

Typhoid fever, complicated by syncope due to relative bradycardia: A case report

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Tam Van Nguyen^{1,2*}, Quan Van Le³, Ha Thi Nguyen³,
Quang Tu^{4,5}, Tuyen Tien Hoang¹, Thang Ba Ta⁶, Tien Viet Tran⁷,
Tuan Dinh Le⁸ , Thang Canh Tran³, Linh Giang Nguyen⁹,
Thuan Duc Nghiem^{10*}, Son Tien Nguyen⁸, An Van Nguyen¹¹,
Khanh Dinh Hoang¹² and Kien Xuan Nguyen^{13*}

Abstract

In a United Nations (UN) staff member headquarters in South Sudan, we present a rare typhoid fever complicated by syncope due to relative bradycardia. A 25-year-old male presented to our hospital with a high fever, diarrhea, and no vomiting. He had no substantial medical background. He was diagnosed with an unspecified digestive disorder and received initial treatment. Two syncope episodes were recorded in the Level I hospital. He was referred to our hospital at the 30th hour and the third fainting occurred. Electrocardiogram showed bradycardia with a heart rate of 40 beats/min. The atropine test was negative; the initial diagnosis was sinus sickness syndrome. Microbiology tests later suggested typhoid infection. Then, the diagnosis changed to relative bradycardia caused by *Salmonella typhi*; and he was orally treated with the third-generation Quinolone antibiotic. He significantly improved and got discharged on the seventh day. In conclusion, typhoid remains a real and present threat to UN staff and civilians in South Sudan.

Keywords

Typhoid fever, bradycardia

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Introduction

A bacteria strain called *Salmonella enterica* serotype typhi causes typhoid fever. *Salmonella typhi* is spread through contaminated food, drink, or water. Symptoms of typhoid

fever include prolonged high fever, fatigue, headache, nausea, abdominal pain, and constipation or diarrhea.¹ Some patients may have a rash. Severe cases may lead to serious complications or even death. Typhoid fever diagnosis was based on travel history, medical symptoms, Widal test

¹Emergency Department, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam

²Outpatient Department, Vietnam Level 2 Hospital, Bentiu, South Sudan

³Functional Diagnostics Department, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam

⁴Aeromedical Evacuation Team, Vietnam Level 2 Hospital, Bentiu, South Sudan

⁵Social Policy, School for Policy Studies, University of Bristol, Bristol, UK

⁶Respiratory Center, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam

⁷Department of Infectious Diseases, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam

⁸Department of Rheumatology and Endocrinology, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam

⁹University of Medicine and Pharmacy, Vietnam National University, Hanoi, Vietnam

¹⁰Department of Otolaryngology, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam

¹¹Department of Microbiology, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam

¹²Ultrasound Department, Imaging Diagnostics Center, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam

¹³Department of Military Medical Command and Organization, Vietnam Military Medical University, Hanoi, Vietnam

*These authors contributed equally to this work.

Corresponding Author:

Kien Xuan Nguyen, Department of Military Medical Command and Organization, Vietnam Military Medical University, 160 Phung Hung Street, Phuc La Ward, Ha Dong District, Hanoi 10000, Vietnam.
Email: nguyensexuan@vmmu.edu.vn



