**Salmonella Enterica Serotype Enteritidis Vertebral Osteomyelitis and Epidural Abscess Complicated with Meningitis**

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Infection with non-typhoidal *Salmonella* often results in a self-limited acute gastroenteritis. Extra-intestinal *Salmonella* infection is relatively rare and occurs predominantly in infants and adults with significant underlying conditions. We describe a 54-year-old Japanese man with a history of heavy alcohol consumption and daily contact with a dog, who developed bacteremia complicated by vertebral osteomyelitis, spinal epidural abscess, and meningitis, due to *Salmonella enterica* serotype Enteritidis. This case suggests that *Salmonella* should be considered as an etiologic pathogen in adult patients with perivertebral infection or meningitis.

**Key words:** *Salmonella* Enteritidis, vertebral osteomyelitis, epidural abscess, meningitis

**INTRODUCTION**

*Salmonella enterica* serotype Enteritidis (SE) is most often a foodborne infection associated with poorly prepared or raw egg or poultry. It may also be contracted from pet animals and contaminated pet food [1]. Infection with non-typhoidal *Salmonella* most often manifests as a self-limited acute gastroenteritis. Among immunocompetent individuals with *Salmonella* infection, 1–4% has positive blood cultures. Extra-intestinal forms of SE infection, with or without bacteremia, are relatively uncommon and predominantly occur in patients with significant underlying disease. Collagen disease, malignancy, diabetes mellitus, human immunodeficiency virus (HIV) infection, immunosuppressive therapy, and sickle cell disease are considered to be predisposing factors. We describe a 54-year-old Japanese man with a history of heavy alcohol consumption and daily contact with a dog, who developed not only bacteremia, but also vertebral osteomyelitis, spinal epidural abscess, and meningitis due to SE. To the best of our knowledge, this is the first report of meningitis, osteomyelitis, and spinal epidural abscess, due to non-typhoidal *Salmonella* in an adult.

**CASE REPORT**

A 54-year-old Japanese man was admitted to Tokai University hospital with a 5-day history of loose stool followed by fever and severe low back pain. He reported living at home with a pet dog that was kept indoors. He denied eating raw eggs, uncooked eggs, or poultry, and having a contact with animals such as rodents or amphibia other than dogs. His past medical history was unremarkable except for a history of heavy alcohol consumption, equivalent to 140 g of alcohol per day, for more than 20 years. On admission, he was mildly confused during conversation and his temperature was 38.5°C. Physical examination was unremarkable with no sign of hepatosplenomegaly, palmar erythema, or spider angioma. Neurological examination revealed no focal deficit; however, neck stiffness, and both Kernig's and Laségue's sign were present. Laboratory examinations revealed the following: white blood cell count, 4,700/µL (83% neutrophils and 8% lymphocytes); hemoglobin, 15.4 g/dL; platelets, 6 × 10^4/µL; erythrocyte sedimentation rate (ESR), 44 mm/h; Immunoglobulin G (IgG), 1620 mg/dL; IgM, 783 mg/dL; and IgA, 69 mg/dL. The antibody against HIV was negative. Lumbar puncture yielded cloudy cerebrospinal fluid (CSF). Glucose, protein, and leukocyte count in the CSF were 54 mg/dL (comitant blood glucose 130 mg/dL), 901 mg/dL, and 587/µL (95% neutrophils, 1% lymphocytes), respectively. A plain lumbar spine radiograph did not show any destructive changes. However, MRI showed decreased signal intensity in the vertebral bodies of L3-S2 and the L4/5 disc on T2-weighted images and increased intensity on T2-weighted images. Spinal epidural abscess was seen adjacent to the L4/5 disc lesion, with peripheral enhancement by gadolinium on T1-weighted images (Figure). MRI of brain was unremarkable. Empiric antibiotic treatment was started soon after all cultures were taken. CSF, blood, and stool cultures showed the growth of SE sensitive to β-lactam and new quinolone antibiotics. Minimal inhibitory concentrations (MIC) of antibiotics were as follows: ampicillin 0.25 µg/mL, cefazolin 8µg/mL, norfloxacin 4µg/mL. The results of MIC were exactly the same among sites of samples. Antibiotics were changed to 300 mg ciprofloxacin and 2 g ceftriaxone given intravenously every 12 hours, after culture results became available. The patient’s temperature and mental state improved promptly. Thereafter, he mentioned he slept together with his dog in the same bed. Repeated blood and CSF cul-
tures became sterile after a week of treatment and the absolute lymphocyte counts were normalized to greater than 2,000/µL. Intravenous ceftriaxone and ciprofloxacin were discontinued after 2 weeks of treatment and oral ciprofloxacin was continued for 3 months. After 3 months of oral antibiotic treatment, the ESR normalized and the spinal epidural abscess was no longer apparent on repeat MRI. He was discharged with no neurologic sequelae.

