

Nontyphoidal *Salmonella* Urinary Tract Infection in a Case of Hyperparathyroidism and Nephrocalcinosis

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ABSTRACT

Nontyphoidal Salmonella infections often present with self-limited gastroenteritis. Extraintestinal focal infections are uncommon but have high mortality and morbidity. Urinary tract infection caused by nontyphoidal *Salmonella* is usually associated with structural abnormalities of the urinary tract. Nephrocalcinosis and nephrolithiasis are the major risk factors. Although primary hyperparathyroidism has been reported to increase the risk of nephrocalcinosis and nephrolithiasis, little is known about the association between hyperparathyroidism and *Salmonella* urinary tract infection. We report the case of a 37-year old man who had a history of primary hyperparathyroidism and bilateral nephrocalcinosis and who developed urinary tract infection. *Salmonella* Group D was isolated from his urine specimen. *Salmonella* should be considered as a possible causality organism in patients with primary hyperparathyroidism and nephrocalcinosis who develop urinary tract infection. These patients need to be aware of the potential risks associated with salmonellosis.

Keywords: Hyperparathyroidism, nephrocalcinosis, *Salmonella*, urinary tract infections

Infección de las Vías Urinaria por *Salmonella* No Tifoidea en un Caso de Hiperparatiroidismo y Nefrocalcinosis

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RESUMEN

Las infecciones por Salmonella no tifoidea se presentan a menudo con gastroenteritis auto-limitada. Las infecciones extra-intestinales focales son poco frecuentes, pero tienen una alta mortalidad y morbilidad. La infección de las vías urinarias causada por la Salmonella no tifoidea se asocia generalmente a anomalías estructurales de las vías urinarias. La nefrocalcinosis y la nefrolitiasis son los principales factores de riesgo. Aunque se ha reportado que el hiperparatiroidismo primario aumenta el riesgo de la nefrocalcinosis y la nefrolitiasis, poco se sabe sobre la asociación entre el hiperparatiroidismo y la infección de las vías urinarias por Salmonella. Damos a conocer aquí el caso de un hombre de 37 años con una historia de hiperparatiroidismo primario y nefrocalcinosis bilateral, que desarrolló una infección de las vías urinarias. La Salmonella del grupo D fue aislada de su muestra de orina. La Salmonella se debe considerar como un posible organismo de causalidad en pacientes con hiperparatiroidismo primario y nefrocalcinosis que desarrollan infección del tracto urinario. Estos pacientes necesitan tomar conciencia de los riesgos potenciales asociados con la salmonellosis.

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Palabras claves: Hiperparatiroidismo, nefrocalcinosis, *Salmonella*, las infecciones del tracto urinario

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INTRODUCTION

Infections with nontyphoidal *Salmonella* often present with self-limited acute gastroenteritis. Extraintestinal focal infections are associated with a higher mortality and morbidity (1, 2). Urinary tract infection caused by nontyphoidal *Salmonella* is uncommon but carries a high risk of relapse and mortality (3). The isolation of nontyphoidal *Salmonella* from urine specimens is commonly related to structural abnormalities of the urinary tract. Nephrocalcinosis and nephrolithiasis are the major risk factors of urinary tract infection by *Salmonella*.

Although primary hyperparathyroidism has been reported to increase the risk of nephrocalcinosis and nephrolithiasis, to our knowledge, no association between primary hyperparathyroidism and *Salmonella* urinary tract infection has been previously described.

Here, we present a case of bilateral nephrocalcinosis due to primary hyperparathyroidism with recurrent *Salmonella* urinary tract infection.

CASE REPORT

A 37-year old man presented to the emergency room with a three-day history of fever, chills, and abnormally coloured urine. Right flank pain and anorexia developed one week before the visit. He did not have headache, neck stiffness, photophobia, shortness of breath, vomiting, diarrhoea, jaundice, or weight loss.

The patient had a history of primary hyperparathyroidism and had undergone partial parathyroidectomy three years earlier. Bilateral nephrocalcinosis was also noted (Figure). He did not have a history of hepatitis, pancreatitis, or



Figure: Abdominal computed tomography scan shows calcifications in the renal medulla of both kidneys.

cholecystitis. But he had a habit of eating undercooked seafood.

On examination, his temperature was 38.9 °C, respiratory rate was 25 per minute, pulse rate was 119 per minute, blood pressure was 113/79 mmHg, and he had an ill appearance. The oropharynx was without exudates, and the neck was supple. The chest was clear on auscultation; the heart sounds were regular, without murmur. The patient's abdomen was not tender. On percussion, the patient had tenderness bilaterally in the costovertebral angles. No splinter haemorrhages or Osler's nodes were seen. A rectal examination revealed no blood or mass lesion. The skin was not jaundiced and there was no rash or ulcers.

The patient's white cell count was 12 100 per cubic millimetre, with a differential count of 87 per cent neutrophils. Urinalysis reported 35 to 50 leukocytes, occasional red cells, and moderate numbers of bacteria per high-power field.

