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CASE REPORT

Is 2 weeks of antibiotic therapy enough to treat elderly patients with nontyphoid *Salmonella* bacteremia? A case report of fatal endovascular infection



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Nontyphoid *Salmonella* (NTS) can cause invasive diseases in the elderly. Notably, the most feared complication of NTS bacteremia is endovascular infection. The risk factors for infected aortic aneurysm include old age and atherosclerosis. Extended use of antimicrobial therapy (> 2 weeks) for NTS bacteremia should be considered for those who demonstrate the risk factors for endovascular infection, even when a metastatic focus is clinically elusive. Herein, we report the case of a 75-year-old patient with diabetes mellitus, hypertension, chronic kidney disease, and myocardial infarction who died of an infected aortic aneurysm despite 3 weeks of antibiotic therapy that was administered to treat the initial NTS bacteremia. Copyright © 2012, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. All rights reserved.

Introduction

Nontyphoid *Salmonella* (NTS) causes invasive disease in humans, and one of the most feared complications is endovascular infection. The risk factors for NTS endovascular infection include old age and underlying atherosclerosis.¹

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Presumably, transient bacteremia from a gastrointestinal source leads to the seeding of the damaged atherosclerotic intima or an overlying thrombus at the site of the vessels.¹ It is reasonable that an adequate duration of effective antibiotics may reduce the occurrence of endovascular infections in patients with NTS bacteremia. However, clinical evidence regarding the use of antibiotics for treating NTS bacteremia is limited. Clinically, patients diagnosed with NTS septicemia but without complications typically receive a course of antibiotic therapy for 7–14 days.^{2,3} In this report, we highlight the importance of prolonged antibiotic therapy for patients at high risk of developing NTS endovascular infection. The present case initially received effective *in vitro* antibiotic therapy for more than 2 weeks to treat bacteremia, but died of relapsing NTS endovascular infection 3 months later.

Case report

A 75-year-old patient with diabetes mellitus, hypertension, chronic kidney disease, and coronary artery disease presented to the emergency room with sudden shortness of breath and chest pain. Laboratory data revealed

leukocytosis (12,500 cells/mm³) and a high level of C-reactive protein (73 mg/L). Non-ST elevation myocardial infarction with acute pulmonary edema was immediately diagnosed. The patient was intubated due to respiratory failure and admitted to the intensive care unit. After extubation, he received percutaneous coronary intervention with stenting to treat coronary arterial stenosis.

The patient received empirical parenteral therapy that consisted of 500 mg/day levofloxacin after admission. However, he developed a fever on the fifth day in the hospital. Blood cultures verified *S. enterica* serogroup B and *Fusobacterium nucleatum*. He received 2 g intravenous ceftazidime every 12 hours and 500 mg metronidazole every 8 hours for 10 days. Computed tomography with contrast enhancement did not detect any evidence of infective vascular lesions (Fig. 1). After discharge, he was prescribed a 7-day course of oral ciprofloxacin (500 mg/day) and metronidazole (500 mg thrice daily).

Three months later, he visited the emergency room and complained of abdominal pain that had been manifesting for 3 days. Abdominal computed tomography showed a mycotic aneurysm (4.5 cm in diameter) over the descending aorta (Fig. 1). Cefepime (2 g every 12 hours) was immediately administered. However, he died when the

