Epididymo-Orchitis and Testicular Abscess Caused by *Salmonella enteritidis* in Immunocompromised Patients in Kuwait

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Introduction

The commonest manifestation of salmonellosis is gastro-enteritis. Focal extra-intestinal infections are not as common and they usually follow complications with bacteraemia. An enlarged testis can be due to infectious and non-infectious diseases and until a diagnosis is made can evoke a great deal of anxiety in the patient as a prominent differential diagnosis is malignancy. Epididymo-orchitis complicating *Salmonella* infection in an immunocompetent or, even, immunocompromised patient is a rare condition. In a review of more than 700 cases of extra-intestinal infections caused by *Salmonella* spp., Cohen et al. [1] found only 12 cases (1.4%) of orchitis or epididymitis. Since then only a handful cases of epididymo-orchitis and testicular abscesses associated with various strains of *Salmonella* spp., particularly in newborn babies and infants, have been reported [2–8]. There have been almost no cases of *Salmonella* epididymo-orchitis or testicular abscesses in adults.

In this communication, we present 2 cases of unusual presentation of *Salmonella* infection, epididymo-orchitis and testicular abscess in immunocompromised patients with systemic lupus erythematosus (SLE) and diabetes.
Case 1

A 55-year-old diabetic (type II) Pakistani man, on oral hypoglycaemic agent for the previous 4 years, was admitted on September 29, 2004 through the Emergency Room because of a 4-day history of painful and swollen left scrotum. It was associated with fever of gradual onset. There was no diarrhea, night sweats or fatigue. On examination, he was found to be in pain, anxious and febrile (oral temperature, 38°C). His blood pressure was 180/110 mm Hg and his left testicle was enlarged, hot, tender and erythematous. Other systems were normal. He was immediately admitted into the surgical ward for investigations and treatment. While in the ward, 3 sets of blood samples were taken for culture, haematological and biochemical investigations, and Brucella agglutination test. On day 2 of admission, urine and stool samples were taken for culture as well. WBC, Hb and platelet count were 6.4 × 10⁹/l, 9.9 g/dl and 137 × 10⁹/l, respectively. Biochemical profile revealed slightly elevated urea (10.6 mmol/l); creatinine and other parameters were all within the normal ranges. Ultrasonography of the abdomen, pelvis, and scrotum showed mild hepatosplenomegaly, normal gallbladder, prostatic volume of 44 ml, normal-size right and left testes, thickened epididymis with decreased echogenicity and increased blood flow on Doppler of the left testicle. On suspicion of epididymo-orchitis, he was started initially on intravenous piperacillin, 2 g 8-hourly and amikacin, 500 mg 12-hourly. On day 4, results of urine and blood cultures revealed the presence of Salmonella enteritidis resistant to amikacin. Consequently, amikacin therapy was discontinued. He improved within 5 days and was discharged home on oral ciprofloxacin, 500 mg 12-hourly for 14 days. He has remained well 6 months after discharge with no recurrence of epididymo-orchitis.

Case 2

A 55-year-old diabetic (type II) Pakistani man, on oral hypoglycaemic agent for the previous 4 years, was admitted on September 29, 2004 through the Emergency Room because of a 4-day history of painful and swollen left scrotum. It was associated with fever of gradual onset. There was no diarrhea, night sweats or fatigue. On examination, he was found to be in pain, anxious and febrile (oral temperature, 38°C). His blood pressure was slightly raised (140/90 mm Hg). All other systems were normal. The left scrotum was swollen, red, hot and tender. Ultrasound of the testes showed increased echo-pattern of the left testis surrounded by free fluid in its upper surface. A solid enhancement mass measuring 2.6 × 2.5 cm was seen in the upper pole of the left testis in the region of the epididymis, which was suggestive of an abscess. A diagnosis of epididymitis and testicular abscess was made. Blood was taken for haematological and biochemical investigations as well as for culture as well. Urine and stool were also sent for microscopy and culture. On day 2 of admission, incision and drainage of the abscess was done and a specimen of pus was sent to the microbiology laboratory for culture. The results of the initial haematological and biochemical investigations were as follows: WBC 13.1 × 10⁹/l (predominantly polymorphonuclear leucocytes); Hb 11.5 g/dl, and platelets 347 × 10⁹/l. Serum electrolytes, liver and renal function tests were normal. Serum glucose was 15.2 mmol/l. Brucella agglutination test and VDRL test were negative. Urine microscopy showed WBC >200/ml and RBC 10/ml but the culture yielded no bacteria. Blood culture was negative. On day 4, culture of the pus yielded growth of Salmonella enteritidis, sensitive to ampicillin, amoxicillin-clavulanic acid, ceftriaxone, chloramphenicol, cotrimoxazole, ciprofloxacin and tetracycline and but resistant to amikacin, cefalothin, cefuroxime and gentamicin. Initial management was intravenous amikacin 500 mg 12-hourly and ceftriaxone 2 g once daily. Upon receipt of results of culture and sensitivity, this was then changed to ceftriaxone 1 g once daily. He improved clinically and made uneventful recovery. He was discharged 7 days after admission on oral ciprofloxacin 500 mg 12-hourly for 2 weeks. At follow-up 26 days later at the Urology OPD, he was well although the wound was still oozing. Culture of the wound and stool did not yield growth of Salmonella spp. He remains well 6 months after completing the above courses of antibiotics.

