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CASE REPORT

Acute epididymo-orchitis due to *Salmonella Typhi* in a young man from Bangladesh

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Abstract
S. typhi infection rarely involves the genitourinary system. We report the first described case of acute epididymo-orchitis due to *S. typhi* in a 14-year-old boy from Bangladesh. A high index of suspicion should be maintained when evaluating patients coming from endemic countries also in case of unusual sites of infection.

Keyword *S. typhi* · Epididymo-orchitis · Salmonellosis · Migration

Case report

In July 2018 a 14-year-old boy came to the Pediatric Emergency Room of Spedali Civili of Brescia because of right testicular pain associated with swelling of the scrotum. He complained of high fever (maximum temperature 40.5 °C) and malaise for 3 days during the previous week. There was no history of abdominal pain, diarrhea, nor dysuria.

The young man moved to Italy from Shariatpur district, Bangladesh, 6 months before and he had been in good general conditions since then. His past medical and family history was unremarkable and he did not take any medications recently. No vaccination against typhoid fever was recorded.

At clinical examination, he was afebrile and he presented a tender right testicle increased in size and consistency, with marked edema of the scrotal layers, reactive hydrocele, thickened and hyperemic scrotal skin; at that time, he was apyretic. The abdomen was soft, non-tender, non-distended, with normoactive bowel sounds in all quadrants and Murphy and Giordano's signs were negative.

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Baseline laboratory results showed leukocytosis (white blood cells 31,590/μL), slight normocytic anemia, normal platelets count, AST 44 U/L and ALT 58 U/L, mild extended coagulation times (PT % 56), with a C-reactive protein of 65.5 mg/L (normal value < 5 mg/L). Chemical-physical examination of urine was normal, no increase in testicular tumor markers (BHCG and AFP), except from a slight increase of neuron-specific enolase. Blood and urine were collected to perform culture.

Testicular doppler ultrasound showed the absence of arterial flow in the right testis, which appeared increased in size compared to the left one and surrounded by a dense hydrocele. No evidence of testicular mass was reported.

As it was not possible to clinically rule out testicular torsion, surgical exploration of scrotum was performed. A severe inflammation of the epididymis, associated with an important thickening and swelling of the tunica albuginea was evident and there was no sign of testicular torsion. Culture test and histological examination of testicular biopsy were performed.

Stool culture and nucleic acid amplification tests (NAATs) for the detection of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* on urine were performed during the hospitalization.

Antibiotic therapy with intravenous cephazolin was started and the patient was discharged after 3 days with oral cefixime.

Blood cultures and NAATs resulted negative, along with the urine and stool culture (performed during antibiotic therapy).

The culture of testicular biopsy resulted positive for *Salmonella enterica* subspecies *enterica* serovar Typhi and, according to the rarity of such isolation, it was ascertained using three different methods: Maldi-Tof, Vitek-II and latex serological test.

The bacterium was first isolated by inoculating the sample into a nutrient broth (BBL™ Brain Heart Infusion Broth—Becton Dickinson). It was incubated over-night at 37 °C and then sown on nutrient blood agar (COS–Biomerieux). After another over-night incubation, it showed the bacterial growth of gram-negative bacilli.

Then, the isolate has been identified by MALDI-TOF (Biomerieux) technology as *S. typhi*. A second isolation on MacConkey agar (Biomerieux) and another identification on Vitek-II (Biomerieux) were performed still obtaining the same strain. The final confirmation was obtained with the agglutination test to use the Kauffmann–White classification.

The antibiogram showed a pansensitive strain (using EUCAST breakpoints): sensitive to amikacin (MIC ≤ 2 mcg/ml), amoxicilline-clavulanate (MIC ≤ 2 mcg/ml), third and fourth generation cephalosporines (MIC ≤ 1 mcg/ml), piperacillin-tazobactam (MIC ≤ 4 mcg/ml), meropenem (MIC ≤ 0.25 mcg/ml), fosfomycin (MIC ≤ 16 mcg/ml), trimethoprim/sulfametossazol (MIC ≤ 20 mcg/ml), gentamycin (MIC ≤ 2 mcg/ml). Therefore, antibiotic therapy was confirmed.

We investigated patient's cohabitants to exclude the presence of chronic carrier among them but stool cultures were negative. Moreover, none of them experienced any pathological event during the days and weeks before and no one had a history of gall bladder stones, biliary tract or urinary tract abnormalities.

The result of histological examination of testicular biopsy showed a pattern of acute inflammation with inclusions of neutrophils granulocytes within the parenchyma. Inside seminiferous tubules, images indicating the presence of bacteria were observed. No sign of granulomatous inflammation was detected.

