JACOBS PUBLISHERS

OPEN ACCESS

Jacobs Journal of Internal Medicine

Case Report

An Unusual Case of *Salmonella* UTI in a Male Teen

Yuan Liu[1], Thomas Waller[1]

[1]*Mayo Clinic Florida*

**Corresponding author: Dr. Yuan Liu, Mayo Clinic, 4500 San Pablo Rd., Jacksonville, FL32224; Email: asydarka@gmail.com*

Received: 07-28-2015

Accepted: 08-17-2015

Published: 09-03-2015

Abstract

Nontyphoid *Salmonella* (NTS) is the leading bacterial cause of gastrointestinal infection globally and in the US. More than 90% of NTS infections are foodborne. NTS mostly causes acute self-limited colitis; bacteremia may develop in hosts with predisposing factors or with certain invasive serovars; focal disease may ensue due to immunosuppression and/or structural defects. Hydration is usually sufficient for colitis. Antibiotics are reserved for those who are immunocompromised, bacteremic, or at risk for severe focal disease. We will share an unusual case of NTS urinary tract infection in an apparently healthy male teen, and our reflections on the universal, diverse, and potentially fatal NTS infection.

Introduction

Salmonella is divided into 2 broad categories based on disease spectrum: typhoid and nontyphoid (Table.1). Nontyphoid *Salmonella* (NTS) refers to all 2500+ *Salmonella* serovars (Box.1) except for the 4 typhoid senovars: *S.* Typhi, *S.* Paratyphi A, B and C, that cause enteric fever and chronic carrier state. NTS is the most common bacterial cause of gastrointestinal infections globally and in the U.S. [1]. NTS has a vast reservoir in nature. More than 90% of NTS infections are foodborne; another 3~5% are from contacts with exotic pets, e.g. turtles, lizards, hedgehogs etc.; human to human transmission is rare.

Table 1. Typhoid versus Nontyphoid Salmonella.

Features	Typhoid	Nontyphoid
Serovar	Typhi, Paratyphi ABC	The other 2500+
Reservoir	Human	Animals, plants
Transmission	Waterborne	Foodborne
Distribution	Developing countries	Worldwide
Diseases	Systemic	Enteric or systemic

Box. 1 Nomenclature of Salmonella.

The genus *Salmonella* consists of rod-shaped, gram-negative, flagellated facultative anaerobes, and belongs to the family Enterobacteriaceae. **Genomically**, *Salmonella* branches into 2 species: *S.* enterica and *S.* bongori, which are further classified into 6 subspecies. Most human infections are caused by the subspecies enterica (*Salmonella enterica* subsp. *enterica*), which only infects warm-blooded animals; the other 5 subspecies colonize cold-blooded animals, plants, and nonbiological environment. **Serologically**, there are 6 serogroups (A, B, C1, C2, D, and E) defined by O-antigen and 2,500+ serovars (serotypes) defined by 3 major antigens (O, H, and Vi). Most isolated serovars worldwide are *S. enteritidis* and *S. typhimurium*. **Clinically**, Salmonellosis is divided into 2 broad categories: typhoid and nontyphoid (Table.1).

We report a case of NTS urinary tract infection (UTI) in an apparently healthy male teen. The unusual presentation of this case prompted us to review and share what we learned about the universality, diversity and potential lethality of

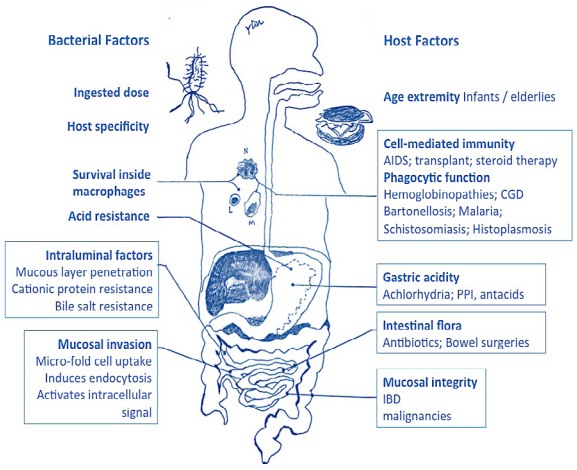
NTS diseases.

