitis and abscess formation [4]. However, the majority of such infections occur in patients with preexisting disease, which may be haemoglobinopathy, especially sickle cell disease; prior joint disease, including rheumatoid arthritis, systemic lupus erythematosus, osteoarthritis and gout; previous trauma; cranial surgery;

hematologic neoplasm; immunosuppressive therapy; or impaired cell-mediated immune response as in AIDS [5].

Pyogenic infections of the sacroiliac joints are uncommon [6]. Pyogenic SI accounts for approximately 1.5% of all suppurative arthritis cases in children but occurs much more commonly in adults who use intravenous drugs [7]. The most common organisms causing pyogenic SI are *Staphylococcus aureus* and *Streptococci*, although *Pseudomonas aeruginosa* may be more common in intravenous drug abusers [8]. Although pyogenic SI due to *Salmonella* is reported in large numbers, *Salmonella typhi* as its causative agent is rare [6]. To the best of our knowledge, this is the first case report of SI caused by *S. typhi* from Turkey.

Case

A previously healthy 22-year-old woman was admitted to the University of Dicle Hospital, Diyarbakir, in the southeastern Anatolia region of Turkey, in September 2006, with complaints of fever, weakness, pain, and inability to walk and bear weight on the left hip. There had been no trauma and injection history. She was not known to have a haemoglobinopathy. She had not had any disturbance of bowel action, vaginal discharge, or eye symptoms. She had no family history of chronic granulomatous disease. Three weeks earlier, the patient had a fever and non-bloody diarrhoea and abdominal pain which

Figure 1. An anterior view of a bone scan ($^{99m}\text{Tc-MDP}$) 10 days after onset of symptoms showing increased uptake of the radioisotope in bilateral sacroiliac joint.



resolved in 72 hours after eating raw meatball and lettuce. She had developed an episode of high-grade fever two days prior to admission and severe low back pain radiating to the left leg. The patient received naproxen sodium for continued fever and pain. Despite treatment, the pain continuously worsened until the patient was unable to walk.

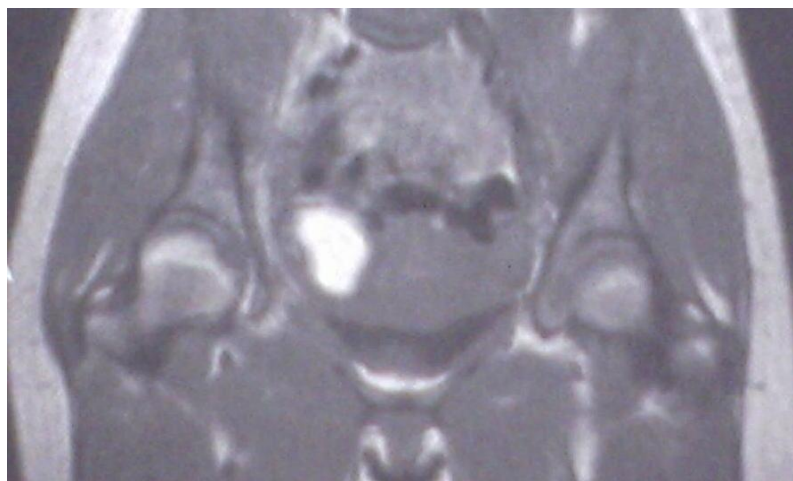
On the day of admission, physical examination revealed that she was in pain and feverish (38.2°C). Fever had a sudden onset without any associated chills or rigors. Blood pressure and pulse were 100/60mmHg and 94/minute, respectively. Her physical examination was normal except for the musculoskeletal system. There were no overlying abnormal skin findings, costovertebral angle or lumbar spine tenderness. Lower extremities were neurovascularly intact. Local examination showed tenderness with increased local temperature and flexion deformity and restricted movement of the left hip joint. She had limited active hip flexion and external rotation, and there was slight pain with passive hip external rotation. The patient's history of fever and marked tenderness to palpitation over the sacroiliac joint suggested the possibility of septic SI.

Laboratory findings included a hemoglobin level of 12.1g/dl (range, 12.2-18.1 g/dl), total leukocyte count of 8580/mm³ (78% polymorphonuclear cells, 14% lymphocytes; range, 4600-10200/mm³), and platelet count 245 K/UL (range, 142-424 K/UL). ALT=24 U/L (range, 10-35 U/L) and AST=20 U/L (range, 10-40 U/L) were within normal limits. Creatine kinase was 384 U/L (range, 38-174 U/L).

