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Case Report

Kidney allograft pyelonephritis caused by *Salmonella enterica* serovar Schwarzengrund

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ABSTRACT

Kidney transplant recipients (KTRs) taking immunosuppressive drugs have a 20-fold greater risk of nontyphoidal *Salmonella* (NTS) infection than the healthy adult population. Among KTRs, the urinary tract is the most common site of infection. However, few cases of urinary tract infection caused by NTS have been documented in KTRs, and only one in Japan. Furthermore, it frequently induces acute allograft rejection with high mortality. *Salmonella enterica* subsp. *enterica* serovar Schwarzengrund (*S.* Schwarzengrund) is now among the more common *Salmonella* serovars isolated in Japan and is likely to be invasive. We present a case of a 45-year old female with vesicoureteral reflux to her transplanted kidney who developed kidney allograft pyelonephritis caused by *S.* Schwarzengrund. She was admitted to our hospital with fever, urodynia, lower abdominal pain, gross hematuria, and cloudy urine. Urine cultures were positive for *S.* Schwarzengrund. Exposure to cats, especially stray cats, were identified as the most likely source. We administered antibiotics for 4 weeks (ceftriaxone then amoxicillin, each for 2 weeks) and educated her about pet safety. She experienced no recurrence of infection or clinical kidney allograft rejection for 3 months post-treatment. NTS should be considered as a possible pathogen of urinary tract infection among KTRs, especially in cases with animal exposure or structural urologic abnormalities. When the pathogen is NTS, appropriate antibiotics and treatment periods are essential for preventing recurrence and allograft rejection after the completion of treatment.

1. Introduction

Nontyphoidal *Salmonella* (NTS) infection is an enduring global public health concern. Use of immunosuppressive drugs, HIV infection, and malignancy are common risk factors for nontyphoidal *Salmonella* (NTS) infection [1]. Kidney transplant recipients (KTRs) are at 20-fold greater risk of NTS infection than the healthy adult population [2]. The urinary tract is the most common infection site among KTRs [3], accounting for 45%–72% of all infections developed in KTRs [3]. Surprisingly, however, very few cases of urinary tract infection caused by NTS among KTRs have been published [2,4–11], and only one of these was from Japan [8]. Urinary tract infection caused by NTS induces acute allograft rejection in 55% of cases [11] with 27%–29% mortality [9,11]. Furthermore, *Salmonella enterica* subsp. *enterica* serovar Schwarzengrund (*S.* Schwarzengrund) identified in the present case is likely to be invasive [12,13], and is detected at progressively increasing frequency in Japan [14–16].

Here we report a case of kidney allograft pyelonephritis caused by *S.* Schwarzengrund in a Japanese KTR.

2. Case report

A 45-year old female was admitted to our hospital because of fever, urodynia, lower abdominal pain, gross hematuria, and cloudy urine. She had been diagnosed with chronic kidney disease of unknown etiology 9.5 years earlier and began hemodialysis 2 years prior to current presentation. Seven months prior to presentation, she received a living donor kidney transplantation from her husband. From the time of surgery to presentation, she took tacrolimus, mycophenolate mofetil, and methylprednisolone as immunosuppressive drugs, and was also on rabeprazole to

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prevent peptic ulcer. She had not traveled abroad since kidney transplantation.

Six months before admission, she developed kidney allograft pyelonephritis caused by *Enterococcus faecalis*, and a month later again developed kidney allograft pyelonephritis due to *Klebsiella pneumoniae*. At that time, she was diagnosed with grade 3 vesicoureteral reflux of her transplanted kidney (Fig. 1). We followed her closely without surgical intervention because pyelonephritis improved quickly following administration of antibiotics. In particular, we administered piperacillin/tazobactam (13.5 g daily for 5 days), ampicillin/sulbactam (9 g daily for 6 days), and amoxicillin (1500 mg daily for 3 days) against the former, and piperacillin/tazobactam (9 g daily for 3 days), ceftriaxone (2 g daily for 8 days), and cefaclor (750 mg daily for 3 days) against the latter. Four months before admission, she was hospitalized and received ganciclovir for cytomegalovirus colitis. After discharge, she continued taking valganciclovir. Twenty-two days before the current admission, she developed urodynia and cloudy urine without fever. She was diagnosed with bacterial cystitis and received levofloxacin (500 mg daily for 5 days), which improved her symptoms by day 3. At that time, *Salmonella* spp. was isolated in her urine culture using the BD Phoenix system (Becton Dickinson, Tokyo, Japan) and the serotype was identified as O4 using *Salmonella* antisera including only O antigen (Denka Seiken, Gosen, Japan). We are not able to identify H antigen technically in our hospital. The minimum inhibitory concentrations of antibiotics against the isolated *Salmonella* as measured using the broth microdilution method of the BD Phoenix system (Becton Dickinson, Tokyo, Japan) were shown in Table 1. The isolated *Salmonella* was confirmed to be nalidixic acid-resistant. Ten days before admission, her symptoms relapsed. She received amoxicillin (750 mg daily for 5 days) under a diagnosis of cystitis caused by *Salmonella* serotype O4 based on the results of antimicrobial susceptibility testing (Table 1). *Salmonella* serotype O4 was detected in her urine culture again. Although her symptoms improved after 2 days' treatment, she developed fever, urodynia, lower abdominal pain, gross hematuria, and cloudy urine with no gastrointestinal symptoms 5 days after the end of treatment. Subsequently, her symptoms progressively worsened and she was admitted to our hospital.