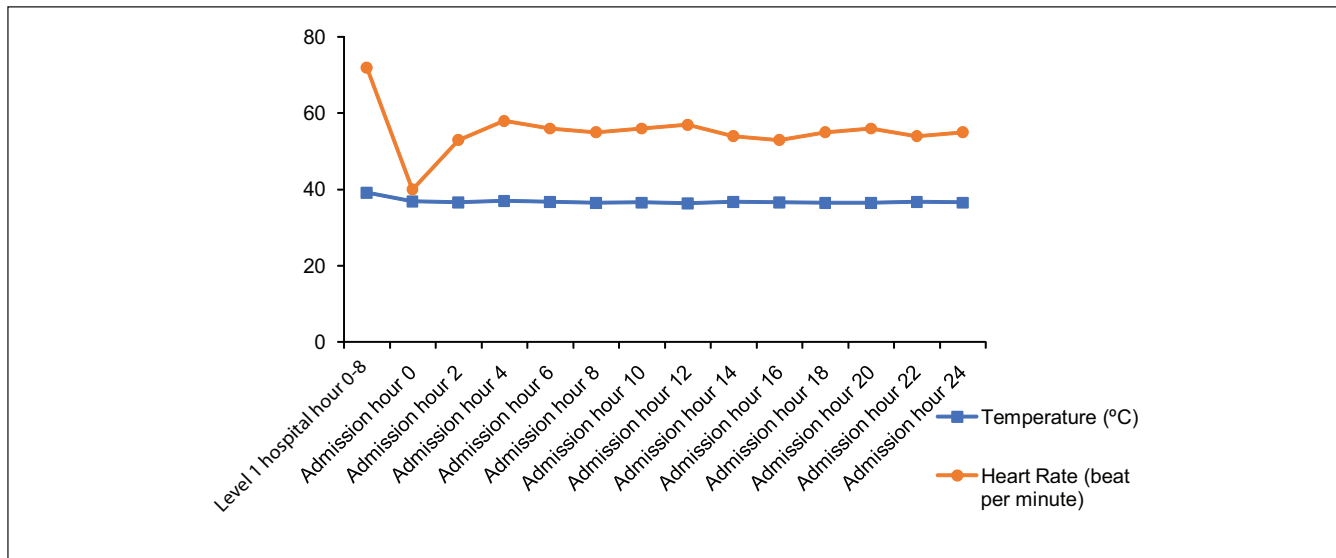


Figure 1. Heart rate and temperature on the first admission day and level I hospital.

(rapid test) orients to typhoid fever, and blood culture.¹ Antibiotic therapy is an effective treatment for typhoid fever.

The presentation, in this case, was initially thought to be a syncope caused by sinus sickness syndrome and thereafter features more associated with relative bradycardia symptoms, which is an uncommon symptom of *S. typhi* infection.

Case presentation

A 25-year-old male presented to the Level 1 hospital with sudden onset symptoms: pyrexia (39.2°C), headache, arthralgia, myalgia, distended abdomen, watery diarrhea four times, no nausea, and vomiting. He previously had been well, and he had never been given a typhoid vaccination before. On examination, blood pressure was 120/65 mmHg; heart rate was 72 bpm. Otherwise, he had no edema, lymphadenopathy, abdominal tenderness, or skin rash. At the Level 1 hospital, the patient was treated for an unspecified gastrointestinal disorder with oral antipyretic medicine and electrolyte-fluid compensation. After 8 h, symptoms of pyrexia and diarrhea ceased.

At the 22nd hour, the first syncope was recorded and lasted for 40 s, accompanied by vomiting once. He was treated with intravenous (IV) transfusion with normal saline (0.9%) and closely monitored. At the 24th hour, he had the second syncope but no fever, vomiting, or convulsion. This syncope lasted for 35 s.

Due to the recurrent syncope, the patient was referred to our hospital at the 30th hour and admitted to the Emergency room. Symptoms and signs on admission were body temperature 36.5°C, blood pressure 105/65 mmHg, respiratory rate 22 bpm, oxygen saturation 93%, palpitation, fatigue, headache, dizziness, and nausea without vomiting. Glasgow Coma Scale was E4V5M6.² The abdomen was initially soft

and mildly distended, with no significant bowel sounds and no tenderness with no visceromegaly or adenopathy. The third syncope occurred while the patient was in the Emergency room and lasted for 30 s, for which he was closely monitored without any treatment.

With three syncopes, mild dyspnea, electrocardiogram presented to change with sinus bradycardia, 40 bpm. IV atropine of 0.04 mg/kg of the body mass was prescribed. After the injection, the heart rate increased to 53 bpm (atropine test negative), suggesting a sickness sinus syndrome; therefore, he was planned to be treated with this diagnosis and indicated pace marker intervention (Figure 1).

On the other hand, due to pyrexia and digestive disorder symptoms, after being admitted to the emergency room, the patient was tested for *S. typhi*; the result was a Widal test positive, and the blood culture was positive for *S. typhi*.

Some medical tests were performed. The results of these tests were shown in Tables 1 and 2.

The patient was treated with oxygen support with a flow of 3 L/min × 120 min, saline 0.9% 500 mL IV, XXX drops/minute, atropine IV 0.04 mg/kg, and ciprofloxacin 500 mg oral × 2 tablets/day × 7 days.

After treatments, he was closely monitored on vital signs, oxygen saturation, and electrocardiogram for 7 days. No more syncope and no fever were recorded, and vital signs were normal. Heart rate increased day by day and remained stable from the sixth day (Figure 2).

Symptoms of headache, arthralgia, myalgia, and distended abdomen decreased and ceased on the sixth day. Electrocardiogram showed sinus rhythm with a heart rate of 72 bpm, and no sinus bradycardia was detected. The patient was discharged on the seventh day.

