



Case Report

A rare case of salmonellosis with multifocal osteomyelitis and pulmonary involvement

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ABSTRACT

Salmonellosis is characterized by gastroenteritis and enteric fever in humans and affects various organs, particularly in endemic regions and in immunocompromised patients. Here, we report on a 45-year-old male patient with multifocal osteomyelitis, pneumonia and colonic ulcers caused by *Salmonella typhi* infection. The patient was admitted to our outpatient department with dysuria, fever and hip pain and had been treated with prednisolone and methotrexate for pemphigus vulgaris for two months. After *Salmonella typhi* was isolated in the urine culture, the patient was hospitalized and treated according to the antibiogram. However, despite antibiotherapy, the patient's ongoing complaints suggested an existing resistance problem or a rare or atypical involvement of *Salmonella* spp. As immunosuppressive agents were not used in high doses or for prolonged periods, this disease course and severity were not expected. For an infectious process with an atypical course or multiorgan involvement, particularly in endemic regions and immunocompromised patients, salmonellosis should be considered in the differential diagnosis.

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Introduction

Salmonellae are gram negative, facultatively anaerobic and motile bacilli. Transmission most commonly occurs via food or water and as a result of faecal contamination by ill or asymptomatic chronic carriers. While salmonellosis is often considered to affect the gastrointestinal tract primarily, infection at other sites may occur, producing characteristic clinical syndromes [1]. Specific salmonella serotypes often produce characteristic clinical syndromes, including gastroenteritis, enteric fever, bacteraemia, vascular infection, localized infections and the chronic carrier state, but infection outcomes differ substantially by serotype [2]. An increase in the use of immunosuppressive drugs to treat autoimmune and rheumatic diseases has led to an increase in atypical invasive manifestations [3]. Here, we report on a patient with acute multifocal osteomyelitis, pulmonary infection and colitis due to salmonellosis after using prednisolone and methotrexate.

Case report

A 45-year-old male was admitted to a dermatology outpatient department with an oral and facial lesion. After pemphigus vulgaris was diagnosed, 80 mg/day of prednisolone and 15 mg/week of methotrexate were initiated. In the second month of therapy, the patient was referred to a hospital with complaints of fever, dysuria, shortness of breath, cough and bilateral hip and thigh pain. The patient had also lost his ability to walk. A routine laboratory analysis revealed the following: AST: 283 IU/mL (normal: 5–34 IU/mL), ALT: 454 IU/mL (normal: 3–45 IU/mL), total leukocyte count (TLC): $15 \times 10^3/\text{mm}^3$ (normal: $4.3\text{--}10.3 \times 10^3/\text{mm}^3$), haemoglobin (hb): 9.7 g/dL (normal: 12.1–16.2 g/dL), platelets (plt): $213 \times 10^3/\text{mm}^3$ (normal: $112\text{--}318 \times 10^3/\text{mm}^3$), C-reactive protein (CRP): 65 mg/l (normal: 0–5 mg/l), erythrocyte sedimentation rate (ESR): 101 mm/h (normal: <20 mm/h) and pyuria. An abdominal ultrasonography revealed hepatomegaly. After the elevated transaminases were detected, the patient was evaluated for viral hepatitis, brucellosis, autoimmune hepatitis and salmonellosis. A Widal test showed titres of 1:200 for *Salmonella typhi* O (somatic) and H (flagellar) antigens. A urine sample was collected and tested positive for *S. typhi* with a titre of 4×10^4 cfu/mL. The patient was hospitalized, and treatment with amoxicillin-