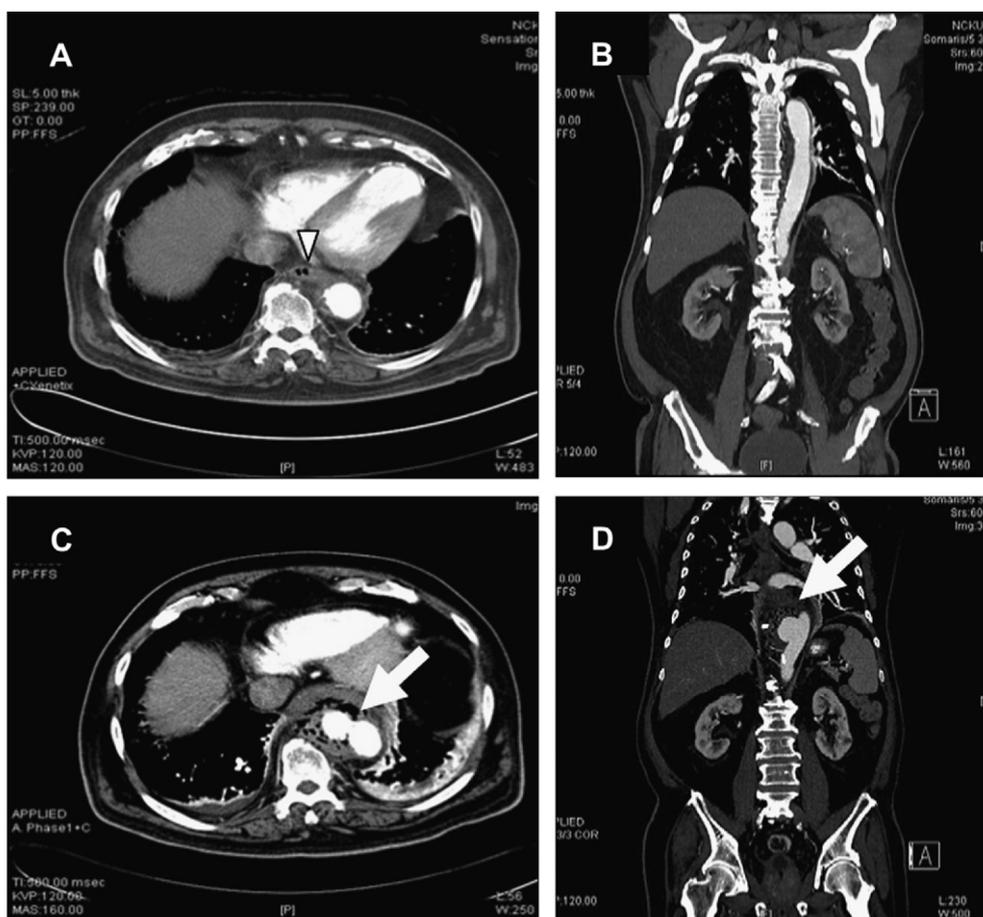


Figure 1. A 75-year-old male was admitted for non-ST elevated myocardial infarction and concurrent nontyphoid *Salmonella* (NTS) bacteremia. He received active *in vitro* antibiotic therapy for 3 weeks. There was no evidence of endovascular infection on computed tomography, which was performed at a similar level during the patient's first hospitalization (A and B). The structures of the vascular wall and esophagus (arrowhead,) were intact (A). Three months later, he was readmitted for recurrent NTS bacteremia with an infected aneurysm over the abdominal aorta (arrows; C and D).

aneurysm ruptured 3 days later. The initial blood culture had indicated *S. enterica* serogroup B, but was later identified as *S. enterica* serotype Typhimurium. Two NTS bacterial isolates of the same genotype were also determined by pulse-field gel electrophoresis using the NotI restriction enzyme. Both isolates had the same antibiogram and were susceptible to nalidixic acid, levofloxacin, cefotaxime, and ceftriaxone.

Discussion

Patients with an underlying immunodeficiency, such as HIV, tend to have recurrent NTS infections.⁴ Here, we present a fatal case of a *Salmonella*-infected aneurysm over the abdominal aorta without a known immunocompromised status. NTS infections can cause severe invasive diseases such as septicemia, meningitis, and endovascular infections.⁵ Of note, endovascular infections are associated with high mortality and morbidity. The risk factors for infected aortic aneurysm in patients with NTS bacteremia include old age and underlying atherosclerosis,⁶ and both of these were noted in the present case. *Salmonella* is traditionally considered to be highly invasive to the endothelium and capable of causing the early rupture of aneurysms.⁷ Moreover, *Salmonella* species have comprehensive mechanisms that facilitate intracellular survival, which makes latent or recurrent infections possible.⁸ However, the interaction between atherosclerosis and *Salmonella* isolates is not clearly understood.