The patient was scheduled to get re-examinations on the 10th day, the first month, and the third month afterward.

Table 1. Results of blood tests.

No.	Test	Result
1	Troponin I	0.02 µg/L
2	CK-MB	4.8 ng/L
3	C-reactive protein	5 mg/L
4	White blood cell	4.7 G/L
5	Electrolytes	Within normal range
6	Liver function, clotting	Within normal range
7	Urine dipstick	Leukocytes & nitrites negative
8	Malaria rapid diagnostic test	Negative
9	Dengue fever rapid diagnostic test	Negative
10	Widal tube agglutination	Positive
11	Blood culture	Positive for <i>Salmonella typhi</i>

Table 2. Results of some imaging tests.

No.	Test	Result
1	Electrocardiogram	Sinus Bradycardia, 40 beats/min
2	Chest x-ray	Normal
3	Echocardiography	The normal size left ventricle, dynamic systolic function (ejection fraction of 86%), and no regional wall motion abnormality
4	Abdominal ultrasound	No hepato-splenomegaly

Results showed that no syncope, no pyrexia, and no digestive disorder symptoms occurred. Normal electrocardiographs with sinus rhythm and heart rate of 70–80 bpm were observed. The patient returns to normal life as usual.

Discussion

Syncope is defined as transient loss of consciousness due to cerebral hypoperfusion, characterized by a rapid onset, short duration, and spontaneous complete recovery.^{3,4} This is a common clinical problem, and the primary goal of evaluation is to determine whether the patient is at increased mortality risk. Syncope is common in the general population, with 6% of medical admissions and 3% of emergency room visits.⁴ Studies of syncope report prevalence rates as high as 41%, with recurrent syncope occurring in 13.5%.⁵ Syncope shares many clinical features with other disorders, presenting many differential diagnoses. Syncope is a symptom that can be due to various causes, ranging from benign to life-threatening conditions.^{3,4} In our patient, syncope happened thrice and lasted 30 to 40s, which is an abnormal and rare symptom in typhoid patients.

Cardiac arrhythmia is a common cause of syncope, and promptly identifying an arrhythmic etiology has diagnostic and prognostic implications.⁶ Syncope is caused by

bradycardia, tachycardia, or hypotension due to low cardiac index, blood flow obstruction, vasodilatation, or acute vascular dissection. When bradycardia and tachycardia are discovered in patients with syncope, determining their causal relationship to syncope often poses challenges for the practitioner.^{3,4}

Along with the history and physical examination, the electrocardiogram is the most important diagnostic tool evaluating of the patient. Bradycardia and conduction blocks are common electrocardiographic findings.⁷ Symptoms are related to the decreased cardiac output that occurs with bradycardia or tachycardia. Most of the symptoms are caused by decreased cerebral perfusion, and 50% of patients have syncope or presyncope.^{3,4}

Sinus node dysfunction should be suspected when a patient describes symptoms of fatigue, syncope, presyncope, or exercise intolerance and is noted to have sinus bradycardia or pauses on the 12 lead-electrocardiogram or during Holter monitoring.^{3,6,7}

Pharmacologic testing may be used to differentiate between sinus node dysfunction and autonomic dysfunction. The total autonomic blockade is achieved after administering atropine 0.04 mg/kg. The resulting intrinsic heart rate represents the sinus node rate, devoid of autonomic influences. Assuming that the formula defines the normal intrinsic heart rate (in beats/min):

$$\text{Intrinsic heart rate} = 118.1 - (0.57 \times \text{age})$$

Then an intrinsic heart rate lower than predicted using this formula is consistent with sinus node dysfunction and an intrinsic heart rate close to the predicted rate with a clinical presentation similar to sinus node dysfunction is suggestive of autonomic dysfunction as the cause of bradycardia. The intrinsic heart rate helps to distinguish patients with true sinus node dysfunction from those with enhanced parasympathetic tone.^{3,7,8} In our case, the electrocardiogram showed sinus bradycardia, 40 bpm, and IV atropine of 0.04 mg/kg of the body mass was given. After that, the heart rate only increased to 53 bpm (atropine test negative).