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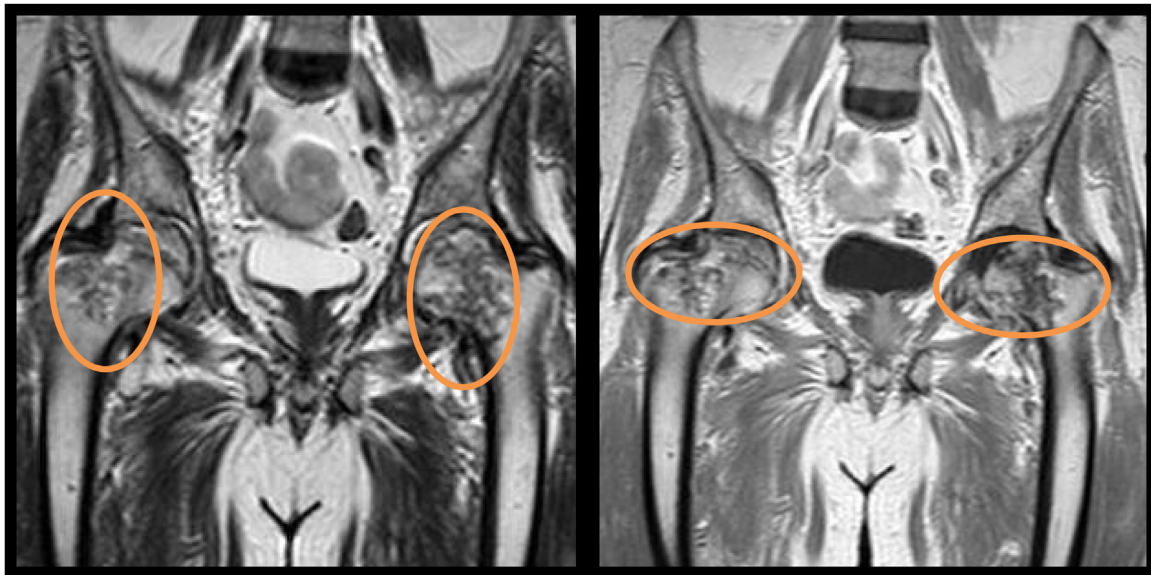


Fig. 1. MRI scan of hips showing the extent of osteomyelitis at the proximal femur.



a) Before antibiotherapy b) Control CT on the fourth week c) Control CT on second month

Fig. 2. CT image of pulmoner consolidation and, regresion with treatment response.

clavulanate and ciprofloxacin was initiated according to the antibiogram.

The patient had a cough and complained of hip and thigh pain, so he underwent further evaluation. As no pathology was observed on plain radiographs, hip and femur magnetic resonance imaging (MRI) scans and a thoracic computed tomography (CT) scan were performed. The MRI revealed osteomyelitis in the proximal femur with microcavities and bone infarcts (Fig. 1). The thoracic CT scan demonstrated infiltration in both the upper and lower lobes and a cavity in the lower right lobe (Fig. 2). These lesions were thought to be septic embolisms. Antibiotherapy was maintained without any changes. *S. typhi* also grew in the blood and sputum cultures. The strain was fluoroquinolone-sensitive.

After experiencing pain relief and fever reduction, the patient was discharged in the fifth week with oral ciprofloxacin. Two weeks after discharge, he returned to the hospital with cough, fever, bilateral shoulder pain and stomach pain. He was hospitalized again and examined to identify the cause of the pain. Urine, blood and sputum cultures were taken, and arm and shoulder MRI scans and an abdominal CT scan were performed. The shoulder MRI revealed osteomyelitis in the proximal humerus and effusion in the glenohumeral joint (Fig. 3). There was no pathology on the abdominal CT scan, but the stomach pain continued, and intermittent diarrhoea was added to his complaints. A colonoscopy identified terminal ileitis, and a biopsy was performed of the colonic

ulcers. A histopathological examination of the colon specimen revealed chronic inflammatory changes. No exact clinical improvement was observed with that therapy, and the treatment was changed to 3 × 1 gr/day of meropenem. Whole-body bone scintigraphy was carried out to identify any other osteomyelitis foci. Uptake increases were detected on the humerus, femur, hip and tibia. Biopsies were carried out via surgical intervention from both hips and shoulders, but there were no specific histopathological findings or growth on cultures. A control thoracic CT scan showed no sequelae images after pneumoniae. Meropenem was continued for four weeks. After discharge, the patient continued his antibiotherapy with oral ciprofloxacin until normal CRP levels were achieved and maintained within four months. During outpatient visits, he reported that his complaints had regressed, and no new and active lesions were observed.

Discussion

Salmonella species usually cause gastroenteritis and enteric fever. However, salmonellosis can also lead to bacteraemia and focal infections in various tissues, including bones and joints [1]. There are some case reports in the literature of abscesses (liver, subphrenic space, ovary, thyroid, psoas muscle) [4]. Salmonella osteomyelitis is rare and represents 0.45% of all types of osteomyelitis [5]. It is most likely to occur in patients with sickle

