

# *Salmonella typhi* Bacteriuria, Predispositions and Complications: Two Case Reports and Review of Literature

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## Abstract

*Salmonella typhi* infection presents most commonly as typhoid fever and infrequently as extraintestinal localized infections of bone, joints, soft tissues, spleen, endocarditis, pulmonary, hepatobiliary, genital and urinary systems. Urinary tract infection (UTI) is rare and clinical presentation is indistinguishable from UTIs due to other etiological agents or may even be asymptomatic. We report two cases of patients with chronic kidney disease with UTI due to *Salmonella typhi*. Renal cyst, nephrolithiasis and urethral strictures were the concomitant findings in one case and renal tubular acidosis with nephrocalcinosis in the other. In patients with relapses and a chronic course with coexisting functional or structural abnormalities of the urinary tract system, the suspicion of salmonella as one of the probable causative agents should be kept in mind so as to ensure appropriate and adequate therapy. Also in the presence of long-standing hypokalemia, one must investigate for renal abnormalities and vice versa.

**Keywords:** Chronic kidney disease; Nephrocalcinosis; Nephrolithiasis; Salmonella; Urinary tract infection

## Introduction

Salmonellosis may manifest as gastroenteritis, enteric fever, localized infection, or carrier state. One million foodborne illnesses in USA are due to salmonella infection [1]. Enteric fever is endemic in many tropical countries.

Predisposing conditions like hemoglobinopathies, joint trauma, surgery, cholelithiasis or other immunosuppressive states have been documented in patients with extraintestinal

manifestations [2]. We present here two cases of UTI due to *Salmonella typhi* and their associated predisposing conditions from our hospital in North India.

## Case Reports

### Case 1

A 56-year-old male patient presented to Indraprastha Apollo Hospitals, New Delhi with complaint of off and on right flank pain for the last 1 month. He was admitted for further evaluation and management. Abdomen ultrasound (USG) and contrast-enhanced computed tomography findings were suggestive of large pelviureteric junction calculus with marked back pressure and left upper pole calculus. 99m Tc DTPA Renal Dynamic Study showed subnormal glomerular filtration rate (GFR), left side non-obstructed kidney and right enlarged partially obstructed kidney with moderately impaired cortical function.

Right DJ stenting was done (Fig. 1). His urine routine microscopy (R/M) showed raised proteins and pus cells full high power field. Patient was started empirically on ofloxacin 200 mg orally 12 hourly. Urine culture showed pure growth of > 100,000 CFU/mL of urine of non-lactose fermenting colonies on MacConkey Agar. These were identified as *Salmonella typhi* on Vitek 2 Compact and Vitek MS (Biomerieux, France). Agglutination with salmonella polyvalent O antisera (Denka Seiken, Japan) and salmonella O antiserum factor 9 (Becton Dickinson and Company, Ltd) were positive.

Antibiotic susceptibility testing done and interpreted following CLSI guidelines [3] showed strain was sensitive to ceftriaxone and cefexime and resistant to ampicillin, nalidixic acid, cotrimoxazole and quinolones. Following the sensitivity report, antibiotic treatment was changed to cefixime 200 mg twice a day for 2 weeks and patient was advised to come for follow-up and evaluation of renal functions. Percutaneous nephrolithotomy (PCNL) was planned if the renal functions improved. On follow-up after 2 weeks, his serum urea level was 75 mg/dL (reference range 10 - 50 mg/dL), serum creatinine was 2.4 mg/dL (reference range 0.5 - 1.3 mg/dL) and urine R/M still showed pus cells full field. Abdomen USG showed right-sided hydronephrosis with renal calculus and left renal cyst. The same antibiotics were continued and his renal parameters were monitored. After 6 weeks, PCNL was performed and urine, stones and DJ cultures were sent to the

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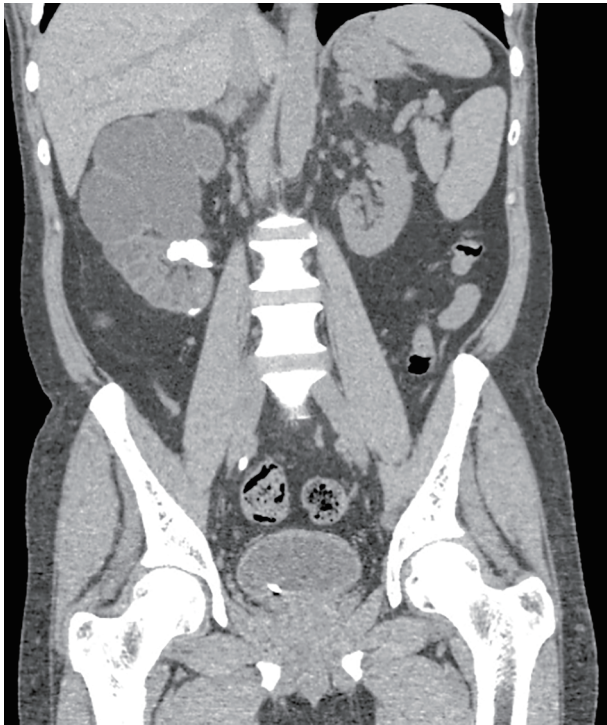
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**Figure 1.** Coronal NCCT image showing gross hydronephrosis involving the right kidney with calculus in the lower major calyx and gross parenchymal thinning. Ureteric stent is also noted on the right side.

