



CASE REPORT

Salmonella osteomyelitis in an immunocompromized patient presenting as a primary lymphoma of the bone

Tobias Schulze*, Angelika Lüdtke, Ilka Rahlff, Per-Ulf Tunn, Peter Hohenberger

Division of Surgery and Surgical Oncology, Charité, Campus Berlin-Buch, Berlin, Germany

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KEYWORDS

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Summary During the past few decades, an increasing number of immunosuppressive drugs have been developed to treat autoimmune and rheumatic diseases, as well as post-transplant patients. In parallel, the incidence of immunocompromized patients in the general population has risen, for example, patients who are HIV positive, undergoing hemodialysis or suffering from diabetes mellitus. In such predisposed patients, infections with organisms of even reduced invasive potential can result in atypical invasive manifestations.

In industrialized countries, an increase in the number of human non-typhoid *Salmonella* infections was observed in the 1980–1990 s [Shimoni Z, Pitlik S, Leibovici L, Samra Z, Konigsberger H, Drucker M, et al. Nontyphoid *Salmonella* bacteremia: age-related differences in clinical presentation, bacteriology, and outcome. Clin Infect Dis 1999;28:822–7]. Beyond the main clinical manifestation of gastroenteritis, there is an increasing prevalence of extra-intestinal infections by this pathogen. We report a patient with acute osteomyelitis due to *Salmonella typhimurium* without any previous signs of gastroenteritis.

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Case report

A 63-year-old male was referred from a district hospital with the diagnosis of lymphoma of the right femur associated with periosteal abscess formation (Figure 1). Painful swelling of the calf had developed, leading to significant function loss of

the leg during the previous eight weeks. These symptoms were accompanied by three episodes of fever up to 38.9 °C and shivering. The patient had a medical history of arterial hypertension, diabetes mellitus controlled by oral antidiabetics, and pulmonary fibrosis treated with oral cortisone (8 mg/day) and azathioprine (100 mg/day) for several years. Deep venous thrombosis had been excluded by duplex sonography. An MRI scan showed an infiltrating intramedullary process replacing normal bone marrow within the right femur, compatible with lymphoma and accompanied by massive myositis. A chest X-ray suggested a polycyclic tumorous enlargement of the left lung hilus. These symptoms had been interpreted as a malignant lymphoma of the femur and

* Corresponding author. Division of Surgery and Surgical Oncology, Robert Roessle Hospital and Tumor Institute at the Max Delbrück Center for Molecular Medicine, Charité, Campus Berlin-Buch, The Humboldt University, Lindenberger Weg 80, D-13125 Berlin, Germany Tel.: +49 30 9417 1407; fax: +49 30 9417 1439.

E-mail address: tobias.schulze@charite.de (T. Schulze).