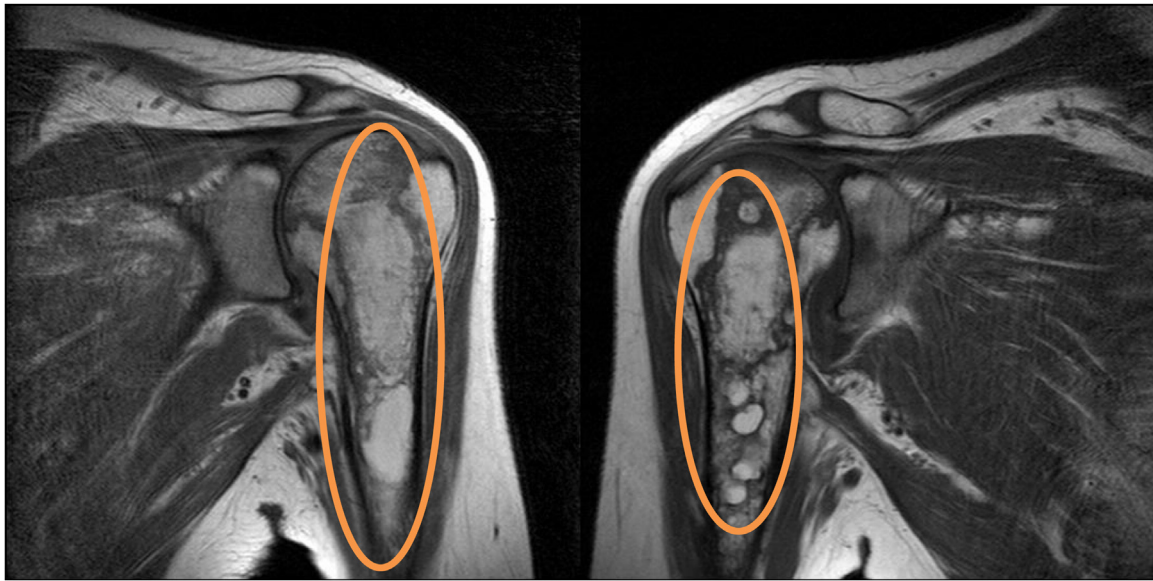


Fig. 3. MRI scan of both shoulders and proximal humerus showing the osteomyelitis.

cell haemoglobinopathy, SLE, neoplasm (particularly haematologic malignancies), immunosuppressive therapy, cranial surgery, trauma, prolonged exposure to the organism or AIDS [6,7].

Translocation of salmonella from the intestinal lumen to the submucosa, mesenteric lymph nodes and distant organs requires disruption of the mucosal barrier or suppression of the host's immunity. In our case, the patient had been treated with a steroid and methotrexate, increasing his susceptibility to salmonella infection. The most important effects of glucocorticoids on the innate and adaptive immune response are downregulation of TNF- α and IFN- γ secretion and the reduction of dendritic cells [8]. Treatment with glucocorticoids also influences the barrier function of the intestines. The histopathology of the intestines in corticosteroid-treated animals demonstrates changes that result in an increase in bacterial adhesion to the mucosa and translocation to mesenteric lymph nodes [9]. However, there are cases of salmonella osteomyelitis that develop in immunocompetent patients in the literature [10,11].

Salmonella infection at various sites requires rapid intervention, correct diagnose and appropriate treatment. The more likely reason of the second hospitalization of our patient is undertreatment because of widespread focal involvements. The antibiotic therapy in Salmonella infections must be given for extended period of time, for up to 4–6 weeks depending upon the site of infection and serotype of Salmonella. Specific surgical intervention is often necessary in conjunction with antibiotic management. Antibiotic resistance in Salmonella is a global concern that includes multi-drug resistant (MDR) strains. With the emergence of MDR *S. typhi*, either fluoroquinolones or third generation cephalosporins are currently recommended for empirical antibiotic treatment. Fluoroquinolone resistance is an important emerging factor and it was reported as 41.8% by CDC [12]. In this case the strain, isolated from blood and the urine culture, was sensitive to fluoroquinolone. Ciprofloxacin was chosen for initial therapy. We based our treatment according to osteomyelitis symptoms and findings, the other organ involvements had already been recovered during the treatment. Gulan et al. treated their patient with Salmonella osteomyelitis for 4 weeks but here we maintained antibiotherapy for 4 months, until symptoms, laboratory and radiological findings were normal [13].

In conclusion, Salmonella are enteropathogenic microorganisms that also have some extraintestinal manifestations affecting

bones, joints, lungs and other the organs. For an infectious process with atypical course and/or multiorgan involvement particularly in the endemic regions, immunocompromized patients with salmonellosis should definitively be included in the differential diagnosis.

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Competing interests

None declared.

Ethical approval

Not required.

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