microbiology laboratory. All the three revealed growth of *Salmonella typhi* with the same antibiotic susceptibility pattern as earlier. Thus, the treatment was continued for another 2 weeks.

DJ stent was removed after 2 months. At this time, the urine culture showed no growth of *Salmonella typhi*. After 2 years, patient presented with pain and swelling of left side of scrotum.

Uroflowmetry was suggestive of obstructive pattern. Retrograde urethrogram and micturating cysto-urethrogram were suggestive of proximal penile urethra stricture. Cystoscopy and optical internal urethrotomy were performed. S. creatinine started improving and patient was discharged in a stable condition.

## Case 2

A 27-year-old male patient presented for evaluation of weakness since last month and complaints of difficulty in walking. Over the last 4 years, he had been hospitalized four times with episode of extreme muscle weakness in his hometown and received I/V therapy for low potassium levels. His past history revealed inability to hear and speak since 4 months of age and persistent hypokalemia since childhood. Patient was thoroughly evaluated and found to have distal renal tubular acidosis with nephrocalcinosis on abdomen USG. Investigations ruled out sickle cell anemia, hypercalciuria, hyperglobulinemia and cirrhosis.

Potassium levels were optimized with oral potassium cit-

rate solution. Urine culture revealed *Salmonella typhi* colony count  $> 10^5/\text{mL}$  and the isolate was sensitive to amoxicillin and clavulanate, cefotaxime, ceftriaxone, cotrimoxazole, nalidixic acid and quinolones. Patient was started on cefexime 200 mg daily till next follow-up after 2 weeks. He was discharged in stable condition.

## Discussion

*Salmonella* enters the urinary tract either hematogenously following a recent episode of typhoid fever once a threshold of the organism is reached in the bloodstream or in chronic carrier states involving the urinary system or by direct invasion of the bladder via the urethra through fecal contamination [4].

The two cases reported by us represent true UTIs, as opposed to colonization or fecal contamination, by virtue of being isolated in pure culture and in high concentrations ( $> 100,000 \text{ CFU/mL}$ ).

*Salmonella* was reported as the cause of 0.056-0.07% of UTIs in Spain and 0.002-0.0037% of UTIs in the United States [5]. Although *S. typhi* bacteriuria is rare even where it is endemic, this specific infection should be kept in mind in patients who have an unidentified chronic UTI.

Interstitial nephritis and renal micro-abscesses can develop as important complications in the course of salmonella UTI. *Salmonella* emphysematous pyelonephritis has been reported in a non-diabetic and non-obstructive end-stage renal disease patient from Taiwan [6].

Recent surveys of salmonella bacteriuria have focused on risk factors associated with acquisition of UTIs. Such risk factors include immunocompromised conditions, underlying urologic abnormalities, neoplasms of the kidney, nephrolithiasis, hydronephrosis, anatomic abnormalities, schistosomiasis, tuberculosis, prostatic hypertrophy, renal transplant recipients, and lupus nephritis [7, 8]. Many of these cases do not have a past history of typhoid fever [8]. In our patients, no past history of typhoid fever was documented.

Many cases of bacteriuria do occur in individuals without known risk factors. An Australian investigation by Paterson and colleagues of 23 persons with *Salmonella* UTIs ( $> 1,000$  leukocytes/mL,  $> 10^5 \text{ CFU/mL}$ ) identified no immunocompromised patients in their study and only three (13%) with urologic abnormalities [9].

In our second case, there was history of treatment with Kanamycin in childhood which is known causes of deafness and renal damage. Hypokalemia results in addition to an alkaline urine and bladder dysfunction leads to urinary stasis and luxuriant bacterial growth.

Antibiotic treatment is challenging and prolonged treatment is indicated due to chronic bacteriuria and relapses [9]. Thus, it is crucial to request for repeat urine cultures in follow-ups. In case of a UTI associated with anatomic obstructive abnormalities, surgical correction may be required in addition to prolonged antimicrobial therapy ( $\geq 6$  weeks) to eradicate infection [10].

Prolonged course of antibiotic treatment with cephalosporins, surgical removal of the calculi and drainage procedure

in conjunction helped in cure in our cases.

### Conflict of Interest

None.

### Funding Source

None.

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