The recommendations found in textbooks and websites regarding the duration of antibiotic therapy for treating NTS bacteremia are summarized in Table 1.^{2,3,5,9,10} In brief, patients diagnosed with NTS septicemia but without specific complications are often administered 1–2 weeks of antibiotics. Documented or suspected endovascular infections should be treated with surgical intervention and

effective *in vitro* antibiotics for 6 weeks. For extra-intestinal nonvascular infections, antimicrobial therapy for 2–4 weeks plus surgical debridement (depending on the site of infection) is usually necessary. Prolonged antimicrobial therapy has been recommended for patients with AIDS and NTS bacteremia.^{3,9,10} However, the boundary between complicated and uncomplicated NTS bacteremia is sometimes clinically indistinct, as in our case.

It is very important to detect persistent bacteremia, which may be associated with endovascular infection. Confirmation of blood sterilization by repeated blood culturing is necessary before discontinuing antibiotics. Early detection of asymptomatic endovascular infection is a clinical challenge. Even after a 2-week course of antibiotic treatment for “uncomplicated” NTS bacteremia, it is still mandatory to closely follow patients and evaluate any new symptoms or signs that suggest focal infections, such as recrudescence of fever, abdominal pain, or joint/bone pain.

For older patients who present with the risk factors for NTS endovascular infections, prolonged antibiotic therapy is reasonable for patients who, if endovascular infection does occur, will develop a disastrous clinical course. Although the clinical and imaging evidence of endovascular infection were not initially apparent in the present case, in retrospect effective *in vitro* antibiotic therapy for 4–6 weeks should have been considered due to the high risk of developing an endovascular infection. In a review of the published accounts of abdominal *Salmonella* aortic aneurysms, some patients presented with a subacute course along with a mean duration of symptoms for 6.7 weeks before diagnosis,¹ indicating that vascular infections may develop late after the onset of NTS bacteremia. With only a single clinical case, it is too early to recommend 4–6 weeks of antimicrobial therapy for all adults with NTS bacteremia. Therefore, the development of a clinical scoring system that can precisely predict the adult

Table 1 Recommended duration of antibiotic therapy for treating uncomplicated nontyphoid *Salmonella* (NTS) bacteremia in adults

Type of source	Origin	Clinical settings	Suggested duration of antibiotics (d)	Reference
Review article	Nontyphoidal salmonellosis. <i>Clin Infect Dis</i> 2001;32:263–9	No persistent blood cultures, suspicion of endovascular focus, or complicated gastroenteritis	10–14	5
Textbook	Salmonellosis. <i>Harrison's Infectious Diseases</i> , 2010	Low-grade bacteremia (< 50% positive blood cultures), non-HIV infection, no relapse of infection	7–14	3
Textbook	<i>Salmonella</i> species, including <i>Salmonella</i> Typhi. <i>Principles and Practice of Infectious Diseases</i> , 2010	Low-grade bacteremia (< 50% positive blood cultures) that does not involve the vascular structures	7–14	2
Textbook, online	<i>Salmonella</i> , nontyphoidal Species (<i>S. Choleraesuis</i> , <i>S. Enteritidis</i> , <i>S. Hadra</i> , <i>S. Typhimurium</i>). <i>Antimicrobial therapy and vaccines</i>	Low-grade bacteremia, non-AIDS patients	10–14	9
Textbook, online	Nontyphoid <i>Salmonella</i> bacteremia. UpToDate 19.2	Nonimmunocompromised host, bacteremia, and the absence of extraintestinal focal infection	14	10

populations with NTS bacteremia who are at high risk of developing complications and subsequent endovascular infections is urgently needed, in addition to more sensitive imaging techniques that can detect early-stage endovascular infections.

Conflicts of interest

The authors have no conflicts of interest to declare.

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