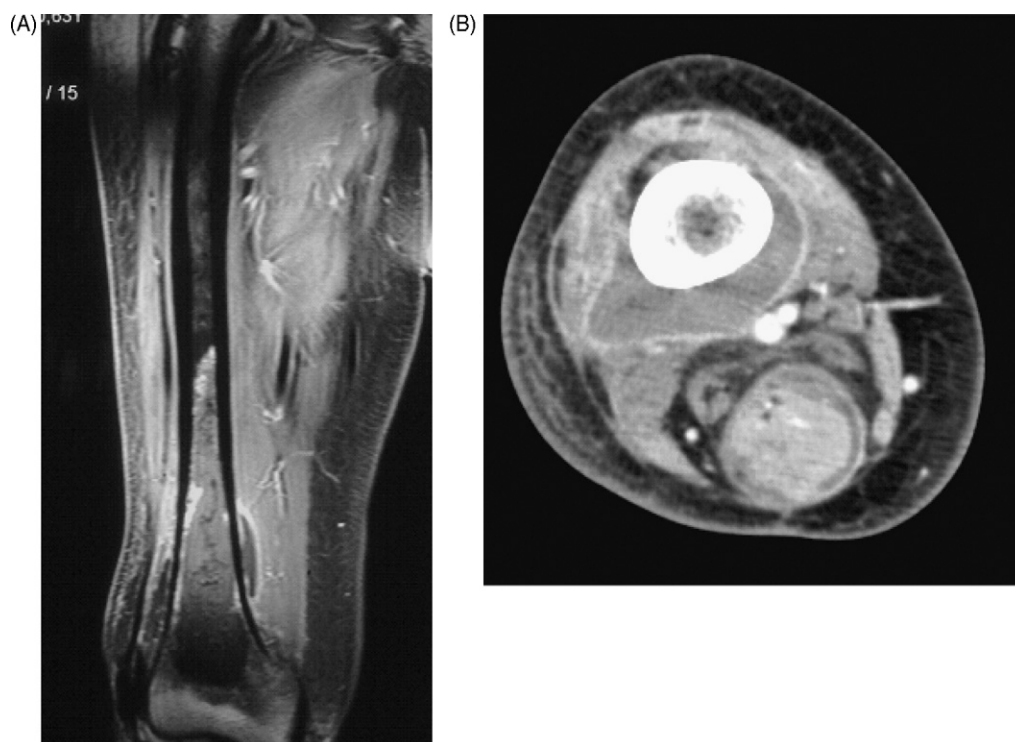


Figure 1 MRI scan of the femur, showing (A) the extent of *Salmonella* osteomyelitis within the distal femur, and (B) periosteal and submuscular abscess formation.

mediastinal lymph nodes, accompanied by B symptoms. Antibiotic therapy with clindamycin had been started in the referring hospital.

The patient was in a reduced physical condition, but blood pressure, heart rate and abdomen did not show any abnormalities. The right knee, calf and thigh were swollen and tender, with elevated temperature and livid color of the overlying skin. WBC count was 19.5×10^9 cells/l and C-reactive protein was 47 mg/l (normal < 5 mg/l). Other blood chemistry was within normal limits. Plain radiographs of the right knee revealed no destruction of bony structures. A CT scan of the thorax confirmed pulmonary fibrosis, but revealed no tumorous lymph nodes. ^{99m}Tc bone scintiscan showed accumulation of activity at the right femur and thoracic vertebrae 7 and 8. A CT-guided biopsy of the soft tissue process and the femur corticalis revealed non-specific myositis and acute destructive osteomyelitis without signs of malignancy. The microbiological workup resulted in *Salmonella typhimurium*. Sequestrotomy, lavage, local antibiotic treatment and drainage were performed. Consequently, local symptoms improved. However, on the fifth post-operative day, the patient developed septicemia with cardiocirculatory and respiratory insufficiency, to which he finally succumbed on day nine. Autopsy revealed severe pseudo-membranous colitis.

Discussion

Infections with non-typhoid *Salmonella* species are most frequently acquired through consumption of contaminated food, in particular uncooked eggs, poultry and meat products. Usually, the incubation period is 7 hours to 2 days, and the infection presents as self-limiting gastroenteritis. *Sal-*

monella serotypes *typhimurium* and *enteritidis* account for 83% of infections,² leading to diarrhea, vomiting, abdominal cramps and low-grade fever. Temperatures return to normal within 48–72 hours and diarrhea resolves within 10 days. Specific antibiotic treatment is not warranted, but fluid and electrolyte replacement might be necessary in elderly patients or those with underlying disease. Hospital admission is required in 13–29% of cases.^{2,3} Less than 6% of immunocompetent patients were reported to be bacteremic. Focal infections of various organs occur during septicemia and can involve almost all organ systems.

Salmonella arthritis and osteomyelitis occur with a frequency of less than 1%, and clinical signs of recent gastrointestinal infection cannot always be seen.^{4–6} Clinical signs of osteomyelitis include fever, bone pain, soft tissue swelling and leukocytosis, and are not indicative of the causative agent. Diaphysis and epiphysis of femur, tibia and humerus, as well as lumbar vertebrae, represent the most affected sites. *S. typhimurium* and *S. enteritidis* are the most common serotypes of human non-typhoid *Salmonella* infections, but recently other serotypes have been observed significantly more frequently.^{7,8}

Immunity to *Salmonella* infection requires interplay between the innate and the adaptive immune systems.⁹ After ingestion, passage of *Salmonella* occurs via the epithelial M cells overlaying Peyer's patches, invasion of enterocytes or shuttling by cells that physiologically breach the epithelial layer, for example, dendritic cells (DCs). The presence of *Salmonella* on the basal site of enterocytes leads to the secretion of chemokines (IL-8, MIP-3 α , MIP-2 and TNF- α), attracting cells of the innate immune system (neutrophils, macrophages, DCs and natural killer [NK] T cells). The expression of co-stimulatory molecules is upregulated soon after

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