Case Report

A 15 year-old Afro-American male presented to our primary care clinic (day1) with dysuria and frequency that developed in the past 6 hours. He denied hematuria, fever, or flank pain; physical exam was unremarkable. A urine sample was collected

for urinalysis and culture; expectant management was adopted. Twelve hours later, the patient presented to the local emergency room with worsening dysuria and gross hematuria; a urinalysis revealed WBC of 461 and RBC of 425 per hpf. He was prescribed Cephalexin 500 mg 4 times a day for presumed pyelonephritis. He returned to our clinic on day 2 with nausea and back pain; denied fever or chills; exam remained unremarkable; he was given tramadol for dysuria. A renal ultrasound was negative for pyelonephritis, urolithiasis, and hydronephrosis. On day 3, the urine culture from day 1 revealed growth of 30,000 *Salmonella* spp.; so the antibiotic was changed to Bactrim; the strain was later tested to be pan-sensitive. By the follow-up on day 8, his gross hematuria had gone away but dysuria persisted. An extensive bloodwork was unremarkable, including 2 sets of blood cultures; the stool culture though did grow *Salmonella* despite absence of diarrheal disease. Urology was consulted; cystoscopy saw multiple erythematous areas on the bladder wall; no cystoureteral reflux was noticed. Post-procedurally he developed abdominal cramps, nausea, and nocturnal fever up to 103°F. Another extensive septic work-up was unremarkable;

Figure 1. Host and Bacterial Factors of Salmonellosis Pathogenesis (Modified from: Camille N Kotton MD. et al., Pathogenesis of Salmonella Gastroenteritis).



CT of abdomen and pelvis reported borderline enlargements of spleen and a left paraaortic lymph node. The majority of his symptoms resolved after Bactrim was discontinued (as medication-induced fever was suspected); nitrofurantoin was given instead and continued for 8 weeks. A thorogh epidemiologic history was unremarkable; previous medical issues include overweight, elevated blood pressure for age, intermittent dysuria and functional constipation with anal fissure.

Discussion

Pathogenesis of Salmonellosis is a multi-round combat between the host defense and bacterial virulence (Figure1). **Macrophage dysfunction** is a unique predisposing factor for more aggressive NTS infections: Hiding inside macrophages is not only a master hand of *S.* Typhi, but also a property of some NTS [1,2]. **Host specificity** is the most important pathogen factor for NTS: Serovars with broader host range tend to cause colitis (*S.* typhimurium, *S.* enteritidis), while those with narrower host range tend to cause bacteremia (*S.* choleraesuis, *S.* dublin) (Table.2). Typhoid serovars cause the most invasive disease because their evolution strategy is to obtain host-specific virulence genes at the cost of degrading "generalist" genes [3].

Table 2. Characteristic Diseases of Representative Serovars.

Serogroup	Serovar	Characteristic disease
A	*S.* paratyphi A	Enteric fever, carrier
B	*S.* paratyphi B	Enteric fever, carrier, colitis
B	*S.* typhimurium	Colitis
C	*S.* paratyphi C	Enteric fever, carrier
C	*S.* choleraesuis	Bacteremia
D	*S.* typhi	Enteric fever, carrier
D	*S.* enteritidis	Colitis
D	*S.* dublin	Bacteremia

NTS infections can present as a broad spectrum of clinical syndromes of various severity, depending on the bacterial and host factors outlined above (Figure.1). **Acute colitis** is the most common NTS disease in developed countries. Diarrhea is self-limiting and indistinguishable from other GI pathogens. Called "gastroenteritis", the histology really features acute diffuse colitis with crypt abscesses, with no gastritis and minimal small bowel enteritis [3,4]. **Bacteremia** can be secondary (with colitis) or primary (without colitis). Primary bacteremia is common in normal infants, but an alarm for immunosuppression in non-infants. Bacteremia in children is usually benign, with only 2.5% of subsequent focal disease, andrarely fatal, while 1/3 bacteremic adults will develop focal disease and may die [4-6]. **Focal disease** comprises 7-12% of all NTS infections. Immunosuppression and structural defects both predispose to focal disease, though their relative importance varies at different sites. Immunosuppression (malignancy, AIDS, steroid) is of greater importance in focal soft tissue and chest infections. Some of the examples of structural causes are: meningitis in infants due to immature blood-brain barrier; osteomyelitis and septic arthritis in sicklers at foci of avascular necrosis; UTI in those with obstruction, stone, or schistoso-

miasis; grafts and prostheses are self-evident [4,7]. **Endovascular infection** is the unique NTS infection of atherosclerotic plaques or aneurysms typically in adults above age 50 in the developed world. Complications such as mycotic aneurysm, rupture, dissection, and septic embolism are vascular emergencies with high mortality [8].

Box 2. Approach to Managing NTS Diseases.

Exposure to NTS: Obtain stool and blood culture if < 3 months.

