Original Article

SALMONELLA TYPHI BACTERIURIA, PREDISPOSITIONS AND COMPLICATIONS-TWO CASE REPORTS AND REVIEW OF LITERATURE

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ABSTRACT

Aims: Salmonella typhi infection presents most commonly as typhoid fever. Infection can less commonly manifest as extraintestinal localize infections of bone, joints, soft tissues, spleen, endocarditis, pulmonary, hepatobiliary, genital and urinary systems. UTI is rare and clinical presentation is indistinguishable from UTIs due to other etiological agents or may even be asymptomatic. Relapses and a chronic course with coexisting functional or structural abnormalities of the urinary tract system should raise the suspicion of Salmonella as one of the probable causative agents. Methods: We report two cases of patients with chronic kidney disease with urinary tract infection due to Salmonella typhi and same organism was isolated additionally from the DJ stent and stones in one of them. Results: Renal cyst, nephrolithiasis and urethral strictures were the concomitant findings in one case and renal tubular acidosis with nephrocalcinosis in the other. Conclusions: In patients with co-existing renal findings Salmonella should be kept in mind so as to ensure appropriate and adequate therapy. Also in the presence of longstanding hypokalemia one must investigate for renal causes.

Introduction

Salmonellosis is endemic in many tropical countries. One million foodborne illnesses in the United States, with 19,000 hospitalizations and 380 deaths are due to Salmonellosis[1]. Incidence of typhoid fever was found to be high in South-Central Asia and South-East Asia in a study conducted to estimate the global burden of typhoid fever considering 22 regions [2].

Salmonellosis may manifest as gastroenteritis, septicaemia with or without localized infection, enteric fever or as carrier state. Salmonella typhi and Nontyphoidal Salmonella may disseminate throughout the body through blood stream to cause other extra-intestinal infections like abscesses involving many organ systems, septic arthritis, etc. Predisposing conditions like haemoglobinopathies, joint trauma, surgery, cholelithiasis or other immunosuppressive states have been documented in patients with extra intestinal manifestations [3,4].

Significant bacteriuria due to Salmonella is rare. We present here two cases of UTI due to Salmonella typhi & their associated predisposing conditions from our hospital in North India.

CASE SERIES

Case 1

56 years old male patient presented to Indraprastha Apollo Hospitals, New Delhi with complaint of off and on right flank pain for the last one month. He was admitted for further evaluation and management. Ultrasound (USG) abdomen and contrast enhanced computed tomography (CECT) 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 GFR, left sdenon obstructed kidney and right enlarged partially obstructed kidney with moderately impaired cortical function.

Right DJ stenting was done. (Figure 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 every 12 hourly. Urine culture send to microbiology laboratory 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 test was put up and interpreted following CLSI guidelines [5]. The strain was sensitive to ceftriaxone and cefexime. It was 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 2.4 mg/dl (reference range 0.5-1.3 mg/dl) and urine R/M still showed pus cells full field. USG abdomen 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 themicrobiology 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 voiding cystourethrogram were suggestive of proximal penile urethral stricture. Cystoscopy and Optical Internal Urethrotomy were performed. S. Creatinine started improving and patient was discharged in a stable condition.

Case 2

27 years 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 4 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 four months of age and persistent hypokalemia since childhood. Patient was thoroughly evaluated and found to have distal Renal Tubular Acidosis with nephrocalcinosis on ultrasound abdomen. Investigations ruled out sickle cell anemia, hypercalciuria, hyperglobulinemia & cirrhosis. Potassium levels were optimized with oral potassium citrate solution. Urine culture revealed Salmonella typhi colony count >10^5/ml and the isolate was sensitive to amoxicillin and clavulanate, cefotaxime, ceftriaxone, cotrimoxazole, nalidixic acid and quinolones. Patient was started on cefixime 200 mg daily till next follow up after 2 weeks. He was discharged in stable condition.

**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.

**DISCUSSION**

Salmonella has been postulated to enter 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 [6,7].

The two cases reported by us represent true urinary tract infections, as opposed to colonization or fecal contamination, by virtue of being isolated in pure culture and high concentrations (>100,000 CFU/ml).

However in our patients no past history of Typhoid fever was documented.

Salmonella was reported as the cause of 0.056–0.07% of UTI in Spain [8, 9] and 0.002–0.0037% of UTI in the United States. The incidence of bacteriuria is reported as 0.6% [10].

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 [12].

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 Nondiabetic and Non-Obstructive End-Stage Renal Disease Patient from Taiwan [13]. More recent surveys of Salmonella bacteriuria have focused on risk factors associated with acquisition of UTIs. Such risk factors include immuno compromised conditions, underlying urologic abnormalities [13]. Nephrolithiasis, hydronephrosis, anatomic abnormalities, schistosomiasis, tuberculosis,
prostatic hypertrophy, renal transplant recipients, lupus nephritis have been found as predisposing conditions [14, 15]. Many of these cases do not have a past history of typhoid fever [14]. Neoplasms of the kidney have all been reported as predisposing factors [16].

While a significant number of Salmonella-associated UTIs are linked to persons with one or more comorbid conditions, many cases of bacteriuria 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 CFU/ml) identified no immunocompromised patients in their study and only 3 (13%) with urologic abnormalities [16]. Four persons had pyelonephritis (two with C1), one had renal failure and one had a renal stone with which Salmonella counts were >100,000 CFU/ml of urine. It was not possible to determine from the information on the submittal forms how many persons had concomitant gastrointestinal infections, but sepsis was indicated for four patients [17].

Barter syndrome is an autosomal recessive condition characterized by renal salt wasting, hypokalemia, metabolic alkalosis, hypercalciuria, and normal serum magnesium levels. Children younger than 6 years typically present with salt craving, polyuria, dehydration, emesis, constipation, and failure to thrive. Severe polyhydramnios, prematurity, and occasionally sensorineural deafness are the hallmark features [18].

However in our second case there was history of treatment with Kanamycin in childhood which is known causes of deafness and renal damage. Investigations ruled out sickle cell anemia, hypercalciuria, hyperglobulinemia & cirrhosis. His antinuclear antibodies profile was normal.

The presence of stones, which may harbor organisms often, leads to multiple relapses or to the development of chronic urinary carrier state. Salmonella paratyphi A has been reported in a 37-year-old Saudi patient who was a known case of nephrolithiasis and hydronephrosis with frequent admission for management of renal stones [19].

Antibiotic treatment is challenging and prolonged treatment is indicated due to chronic bacteriuria and relapses [9]. Recurrent infection needs to be ruled and 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 (≥ 6 weeks) to eradicate infection [10].

**CONCLUSION**

Specific management depends on the culture and sensitivity results plus the ability to resolve underlying or associated comorbid states. Regardless of the drug used, a patient's failure to respond may represent resistant bacteria or inadequate urine concentrations of the prescribed drug. Prolonged course of antibiotic treatment with cephalosporins, surgical removal of the calculi and drainage procedure in conjunction helped in cure in our cases.

**REFERENCES**