Case Report

Salmonella enterica serovar Minnesota urosepsis in a patient with Crohn's disease in the absence of recent or current gastrointestinal symptoms

Niels Steinebrunner,1 Catharina Sandig,1 Stefan Zimmermann,2 Wolfgang Stremmel,1 Christoph Eisenbach1 and Alexander Mischnik2

1Department of Gastroenterology, Intoxications and Infectious Diseases, Heidelberg University Hospital, Im Neuenheimer Feld 410, 69120 Heidelberg, Germany
2Department of Infectious Diseases, Medical Microbiology and Hygiene, Heidelberg University Hospital, Im Neuenheimer Feld 324, 69120 Heidelberg, Germany

Salmonella enterica serovar Minnesota is a rarely isolated organism in clinical samples mainly grown from stool cultures. Sepsis due to Salmonella is known in severely immunocompromised patients, but so far urosepsis due to S. enterica serovar Minnesota has not been described. We report a case of a 31-year-old patient suffering from Crohn's disease treated with infliximab and azathioprine, in whom was implanted a double-J ureteric catheter for urolithiasis. The patient presented with urinary tract infection and severe sepsis. S. enterica serovar Minnesota was grown from urine and blood cultures. After empiric antimicrobial treatment with meropenem and vancomycin, treatment was changed to ceftriaxone. Antimicrobial treatment was continued for a total of 3 weeks without evidence of Salmonella recurrence on follow-up visits. Salmonella spp. rarely cause urinary tract infection and sepsis. However, in immunocompromised patients, non-typhoidal salmonellosis merits a thorough clinical and microbiological evaluation.

Introduction

Salmonella enterica serovar Minnesota first emerged in literature in the 1950s (Borbolla et al., 1956; McCracken, 1954). Since the initial description, the organism has only rarely been isolated from clinical patient specimens. Salmonella infection is mostly associated with gastro-enteritis, or can rarely cause typhoid-like illnesses, even in immunocompromised patients (Eckerle et al., 2010). To the best of our knowledge, urosepsis due to Salmonella spp. without presenting gastrointestinal symptoms has not been described previously.

Case report

A 31-year-old male patient was admitted to the emergency department with somnolence, high fever (39.8 °C), tachycardia and acute renal failure. On admission, his medication consisted of infliximab (5 mg kg⁻¹ every 4 weeks) and azathioprine (150 mg daily) for treatment of Crohn’s disease. The patient denied the use of any other medication. Nine years previously, a loop ileostomy was created due to perianal fistulas. Current stool consistency and frequency was unchanged with eight to ten ileostomy bag changes per day. Physical examination showed abdominal guarding and a right flank pain.

Laboratory findings revealed a leukocyte count of 4.25 nl⁻¹ (normal 4–10 nl⁻¹), a C-reactive protein level of 184.1 mg l⁻¹ (normal <5 mg l⁻¹), a procalcitonin level of 440.05 ng ml⁻¹ (normal <0.05 ng ml⁻¹), a serum creatinine level of 15.66 mg dl⁻¹ (normal 0.1–1.3 mg dl⁻¹) and a urea nitrogen level of 308 mg dl⁻¹ (normal <45 mg dl⁻¹). His international normalized ratio was elevated to 1.29. Arterial blood gases showed a pH of 7.32, a pCO₂ of 11 mmHg, a pO₂ of 98 mmHg and a base excess of −18.2 mmol l⁻¹. His lactate level was not elevated at 0.80 mmol l⁻¹ (normal 0.9–1.6 mmol l⁻¹).

Because of compensatory hyperventilation due to acidosis and imminent respiratory failure, the patient was intubated and mechanically ventilated. After collection of urine and blood cultures, empiric antibiotic treatment with meropenem and vancomycin was started. Immunosuppressive therapy was discontinued.

Urinalysis revealed 10 702 leukocytes μl⁻¹ and was strongly positive for bacteria. Five months earlier, a double-J catheter had been placed in the right ureter because of an obstruction of urinary flow due to urolithiasis causing hydronephrosis and post-renal kidney failure. The double-J catheter was promptly exchanged and replaced by two bilateral externally draining single-J catheters. Fluid
resuscitation was started and the initially high demand for catecholamines following intubation could incrementally be tapered.

Clinical work-up revealed no infectious focus other than the urinary tract system. Abdominal ultrasound revealed a minimally dilated renal pelvis on the right side and no signs of abscesses. Transthoracic echocardiography and chest and abdominal X-rays were normal.

On the second day following admission, urine culture ($10^5$ c.f.u. ml$^{-1}$) as well as blood cultures yielded *Salmonella enterica*. The National Reference Center for Salmonellae and Other Enteric Pathogens (Robert Koch-Institut, Wernigerode, Germany) identified *S. enterica* serovar Minnesota by agglutination testing and lysotyping. Antimicrobial susceptibility testing revealed resistance to ampicillin, cefuroxime and aminoglycosides according to the European Committee on Antimicrobial Susceptibility Testing guidelines (EUCAST, 2013).