Acute diarrhea: Do no cultures if diarrhea is not dysentery-like, nonbloody, nonfebrile, and < 5 days. Obtain stool culture if > 5 days. Obtain stool and blood culture if dysentery-like or bloody diarrhea, febrile or ill-appearing.

Positive stool culture: Do not treat (with antibiotics) well-appearing, immunocompetent individuals aged 2 to 50 years. Treat febrile infants if < 3 months for 5~7 days and observe if > 3 months. Treat all that are ill-appearing or hospitalized for >=7 days. Treat immunocompromised ones for >=14 days (preemptive). Treat adults > 50 years with various prostheses (preemptive). Healthcare staffs and Food handlers should not work till diarrhea stops. Do not stool culture to test clearance.

Positive blood culture: Obtain CSF culture if < 3 months. Obtain CSF culture if pediatric patients < 16 years are ill-appearing or immunocompromised. Watch for focal disease in those with no diarrhea and with the predisposing factors (Figure.1). Treat all that are bacteremic: immunocompetent >=14 days; immunocompromised >=4 weeks.

Focal infection: Frequently requires surgical drainage /debridement and prolonged antibiotic. Manage case-by-case.

Diagnosis of NTS disease is simply microbiological. However, knowing when to watch for more invasive disease and obtain appropriate culture is crucial to a complete evaluation. The central issue regarding treatment is to whom we give antibiotics and to whom not (Box.2) [5,9].

Globally, resistance to chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole is universal; resistance to fluoroquinolone and 3rd generation cephalosporins is rising; multidrug resistant, extended-spectrum beta-lactamase (ESBL) producing, and carbapenem-resistant strains are also emerging. Resistance data via the CDC or local health agency is helpful if the infection is acquired domestically [1, 5].

In the end, do not forget to tell your patients that they can find updated information about how to avoid foodborne NTS at the CDC website and to keep their young children away from exotic pets.

Conclusion

Exposure to NTS is not uncommon, but retention of NTS in genitourinary tract causing infection reflects, despite negative blood cultures, the occurrence of bacteremia, which in the absence of diarrhea is a sign of immunodeficiency. HIV infection was ruled out. Macrophagic dysfunction has been a consideration: either from hemoglobinopathy related iron overload (his typical CBC profile suggests thalassemia trait, though hemoglobin electrophoresis was not obtained) or chronic granulomatous disease (CGD), the congenital immunodeficiency most frequently related to NTS bacteremia [4]. NTS UTI always suggests an underlying defect of the urinary tract; no obvious anatomic reason was found by cystoscopy or CT scan; however it is not clear if a history of voiding dysfunction renders him susceptible.

Serogrouping by a state microbiology lab was "D," which includes *S.* enteritidis and *S.* dublin. It is also possible the invasive serovar, rather than the host factors, has led to the silent bacteremia. No serotyping was obtained unfortunately.

Conflict of Interests

The authors declare that there is no conflict of interest regarding the publication of this paper.

References

1. Sanchez-Vargas FM, Abu-El-Haija MA, Gomez-Duarte OG. Salmonella infections: an update on epidemiology, management, and prevention. Travel Med Infect Dis, 2011. 9(6): 263-277.

2. Kotton CN, Elizabeth L Hohmann. Pathogenesis of Salmonella gastroenteritis. UpToDate, 2013.

3. Feasey NA, Gordon Dougan, Robert A Kingsley,Robert S Heyderman,Melita A Gordon. Invasive non-typhoidal salmonella disease: an emerging and neglected tropical disease in Africa. Lancet. 2012, 379(9835): 2489-2499.

4. Gordon MA. Salmonella infections in immunocompromised adults. J Infect. 2008, 56(6): 413-422.

5. Christenson JC. Salmonella infections. Pediatr Rev. 2013, 34(9): 375-383.

6. Tsai MH, HuangYC, Chiu CH, Yen MH, Chang LY et al. Nontyphoidal Salmonella bacteremia in previously healthy children: analysis of 199 episodes. Pediatr Infect Dis J. 2007, 26(10): 909-913.

7. Dhanoa A, QK Fatt. Non-typhoidal Salmonella bacteraemia: epidemiology, clinical characteristics and its' association with severe immunosuppression. Ann Clin Microbiol Antimicrob. 2009, 8: 15.

8. Hennedige T et al. Spectrum of imaging findings in Salmonella infections. AJR Am J Roentgenol. 2012, 198(6): W534-W539.

9. Hohmann EL. Approach to the patient with nontyphoidal Salmonella in a stool culture. UpToDate,2013.