Microbiological Investigations and Results

In the Microbiology Laboratory, blood culture bottles were incubated inside the BACTEC 9240 blood culture machine (Becton, Dickinson & Co., Sparks, Md., USA) and the midstream urine sample was inoculated onto cystine-lactose-electrolyte-deficient agar (Becton, Dickinson & Co.) and blood agar (Tryptone Soya Agar, Oxoid Ltd., Basingstoke, Hampshire, England) supplemented with 5% sheep blood and incubated in air at 37°C for 24 h. The pus sample was inoculated onto a set of selective and non-selective media and incubated aerobically and anaerobically. Both blood and urine cultures from case 1 yielded growth of Gram-negative bacilli which were later identified as Salmonella enteritidis by the Vitrek Aerobic Identification System (ID-GNI; REF 21312) (BioMérieux Inc., Marcy-l’Etoile, France) and manual serogrouping with commercial antisera (Wellcome Diagnostics, Dartford, UK). The stool culture was negative. Only the pus obtained from case 2 also yielded Salmonella enteritidis.

Susceptibility testing was initially done in the Vitrek machine using AST-N200 REF 22029, and the results obtained tallied with those obtained by determining the minimum inhibitory concentrations using the Etest strips (AB Biodisk, Sweden). The three isolates were susceptible to ampicillin, ciprofloxacin, cefotaxime, ceftriaxone, chloramphenicol, piperacillin, and piperacillin-tazobactam, but resistant to amikacin, cefalothin and cefuroxime. Brucella agglutination test was negative.

To determine if both isolates obtained from case 1 were indeed related strains, DNA extracts of the blood and urine isolates were subjected to pulse-field gel electrophoresis (PFGE) typing. Briefly, the organisms were grown overnight in tryptic soy broth and then used to prepare agarose blocks using the lysis solution containing lysozyme (1 mg/ml) instead of lysostaphin. Blocks were digested with XbaI (Gibco BRL) according to manufacturer’s instruction. Electrophoresis was performed with 1% agarose gel in ×0.5 TBE buffer using a CHEF DR III apparatus (Bio-Rad Laboratories). The gel was run at 14°C, 6 V/cm and 120° switch angle for 22 h. Linear ramp of switch times was 0.5–40 s. The gels were stained in 0.5 mg/l ethidium bromide and photographed under UV illumina-
Acute Epididymo-Orchitis Caused by S. enteritidis

Discussion

Salmonella infections can present in many ways. Prominent amongst these is the gastro-enteritis, which occurs in about 68% of cases, followed by enteric fever (8.8%), often presenting as 'pyrexia of unknown origin', focal manifestations (7.4%) and asymptomatic carriers (15.8%) [9]. Involvement of the genito-urinary tract is unusual and is often associated with congenital abnormalities, malignancy and immunosuppression. In one of the largest, and often quoted, series of cases ever reported on Salmonella infections from New York Salmonella Center, Saphra and Winter [9] indicated that of the 7,779 cases studied, only 49 (0.6%) involved the genito-urinary tract, mainly pyelonephritis. It is noteworthy that there was no single case of epididymitis or orchitis in this large series. Since then only a few sporadic cases of epididymitis and/or orchitis caused by Salmonella spp. have been reported, mainly in infants [2, 5, 6, 8]. These illustrate the rarity of the infection in adults.