One week after discharge, a severe persistent inflammation of the testis was reported at the clinical examination, and consequently, antibiotic therapy was continued for another week and then stopped (2 weeks antibiotic course).

At ultrasound the right testis appeared still pathologic, reporting a heterogeneous testicular echotexture, increased the volume of the epididymis, reduced testicular vascularization and a widespread thickening of all the scrotal layers.

Moreover, abdominal ultrasound was performed and it excluded any abdominal infectious foci or other abnormalities.

One month after surgery the patient was asymptomatic but, because of local persistent inflammation, he was readmitted. At that moment, blood exams were performed with evidence of normal inflammation values (white blood cells 9760/μL, C-reactive protein ≤ 2.9 mg/L). Cystography excluded any possible urinary tract abnormalities. The patient was then discharged in good general conditions, still presenting a mild local inflammation with a slightly tenderness at testicular palpation. To avoid chronical carriage and because of slow resolution of ultrasound findings, cefixime 400 mg every 24 h was restarted to complete additional 4 weeks of therapy.

Widal-Wright serology, negative at presentation, was performed after 1 month and resulted positive (titer of 1:200 for antibodies against somatic O antigen and 1:800 for antibodies against flagellar H antigen of *S. typhi*).

To explore possible predisposing factors the following assessment were prescribed: HIV antibodies, hemoglobin electrophoresis and serological tests for *Schistosoma* spp. (ELISA and Western Blot) resulted negative. The serum levels of IgA, IgG, IgM and lymphocyte typing were investigated in order to rule out underlying immunodeficiency: the immunoglobulins titers were normal, while the lymphocyte analysis showed a CD3+ 2889 cell/uL (normal < 1880/ul), CD3+ CD8+ 1289 cell/uL (normal < 730), TCR gamma-delta+ 18.6% (normal < 8%). The pediatric immunologist confirmed that the pattern supported the hypothesis of a intracellular bacterial infection.

Urinalysis, stool and urine specimens were collected again, and the result was normal.

One month after the antibiotic discontinuation, the patient presented no symptoms and signs of local inflammation had disappeared.

Discussion

Salmonella enterica subspecies *enterica* serovar Typhi (*S. typhi*) is a facultative intracellular human-restricted pathogen, capable of living and reproducing either inside or outside cells. The human infection occurs through ingestion of fecal contaminated food, milk or water and it's more commonly among people after travel to, or residence in developing countries where sanitation is poor. Incubation period of *S. typhi* ranges from 5 to 21 days and 1–5% of infected subjects become chronic carriers by harboring *S. typhi* in the gall bladder or rarely in the urinary tract despite antibiotic therapy [1]. Chronic carriers in urinary tract are almost always associated with an abnormality in the urinary tract (eg urolithiasis, prostatic hyperplasia) or concurrent bladder infection with Schistosoma [2]. *S. typhi* infection usually presents as typhoid fever and infrequently as extra-intestinal localized infections, including the rare involvement of genitourinary system (< 1%) [1, 2]. The genitourinary tract can be reached by *Salmonella* with two modes: hematogenous spread following a recent episode of typhoid fever or by direct invasion through the urethra (fecal contamination) [3].

Table 1 Predisposing conditions for genitourinary infection by *Salmonella* spp

Functional or structural abnormalities of the urinary tract
Renal transplant recipients
Lupus nephritis
Hemoglobinopathies (eg. sickle cell disease)
Immunocompromised systemic conditions (eg. diabetic patient, immunosuppressive therapy, LES, HIV infection)
Concomitant local infection (e.g. schistosomiasis and tuberculosis)
Previous trauma
Sexually transmitted diseases (e.g. gonorrhea)

Involvement of genitourinary tract is usually associated with predisposing conditions [1, 3–8] (see Table 1).

Epididymo-orchitis due to *Salmonella spp* is rare, it occurs usually in male babies and adolescent boys and the few cases described since now see nontyphoidal *Salmonella* as responsible agent [4–6, 8, 9]. *S. typhi* has been described as etiological agent of a few cases of kidney infection (renal abscess, pyelonephritis) and symptomatic bacteriuria [3, 7, 10], but this bacterium has never been associated with acute epididymo-orchitis until now.