Erythrocyte sedimentation rate (ESR) was 86 mm/h (range, 8-15 mm/h) with a C-reactive protein (CRP), measuring 117 mg/dl (range, 0-8 mg/dl). Antinuclear antibody, Rheumatoid factor, and HLA-B27 were negative. Serum C3, C4 and complement function were normal. Hemoglobin electrophoresis showed nothing abnormal, thus excluding haemoglobinopathy. Serum immunoglobulin concentrations were normal when measured during her convalescence, showing that she did not have obvious immunodeficiency. The Widal test showed titers of 1/320 for TO and TH for *S. Typhi* (cut off value was > 1/160). Urinalysis revealed no evidence of infection; urine and blood pregnancy tests were negative. Blood, stool, urine and throat cultures had been performed before the antibiotic therapy was started. Empirical therapy with cefazolin was started.

In the present study, specimens were plated in eosin-methylene blue agar and 5% sheep blood agar. These cultures were incubated at 37°C for 24-48 hours. The specimens on eosin-methylene blue agar were incubated in air, and sheep blood agars were incubated in 5% carbon dioxide. Smears from colonies which grew were stained with Gram stain. The isolated microorganism was identified with use of conventional techniques and Sceptor system (Becton-Dickinson, Maryland, USA). Its susceptibility was evaluated using disc diffusion testing at our clinic laboratory as recommended by the National Committee for Clinical Laboratory Standards (NCCLS) [9], and ciprofloxacin MIC

Figure 2. An abnormal signal in the left sacroiliac joints and abscess formation near the inner part of acetabulum were found on MRI.



values were determined by E-test (AB Biodisk, Solna, Sweden).

The sacroiliac joints, pelvis, lumbosacral spine, hip joints and chest were radiologically normal. A bone scan with technetium-99m methylene diphosphonate (^{99m}Tc -MDP) showed increased uptake of the radioisotope over the sacroiliac joints with no indication of adjacent bone involvement (Figure 1). However, an abnormal signal in the left sacroiliac joint and abscess formation near the inner part of the acetabulum were found on magnetic resonance imaging (MRI) (Figure 2).

The patient was initially treated with cefazolin 3 g/day with no improvement. The abscess was drained radiologically. Her stool, synovial aspiration, urine and abscess drainage cultures were negative. After three days, the blood culture grew *S. typhi* that was susceptible to all tested antibiotics such as amikacin, amoxicillin-clavunate, ampicillin, ceftriaxone, ceftazidime, chloramphenicol, ciprofloxacin, imipenem and trimetoprim-sulfamethoxazole. Ciprofloxacin MIC value was ≤ 0.5 . Cefazolin was discontinued upon the return of blood culture sensitivity results. Therapy was changed to intravenous ciprofloxacin 400 mg every 12 hours for a week, and then was changed to oral ciprofloxacin 500 mg twice daily for another five weeks. She responded well to treatment; her fever subsided three days after starting ciprofloxacin, and pain in the buttock gradually improved. Her ESR and CRP normalized within three weeks. She recovered completely at the six-month follow-up. X-ray examination showed sclerosis on the left sacroiliac joint and irregularities of the joint margins. Follow-

up after one year showed no residue from the sacroiliac joint infection.

Discussion

Of the clinical manifestations of Typhi, enteric fever is the most common presentation. The others include: Neuropsychiatric manifestations (seizures, meningitis, encephalomyelitis, psychotic syndromes including schizophrenia-like illness and depression); cardiovascular manifestations (myocarditis and pericarditis); hepatobiliary manifestations (acute or chronic cholecystitis); genitourinary manifestations (immune complex-mediated glomerulonephritis, pyelonephritis and cystitis). Occasionally, focal lesions such as osteomyelitis, SI, brain abscess, and spleen and liver abscess have been reported [10].

Although any skeletal site can become infected, *Salmonella* infections of bone typically involve the long bones, the chondrosternal junctions, the knee, the shoulder, the hip, the sacroiliac joints and the spine. Skeletal infection is particularly common at sites of skeletal injury or abnormality, at sites of trauma, in areas that have been injured in the setting of sickle cell disease, and on skeletal prostheses. The most common causative serotype is *Salmonella typhimurium* [11]. Reactive arthritis of the sacroiliac joint following *Salmonella* infection is a well-known clinical entity occurring mainly in patients who are positive for HLA-B27 antigen. However, pyogenic SI due to *Salmonella* is very rare [12]. The most common causative serotypes of salmonella that cause SI were *S. typhi*, *S. virchow*, *S. enteritidis*, *S. chloraesuis*, *S. okatie* and *S. schwarzengrund*, and *S. heidelberg* [4,6].