Epididymo-orchitis is an inflammatory reaction which may be due to infectious or non-infectious aetiology. Bacterial aetiological cause is always a possibility but the least expected is Salmonella spp., especially in adult patients with no known compelling predisposing factor such as sickle cell disease. However, SLE, which was the co-morbidity in the first case, corticosteroid therapy and lymphoma are also major predisposing factors for invasive extra-intestinal Salmonella infections, where it presents mainly as bacteremia [10]. Patient 1 with SLE was on double immunosuppressive therapy including steroids and azathioprine. Urinary tract infection caused by Salmonella spp. is not totally unexpected in this patient but epididymo-orchitis has hardly ever been described as a complication of this infection in SLE patients and there is no record of such an infection reported in the Middle East literature.

The most probable route of infection in infective epididymo-orchitis or testicular abscess is the haematogenous route [2, 3] originating from the bladder as in the first case. This is hardly surprising as spontaneous septicaemia in adult males usually has as its main source urinary tract infections. Positive blood and urine cultures in our first patient support this assertion. However, bacteremia may be intermittent and the culture may be negative as in the second patient. Ascending infection is another route of infection via the urethra and vas deferens as well as outflow obstruction due to benign prostate hypertrophy. All these conditions were present in the SLE patient. The bacterial strains recovered from the blood and urine culture were phenotypically and genotypically identical, an indication that they were from the same source, most probably the gut. Although the culture of the stool specimens from both patients did not yield Salmonella spp., that the gut is the most probable source of both infections is high on the list of routes of infection. It is believed that immunosuppression in these patients was a major predisposing factor.

Our second case was a diabetic patient whose condition was poorly controlled and comes from an Asian country where Salmonella infection is endemic. Although Salmonella infection is a widespread zoonotic infection in developing countries, complication with epididymo-orchitis is very rare. Diabetes mellitus as a predisposing factor is even rarer. As far as we could find in the literature this is the second reported case of this infection in a diabetic patient. The first, and only, case until now was a 56-year-old insulin-dependent diabetic patient with recurrent Salmonella septicaemia and previous history of diarrhoea [11].
A summary of reports on genito-urinary tract *Salmonella* infections gathered from the literature shows that *S. enteritidis* is the commonest species that causes focal lesion of the male genital tract infection [4–6]. Our finding of *S. enteritidis* in our patients is concordant with these reports.

As far as we are aware these are the first case reports of *Salmonella* epididymo-orchitis and testicular abscess in SLE and diabetic patients, in particular in Kuwait and in the Middle East as a whole. This rarity of epididymo-orchitis caused by *Salmonella* in Kuwait is also supported by our own personal experience. For instance, of the 235 patients with epididymo-orchitis treated in the Urology Unit of Mubarak Hospital from January 1999 till November 2004, this is the first case caused by *Salmonella* [Kehinde, unpublished observation]. In our experience, the few cases of infective epididymo-orchitis seen in Kuwait have been due *Brucella* spp. [12].

The management of this condition in the diabetic patient required surgical drainage as well as intravenous antibiotic therapy. About three decades ago, cases of *Salmonella* orchitis and/or epididymitis were eventually managed by orchiectomy to effect bacteriological cure. This was a needless line of management as the conditions are amenable to conservative antibiotic therapy. Our patients responded well to the antibiotic regimens and were discharged home well. The more recent line of management involves surgical exploration, which is performed in the majority of cases because of the strong suspicion of incarcerated hernia rather than infection, especially in children. The first patient improved dramatically on antibiotic therapy alone while the second one required surgical drainage of an abscess and antibiotic therapy. Although antibiotics are not recommended for treating *Salmonella* gastro-enteritis, antibiotic therapy is needed for extra-intestinal infections.

**Conclusion**

These cases show that it is important to consider *Salmonella* infection in the differential diagnosis of inflamed and tender testis in immunocompromised patients and to include blood, urine and stool cultures in all cases.

**References**