At first, intravenous cefazolin was given for empirical treatment of urinary tract infection. The patient's urine culture yielded more than 100 000 colony-forming units of *Salmonella* Group D, but blood cultures showed no growth. The isolate was resistant to ciprofloxacin and trimethoprim-sulfamethoxazole. Antimicrobial therapy was changed to ceftriaxone according to the susceptibility result.

Urinary abnormalities subsequently decreased with treatment, and a culture of urine obtained after two weeks of antimicrobial therapy revealed no evidence of bacteria.

DISCUSSION

Nontyphoidal *Salmonella* is a facultative intracellular bacterium. The infections begin with the ingestion of contaminated food or water and generally results in self-limited acute gastroenteritis, with symptoms including diarrhoea, abdominal cramps and fever. Extra-gastrointestinal tract focal infection includes urinary tract infections, meningitis, pneumonia, septic arthritis, or cholangitis (2). Urinary tract infection due to *Salmonella* is uncommon. The reported incidence of urinary tract infection due to nontyphoidal *Salmonella* varies between 0.015% and 0.033% (3). About 18% of them become chronic urinary carriers (4).

Isolation of *Salmonella* organisms from cultures of urine, blood, or other clinical samples is diagnostic. Because it is difficult to differentiate *Salmonella* urinary tract infection from urinary tract infection caused by other bacteria based on symptoms alone, submission of urine specimen for culture is mandatory in susceptible hosts.

Structural abnormality of the urinary tract, immunodeficiency and chronic illness are predisposing factors for nontyphoidal *Salmonella* urinary tract infection. Among them, structural abnormality of the urinary tract may play a more important role. In a study by Ramos *et al*, 52% of *Salmonella*

urinary tract infection had urologic abnormalities (3). Additionally, Hsu and Lin reported 25% to 33% of nontyphoidal salmonellosis in renal transplant recipients presenting with urinary tract infection, while no heart transplant recipients with nontyphoidal salmonellosis presented with urinary tract infection (5). Moreover, calcification in the urinary tract is associated with relapse of the infection (4).

Our case had primary hyperparathyroidism with extensive renal calcification and nephrolithiasis; both are known risk factors for *Salmonella* urinary tract infection. Primary hyperparathyroidism is associated with increased risk of nephrolithiasis. The prevalence of primary hyperparathyroidism in nephrolithiasis is 2–8% (6). In a study of 271 patients with primary hyperparathyroidism, 7% had renal stones (7). Moreover, male gender and a young age at the time of diagnosis of primary hyperparathyroidism provide additional risks for the development of renal stones (8). Although hypercalciuria (9), increased plasma 1,25-dihydroxyvitamin D levels (10) and polymorphism in the calcium-sensing receptor (11) have been proposed as causes of the development of nephrolithiasis, the precise relationship between primary hyperparathyroidism and nephrolithiasis remains unclear (8). Computed tomography is the radiographic test of choice for diagnosis, with parenchymal calcifications being pathognomonic. Parathyroidectomy is considered to be indicated in primary hyperparathyroidism with nephrolithiasis (12), but the risk of renal stones is still increased until 10 years after the surgery (13).

The most frequent pathogenesis of *Salmonella* upper urinary tract infection is probably haematogenous. *Salmonella* enters the body through ingestion and colonizes the ileum and colon. When *Salmonella* invades the blood stream, it can seed distant target organs, such as kidney and cause pyelonephritis. Another route is through fecal contamination of the urinary tract, resulting in cystitis (14). In their 11-year retrospective study of *Salmonella* focal infection, Rodrigues *et al* reported 85% of patients with *Salmonella* cystitis had concurrent diarrhoea, whereas all patients with *Salmonella* pyelonephritis had concurrent bacteraemia (2). In addition, adults are more likely to have primary bacteraemia and have a higher incidence of secondary focal infections (15).

It is assumed that the index case developed salmonellosis from ingestion of contaminated food, probably from undercooked seafood. Outbreaks of nontyphoidal *Salmonella* have been associated with fish, shrimp, oysters and clams (16). Seafood can acquire *Salmonella* from contaminated waters and improper storage or processing. Extensive contamination is possible; a two-year survey in southeast Asia has shown that *Salmonella* were present in 16% of prawns and 22.1% of mud/water samples (17). We suggest that patients with primary hyperparathyroidism and nephrocalcinosis need to be aware of the potential risks associated with salmonellosis. The infections can be prevented by adequate cooking, careful storage and proper handling of foods to avoid cross-contamination (16).

The reported duration of antibiotic therapy in *Salmonella* urinary tract infection ranges from two (for mild infections) to over six weeks (4, 14). Longer duration of treatment was suggested by some experts, due to the high frequency of complicating conditions (18, 19). However, prolong antibiotic therapy is of little benefit so long as the structural lesions remain (3, 4, 19).

In conclusion, *Salmonella* should be considered as a possible causality organism in patients with primary hyperparathyroidism and nephrocalcinosis who develop urinary tract infection. Suspicion of indicative clinical features should prompt the performance of urine culture. Early treatment is mandatory.

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