Table 1. The results of positive cultures in reported cases of SI caused by *S. typhi*.

| Case | Author | Publication year | Positive culture |
|------|---------------------------------|------------------|-------------------------------|
| 1 | Oka and Mottonen (13) | 1983 | Blood |
| 2 | Govender and Chotai (14) | 1990 | Blood |
| 3 | Govender and Chotai (14) | 1990 | Synovial aspiration |
| 4 | Govender and Chotai (14) | 1990 | Blood |
| 5 | Menon and Gupta (15) | 1993 | Blood |
| 6 | Menon and Gupta (15) | 1993 | Blood |
| 7 | Siam <i>et al</i> (16) | 1993 | Synovial aspiration |
| 8 | Osman and Govender (17) | 1995 | Blood and synovial aspiration |
| 9 | Osman and Govender (17) | 1995 | Blood |
| 10 | Osman and Govender (17) | 1995 | Blood |
| 11 | Osman and Govender (17) | 1995 | Synovial aspiration |
| 12 | Alsoub (6) | 1997 | Synovial aspiration |
| 13 | Alsoub (6) | 1997 | Blood |
| 14 | Uluğ <i>et al</i> (This report) | 2006 | Blood |

The disease usually affects immunocompetent adolescents and the mean age of these patients in the literature is 18.8 years [2]. This data is in agreement with the demographic of our patient, who was 22 years old. The clinical features of *S. typhi* SI reported in the literature is similar to those caused by other organisms. All presented with fever and pain symptoms involving the hip, back or buttock. All patients with pain reported it as unilateral, and there appeared to be no tropism for a particular side [6]. These data also agree with the symptoms of our patient.

The diagnosis hinges on adequate cultures being performed before the antibiotic therapy is started. Blood cultures are frequently positive. The high incidence of positive blood cultures in both *Salmonella* osteomyelitis and septic arthritis suggests that most cases are hemotogenous in origin [11]. Stool and synovial fluid cultures were positive approximately 35% and 42%, respectively; ESR and CRP were also elevated in most cases [4]. The results of positive cultures in reported cases of SI caused by *S. typhi* can be seen in Table 1 [6, 13-17]. In our case, blood cultures were positive, and stool, synovial aspiration and abscess cultures were negative. ESR and CRP were also elevated.

There was often a delay in diagnosis of septic SI. The delays were compounded because patients were treated for the more common agents that cause pyogenic SI before it was determined that *Salmonella* was the bacterial culprit [4]. The mean time to diagnosis of SI caused by *Salmonella* spp. is 12 days (range, 3-21 days) [4,6], which is not similar to the time frame in this study.

The course of *Salmonella* infection in bone or joints may be chronic and treatment may be required for many weeks [18], but response to antibiotic therapy was favorable and a cure was achieved in 85% cases [6]. Initially, antibiotics should be given parenterally during a two-week period, followed by a prolonged course of oral treatment (> 4 weeks) to prevent recurrence. Quinolones and third-generation cephalosporins, especially ceftriaxone, have been used most commonly, but ampicillin, amoxicillin and trimetoprim-sulfamethoxazole have performed well in the past. Zimmerman *et al.* [19] reported that most authors recommend a minimum of four weeks of parenteral antibiotic therapy followed, in some cases, by a course of oral antibiotics. On the other hand, we used intravenous ciprofloxacin for a week and oral ciprofloxacin for another five weeks. Immobilization of the joint appears to be unnecessary. Surgery is indicated for the following conditions: for drainage of an abscess or for sequestrectomy; for biopsy when there is a poor clinical response to antibiotics; or when accurate bacteriology is felt to be essential [20]. In the present case, the abscess was drained.

Plain radiographs of the sacroiliac joints are usually normal in the first two weeks in SI [21]. Bone scan showed an increased uptake of the radioisotope in the involved joints, but the possibility of the diagnosis must first be considered. Computed tomography (CT) and MRI are helpful in making early diagnosis, as they can show abnormalities earlier than conventional X-ray and occasionally even before bone scan [8], and they can define the anatomy of the sacroiliac joint, as well as demonstrate fluid collection which can be aspirated under CT guidance, thus aiding in establishing microbiologic diagnosis [22]. In this study although

plain radiographs were normal initially, SI and abscess formation was determined by scintigraphy and MRI.