The present clinical case reports an acute epididymo-orchitis due to *S. typhi* in a young boy born and lived in Bangladesh until 6 months before fever onset. The patient comes from Shariatpur district in Dhaka Division of central Bangladesh. Recent report from this country suggests a very high burden of the disease in this area with an incidence of 3.9 episodes/1000 person-years during fever surveillance in urban slums [11]. It is an etiology that should be suspected in case of genitourinary tract infection, especially in a young male patient, coming from an endemic area. Other factors that suggest genitourinary tract infection by *Salmonella* spp. are: cohabitation with persons known to be chronic carriers or with risk factors for being such (e.g. gall bladder stones, biliary and/or urinary tract abnormalities), predisposing factors for extra-intestinal localization of *S. typhi* (see Table 1), acute onset and slow clinical remission of an extra-intestinal infection despite a suitable antibiotic therapy.

In this case, our patient developed an acute epididymo-orchitis despite immunocompetence, HIV negative, no previous local trauma or hemoglobinopathies, no STIs, no schistosomiasis and without genitourinary abnormalities.

Moreover, no intestinal chronic carriers were found among cohabitants and family members. Urinary carriage was not investigated.

According to the rarity of such isolate it is mandatory to check the reliability of laboratory techniques to identify the strain: Maldi-Tof, Vitek-II and latex serological test were performed to confirm the isolation.

Genitourinary infections caused by *S typhi* should be treated with antibiotics for 7–14 days [1].

Fluoroquinolones (FOs) were the first line treatment of enteric fever after the emergence of widespread resistance against amoxicillin, trimethoprim-sulfamethoxazole and chloramphenicol. However, within few years FOs resistance reports started appearing mostly in Central Asia. Thereafter, cephalosporins became the first option against *S. typhi* but currently, because of emerging resistances, the treatment banks primarily on macrolide (e.g. azithromycin) [12]. In our case, we isolated a pansensitive *S. typhi* strain but FOs sensitivity was not tested. So that, despite a better penetration of FOs into epididymis and testis tissue, we preferred cephalosporins also considering the potential drug-related tendinopathy. The 4 weeks of cefixime prescribed following the resolution of the acute event had the purpose to prevent the state of chronic carrier and irreversible testis damage in a young boy.

Conclusion

To our knowledge, this is the first reported case of acute epididymo-orchitis caused by *S. typhi*. This bacterium should be suspected in the presence of an extra-intestinal infection after a recent fever, especially in young patients from endemic areas.

Because of increasing migration and international travels, we consider that such rare infection will become more and more frequent in high-income countries. Then, unusual infective etiologies must be considered in routinely clinical practice. Finally, vaccination against thypoid fever in travelers to endemic areas might be always recommended.

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Compliance with ethical standards

Conflict of interest The authors have no conflict of interests to declare.

Ethical approval A consent for the use of the clinical data was provided.

References

1. Huang DB, DuPont HL. Problem pathogens: extra-intestinal complications of *Salmonella enterica* serotype Typhi infection. Lancet Infect Dis. 2005;5:341–48.
2. Farid Z, Bassily B, Kent DC, et al. Chronic urinary salmonella carriers with intermittent bacteraemia. J Trop Med Hyg. 1970;73:153–5.

3. Dawar R, Jasuja S, Imdadi F, et al. *Salmonella typhi* bacteriuria, predispositions and complications: two case reports and review of literature. World J Nephrol Urol. 2017;6:32–4.
4. Svenungsson B. Suppurative epididymo-orchitis due to *Salmonella enteritidis*. J Infect. 1984;8:64–6.
5. Bansal N, Kaistha N, Chander J. Epididymo-orchitis: an unusual manifestation of salmonellosis. J Microbiol Immunol Infect. 2012;45:318–20.
6. Hakim A, Bradley H. Salmonella epididymo-orchitis in infancy and childhood. Clin Pediatr, 1992; 120–122.
7. Mathai E, John TJ, Rani M, et al. Significance of *Salmonella typhi* bacteriuria. J Clin Microbiol. 1995;33:1791–2.
8. Al-Obeid K, Al Khalifan NN, Jamal N, et al. Epididymo-orchitis and testicular abscess caused by *Salmonella enteritidis* in immunocompromised patients in Kuwait. Med Princ Pract. 2006;15:305–8.
9. Foster R, Weber TR, Kleiman M, et al. *Salmonella enteritidis*: testicular abscess in a newborn. J Urol. 1983;130:790–1.
10. Kaur A, Sarma S, Kumar N, et al. Renal abscess caused by Salmonella Typhi. J Lab Physicians. 2015;7:121–3.
11. Brooks WA, Hossain A, Goswami D, et al. Bacteremic typhoid fever in children in an urban slum, Bangladesh. Emerg Infect Dis. 2005;11:326–9.
12. Britto CD, Wong VK, Dougan G, et al. A systematic review of antimicrobial resistance in *Salmonella enterica* serovar Typhi, the etiological agent of typhoid. PLoS Negl Trop Dis. 2018;12:e0006779.