DISCUSSION

Etiologic pathogens for pyogenic vertebral osteomyelitis of hematogenous origin have been well described in the literature. Staphylococcus aureus accounts for 50–80% of cases. Less than 1% of patients with osteomyelitis have Salmonella as the causative agent [2]. Osteomyelitis due to Salmonella occurs predominantly in individuals with significant underlying conditions, such as collagen disease, malignancy, diabetes mellitus, or sickle cell disease. The relationship between sickle cell disease and Salmonella osteomyelitis has long been recognized. More than 70% of cases of osteomyelitis seen in patients with sickle cell disease are due to Salmonella [3]. However, the mechanism for the increased susceptibility to Salmonella in sickle cell patients is not completely understood. There have been only 18 cases of vertebral osteomyelitis due to Salmonella in the absence of sickle cell disease reported over the last three decades [2, 4–19]. The lower thoracic spine was most often affected followed by the lumbar spine [7]. Only two cases had cervical spine involvement. In terms of predisposing conditions, two patients had diabetes mellitus, one had leukemia, one had collagen disease, one had alcoholism, and three cases were reported from an endemic area.

In an experimental model, alcohol was shown to have deleterious effects on leukocyte mobilization, phagocytosis, intracellular killing of bacteria, and T-helper 1 lymphocytes-mediated cellular response [15–17]. In our patient, heavy alcoholic consumption and close contact with his dog were considered to contribute to the development of his extensive Salmonella infection, similar to a case reported by Akagi et al. [18]. The estimated prevalence of Salmonella infection in healthy dogs is 1–36%, which is higher than expected. Contaminated raw food, or water, and coprophagia from infected rodents infected non-typhoidal Salmonella to most dogs via oral route. Extra-intestinal infections were closely related to non-typhoidal Salmonella, mainly Salmonella Enteritidis and Salmonella Typhimurium. Non-typhoidal Salmonella bacteremias are usually due to strains encoding the spv locus [19]. Resistance to spv-expressing Salmonella causing disseminated infection appear to require acquired immunity mediated by CD4+ T cells as demonstrated in mice and by the high incidence of spv+ non-typhoid Salmonella bacteremia in HIV infection. Unfortunately, we could not investigate the SE encoding spv gene in this case. In the multivariable model of Canadian SE study [20], there was positively association with contact with dogs and SE phage type 8 (PT8) infection when compared to the non-PT8/non-PT13a groups while accounting for age and gender (odds ratio = 2.17, 95% confidence interval: 1.01-4.68). Further investigations are needed to confirm these findings in other countries or larger cohorts. On the other hand, immunocompetent hosts are shown to be older and have symptoms of gastroenteritis more
frequently than immunocompromised hosts, in adults with non-typhoidal *Salmonella* bacteremia [21]. This concept is consistent with our case, and heavy alcohol consumption can affect his macrophage function and susceptible to log-term intracellular SE growth in gut, leading to secondary bacteremia causing osteomyelitis, epidural abscess complicated with meningitis.

The formation of an epidural abscess due to *Salmonella* is a rare event. Most cases of cranial epidural abscess due to *Salmonella* reported to date occurred without adjacent osteomyelitis, suggesting a hematogenous spread of infection. In contrast, spinal epidural abscesses mostly occurred in association with adjacent osteomyelitis, suggesting direct extension of the infection. This may be explained by the presence of infected intervertebral discs. Our patient clearly showed signs of discitis on MRI, and it is reasonable to assume the drainage of pus from disc led to the formation of the spinal epidural abscess. Meningitis due to *Salmonella* is an extremely rare complication and primarily occurs in infants with a high mortality rate [22]. It has been reported that the CSF accounts for less than 1% of *Salmonella* isolation sites [23]. Several cases of meningitis caused by *Salmonella* in adults without significant predisposing conditions have been reported [24–27]. However, most were caused by species other than SE. Since meningitis can occur without infection of the adjacent tissue, possibly by hematogenous spread, it is difficult to speculate whether meningitis in our case was due to direct extension of the epidural abscess or hematogenous spread.

Despite the extensive extra-intestinal involvement, our patient was successfully treated with intravenous antibiotics without the need for surgical intervention. This may suggest that the lack of significant underlying conditions, besides heavy alcohol consumption, had a favorable effect on successful medical treatment. In addition, seeking medical attention early in the course of disease before bone destruction began may have also contributed to the good result. It should be emphasized that *Salmonella* should be a differential diagnosis in patients with perivertebral infection and/or meningitis who are alcoholic or have close contact with dogs in addition to other predisposing factors.

All authors declare no conflict of interests.

**REFERENCES.**