Conclusion

Pyogenic SI due to *S. typhi* remains a very rare disease in spite of the large number of patients with *S. typhi* infection, and no case has yet been reported from Turkey. This case is being reported to highlight the unusual presentation of *S. typhi*. Blood cultures should always be performed before antibiotic treatment is started. Bone scan and MRI are very sensitive for making early diagnosis. Therapy with antibiotics for four to six weeks or longer is associated with a successful outcome. In conclusion, physicians should be aware of rare manifestations of *Salmonella* infections, especially in endemic areas. Timely intervention, correct diagnosis, and treatment saved the affected sacroiliac joint, which otherwise would have been damaged for the patients' lifetime.

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References

- Meldrum R, Feinberg JR (2004) Septic arthritis of the ankle due to *Salmonella enteritidis*: A case report. *South Med J*. 97: 77-79.
- Singh S, Singh K, Grover AS, *et al.* (1995) Two-layer closure of typhoid ileal perforations: a prospective study of 46 cases. *Br J Surg*. 82: 1253.
- Ministry of Health, Republic of Turkey (1994) The distribution of the hospitalized patients according to their diseases. (Ministry of Health annual reports A1-A30). Ankara, Turkey: Ministry of Health, 5-7.
- Feldman LS (2006) *Salmonella* septic sacroiliitis case report and review. *Pediatr Infect Dis J*. 25: 187-189.
- Agnihotri N, Dhingra MS, Gautam V, Gupta V, Kaushal R, Metita D (2005). *Salmonella typhi* septic arthritis of hip-a case report. *Jpn J Infect Dis*. 58: 29-30.
- Alsoub H (1997) Sacroiliitis due to *Salmonella typhi*: A report of two cases. *Ann Saudi Med*. 17: 331-333.
- Schaab UB, McCracken GH, Nelson JD. (1980). Pyogenic arthritis of the sacroiliac joint in pediatric patients. *Pediatrics*. 66:375-379.
- Vyskocil JJ, McIlroy MA, Brennan TA, Wilson FM (1991) Pyogenic infection of the sacroiliac joint. Case reports and review of the literature. *Medicine (Baltimore)*. 70: 188-197.
- National Committee for Clinical Laboratory Standards. Performance standards for antimicrobial susceptibility testing. NCCLS document M2-A7. Villanova, PA: National Committee on Clinical Laboratory Standards, 2000.
- Epstein JE, Hoffman SL (2006) Typhoid fever. In: Guerrant RL, Walker DH, Weller PF eds. *Tropical Infectious Diseases Principles, Pathogens and Practice*. 2nd ed. Philadelphia: Churchill Livingstone, Elsevier. 220-240.
- Kim AY, Goldberg MB, Rubin RH (2004) *Salmonella* Infections. In: Gorbach SL, Barlett JG, Blacklow NR eds. *Infectious Diseases*. Philadelphia: Lippincott Williams & Wilkins. 618-632.
- Pegues DA, Ohl ME, Miller SI (2005) *Salmonella* species, including *Salmonella typhi*. In: Mandell GL, Bennett GE, Dolin R eds. *Principles and Practice of Infectious Diseases*. Philadelphia: Churchill Livingstone. 2636-2654.
- Oka M and Mottonen T (1983) Septic sacroiliitis. *J Rheumatol*; 10: 475-478.
- Govender S, Chotai PR (1990) *Salmonella* osteitis and septic arthritis. *J Bone Joint Surg (Br)* 72: 504-506.
- Menon KP and Gupta A (1993) Atypical salmonellosis: two cases of sacroiliitis. *Indian J Pathol Microbiol* 36: 84-86.
- Siam AR, Hammoudeh M, Uwaydah AK (1993) Pyogenic sacroiliitis in Qatar. *Br J Rheumatol* 32: 699-701.
- Osman AA and Govender S (1995) Septic sacroiliitis. *Clin Orthop Relat Res* 313: 214-219.
- Richardson SB, Uttley AH, Rettingale KW (1977) Acute sacroiliitis due to *Salmonella okatie*. *BR Med J* 1: 1449-1450.
- Zimmerman B, Mikolich DJ, Lally EV (1996) Septic sacroiliitis. *Semin Arthritis Rheum*. 26: 592-604.
- Shanahan MD, Ackroyd CE (1985) Pyogenic infection of the sacroiliac joint: A report of 11 cases. *J Bone Joint Surg Br* 67: 605-608.
- Braun J, Sieper J, Bollow M (2000) Imaging of sacroiliitis. *Clin Rheumatol*. 19: 51-57.
- Klein MA, Winalski CS, Wax MR, Piwnica-worms DR (1991) MR imaging of septic sacroiliitis. *J Comput Assist Tomogr*. 15: 126-132.

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