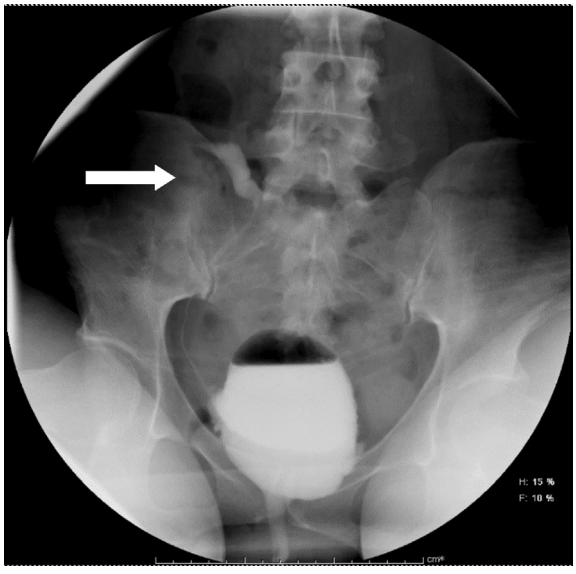

Fig. 1. Voiding cystourethrogram revealed grade 3 vesicoureteral reflux of her transplanted kidney (white arrow).

Table 1
The minimum inhibitory concentrations of antibiotics against the isolated *Salmonella*.

Antibiotics	MIC[a] (μg/mL)
Ampicillin	≤4
Cefotaxime	≤1
Meropenem	≤1
Ciprofloxacin	≤0.5
Trimethoprim-sulfamethoxazole	≥152
Nalidixic acid	Resistant[b]

[a] MIC, minimum inhibitory concentration.
[b] It was confirmed by the disk diffusion susceptibility method (Becton Dickinson, Fukushima, Japan).

She had a history of artificial abortion 6 years earlier. She also cared for 10 or more cats including stray cats but no reptiles. On examination, her Glasgow Coma Scale was 15 (E4V5M6), blood pressure 124/92 mmHg, heart rate 78 beats/min, respiratory rate 20 breaths/min, oxygen saturation while breathing ambient air 98%, and body temperature 38.8 °C. Abdominal examination revealed tenderness of her right (transplant side) lower abdomen and suprapubic area. There was no evidence of costovertebral angle tenderness or skin rash. Results of initial laboratory and urine analyses were as follows: white blood cell count 8700/mm^3, differential 85.5% neutrophils, 6.9% monocytes, 7.0% lymphocytes, hemoglobin level 12.4 g/dL, platelet count 206,000/mm^3, C-reactive protein level 0.28 mg/dL, tacrolimus trough level 5.7 ng/ml, mycophenolic acid trough level 0.5 μg/mL, gross hematuria, and urinary gram stain 3+ for white blood cells and a few gram-negative bacteria. An unenhanced computed tomography scan revealed no hydronephrosis, renal or perirenal abscesses of transplanted kidney, vascular lesions such as infected aneurysm, or disseminated lesions. Diagnosis was kidney allograft pyelonephritis caused by *Salmonella* serotype O4, and we initiated ceftriaxone at 2 g daily. By hospital day 2, she was afebrile and by hospital day 4 all of her symptoms (urodynia, lower abdominal pain, gross hematuria, and cloudy urine) had improved. On hospital day 3, *Salmonella* serotype O4 with unchanged antimicrobial sensitivity was still detected in her urine culture. *Salmonella* did not grow in any stool culture obtained on admission day or in blood cultures obtained on admission day, hospital day 2, and 4. The *Salmonella* isolated in her urine was identified as *S. enterica* subsp. *enterica* serovar Schwarzengrund [*S.* Schwarzengrund (O4: d: 1, 7)] using *Salmonella* antisera against both O and H antigen (Denka Seiken, Gosen, Japan) at the Shizuoka City Institute of Environmental Sciences and Public Health. We administered ceftriaxone for 14 days in hospital and amoxicillin (2 g daily) for 14 days after discharge (Fig. 2). There was no evidence of pyelonephritis relapse or kidney allograft rejection 3 month after completion of treatment. We have continued to monitor her closely for potential relapse and allograft rejection.

3. Discussion

Although there is no database for NTS infections in Japan, statistics managed by the Ministry of Health, Labour and Welfare in Japan show that about 2000 persons annually develop food poisoning caused by *Salmonella*, accounting for 8.4% of all reported cases [17]. Use of immunosuppressive drugs, HIV infection, and malignancy are strong risk factors for NTS infection [1]. In particular, KTRs have a 20-fold greater risk of developing NTS infection compared with normal adult population [2]. NTS infection develops in 2%–3% of all KTRs [2,4,5] and tends to occur within half a year after transplantation [2]. *Salmonella* is detected in 0.015%–0.118% of all culture positive urine samples [7,10], and 1.4%–3.4% of all specimens *Salmonella* is isolated in Refs. [18,19]. Although