Haemodialysis was performed on days 1, 2 and 6 following admission until spontaneous urine production returned and retention parameters declined. After 3 days on mechanical ventilation, the patient was extubated. At this time, laboratory findings showed a leucocyte count of 3.30 nl$^{-1}$, a C-reactive protein level of 169.9 mg l$^{-1}$, a procalcitonin level of 126.15 ng ml$^{-1}$, a serum creatinine level of 3.11 mg dl$^{-1}$, a urea nitrogen level of 85 mg dl$^{-1}$ and an international normalized ratio of 1.08. Urinary white blood counts were still high but had dropped to 4723 ml$^{-1}$. Antibiotic treatment with meropenem and vancomycin was downscaled to ceftriaxone and subsequently applied for a total of 3 weeks until cultures of urine were negative for *Salmonella*. Several stool cultures taken on days 4, 5 and 17 during hospitalization did not yield the organism.

**Discussion**

Strains of *Salmonella* are categorized as typhoidal and non-typhoidal, corresponding to the symptoms caused by infection. Strains of non-typhoidal *Salmonella* (NTS) usually cause an intestinal infection (accompanied by diarrhea, fever and abdominal cramps) that might last 1 week or longer (Hohmann, 2001). *Salmonella* is not a common microorganism to cause sepsis. When causative, *Salmonella* sepsis can be a very dangerous disease (Lee et al., 1994b). Nevertheless, the incidence of NTS infections has risen in recent years (Weinberger et al., 2004). Most NTS infections cause gastroenteritis. Invasive diseases are only seen in 3–8% of patients infected by NTS (Mandal & Brennand, 1988). The patient reported here never presented abdominal symptoms although suffering from Crohn’s disease, which is remarkable. Current stool consistency and frequency was unchanged with eight to ten ileostomy bag changes per day and no abdominal pain. To the best of our knowledge, the patient was not vaccinated against typhoid fever, which could potentially have explained the attenuated clinical course.

Patients experiencing severe *Salmonella* infections are typically immunocompromised due to co-morbidities such as malignancy, human immunodeficiency virus infection, diabetes and treatment with corticosteroids or other immunotherapy agents (Yen et al., 2007). In our patient, Crohn’s disease and treatment with infliximab and azathioprine were important risk factors to explain the susceptibility for *Salmonella* sepsis. In immunocompromised patients, NTS bacteraemia mostly occurs without gastroenteritis (Ramos et al., 1994).

Extra-intestinal *Salmonella* infections may occur at different sites of infection. Urosepsis due to *Salmonella* is a rare disease, and there are only a few cases published in the literature (Cohen et al., 1987; Ramos et al., 1996). In a series of 7779 *Salmonella* infections reported by Saphra & Winter (1957), 49 (0.6%) involved the urinary tract. The four most common serotypes among urinary infections were *Salmonella typhimurium* ($n=16$), *Salmonella oranienburg* ($n=7$), *Salmonella paratyphi C* and *Salmonella choleraesuis* ($n=6$), and *Salmonella montevideo* ($n=3$).

Treatment options usually comprise fluoroquinolones. Third-generation cephalosporins are a reasonable treatment alternative. There are no clinical data that suggest that combination therapy (e.g. a fluoroquinolone plus a third-generation cephalosporin) is more effective than treatment with a single agent (Hohmann, 2001). Antimicrobial resistance, particularly multiple drug resistance, has been noted in several NTS and is a rising problem (Lee et al., 1994a; Stevenson et al., 2007). Treatment with the appropriate antimicrobial agent is crucial for patients with invasive *Salmonella* infections, and the susceptibilities of these isolates should be reported as soon as possible (Lee et al., 1994a). Because of the severity on admission, an initial treatment with meropenem plus vancomycin was given according to the guidelines for treatment of sepsis (Dellinger et al., 2004). When the results of the susceptibility testing became available, treatment was de-escalated to ceftriaxone.

The most interesting point of the case report is the source of infection, which remains unknown. Animal contact is an important source of human non-typhoidal infection (Hoelzer et al., 2011). The range of animals that harbour *Salmonella* spp. is wide and even includes reptiles (Hinshaw & McNeil, 1945). In the present case, the organism could not be isolated from various faecal samples. The patient did not have any pets or contact with other animals. Before admission, he had not been travelling abroad or visited zoos. From his work in a museum, he had much contact with visitors, which did not seem to be a relevant reservoir for *Salmonella* spp.

In conclusion, *Salmonella* spp. rarely cause urosepsis or severe sepsis. However, in immunocompromised hosts, salmonellosis may present as a severe disease. To the best of our knowledge, this is the first case of urosepsis due to *S. enterica* serovar Minnesota in a patient with Crohn’s disease without abdominal symptoms. Therefore, extra-intestinal *Salmonella* infections have to be taken into
consideration in immunocompromised patients presenting with sepsis. Immunocompromised patients should be aware of the risk of transmission when having contact with human carriers of Salmonella spp. or with reptiles.

Acknowledgements

We thank the National Reference Center for Salmonellae and Other Enteric Pathogens, Robert Koch-Institut, Wernigerode, Germany, for specification of the isolate.

References