Relative bradycardia is an important diagnostic finding in various infectious and noninfectious diseases. Relative bradycardia can be an essential clinical tool for diagnosing infectious and noninfectious etiologies. Relative bradycardia may be a valuable marker for diagnosis when other signs and symptoms are confusing or less clear to reveal disease etiology. Relative bradycardia may be used for different infectious diseases in selected clinical situations.^{9–13} Physiologically, for each degree increase in temperature in degree Celsius, there is a commensurate increase in the heart rate of 10 bpm, Carlvon Liebermaster’s rule.^{12,13}

As relative bradycardia is poorly understood pathogenetically, various mechanisms have been proposed. That proposal could be listed as the release of inflammatory cytokines, increased vagal tone, direct pathogen effect on the

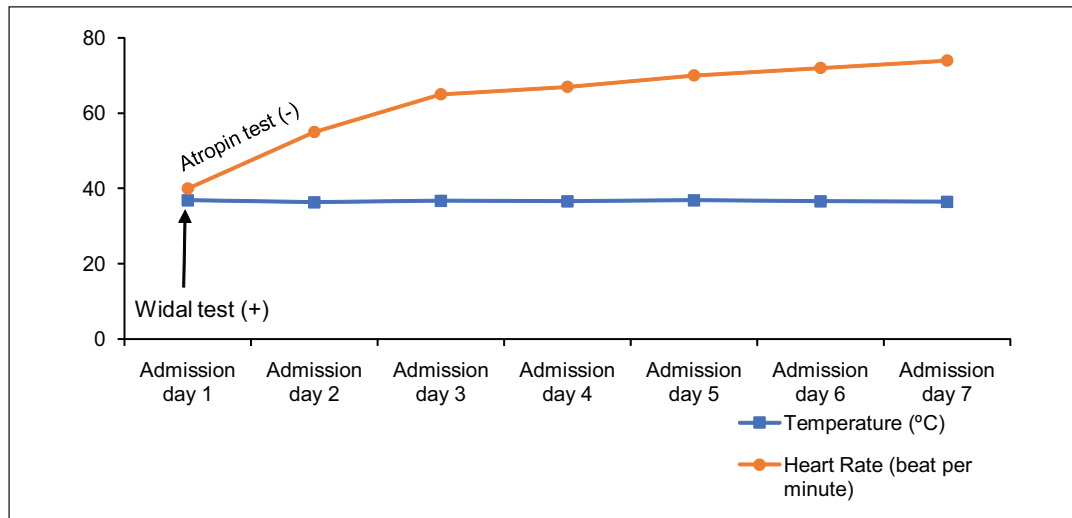


Figure 2. Heart rate and temperature during inpatient treatment time.

myocardium, and electrolyte abnormalities.^{14,15} Some of these proinflammatory cytokines such as tumor necrosis factor (TNF)- α , interleukin (IL)-1, and IL-6 increase vagal tone, therefore, decreasing heart rate.¹⁵

Infectious diseases associated with relative bradycardia have important diagnostic significance for the individual patient as well as for the type of infection.¹¹ In a study by Ostergaard et al.,¹⁰ it is confirmed that typhoid fever, Legionnaire's disease, and psittacosis (*Chlamydia psittaci*) are associated with relative bradycardia. Relative bradycardia is also common among typhoid fever patients, although the sensitivity was low (15%–20%).¹⁶

Typhoid is recognized by the sudden onset of sustained fever, relative bradycardia, severe headache, nausea, and severe loss of appetite; it is sometimes accompanied by a hoarse cough and constipation or diarrhea.^{14,17,18}

Our patient had a sudden onset of a high fever of 39.2°C (102.6°F) but not lasting for a long time (only 8 h). This is an unusual and rare symptom in typhoid patients because they commonly have a high fever $\geq 102^\circ\text{F}$ for about 5–7 days.^{9,17,18} Yaita et al.¹⁶ reported a typhoid fever patient with a fever ($>38.5^\circ\text{C}$) that had persisted for 5 days. Neopane and Panta¹⁸ showed 114 typhoid fever cases with a history of fever $>100^\circ\text{F}$ for more than 5 days. Shah and Dubrey¹⁴ showed a typhoid fever, complicated by myocarditis, in a traveler returning to the United Kingdom, which remained a 5-day pyrexial.

Treatment is increasingly complicated by emerging drug resistance and has led to the use of third-generation cephalosporins or fluoroquinolones.¹⁹ Our patient was successfully treated with ciprofloxacin 500 mg orally twice a day for a 7-day course. Bereda¹ was treated successfully for typhoid fever due to eating over-ripened pineapple by using ciprofloxacin 500 mg was given twice a day orally for 7 days. Effa et al.¹⁹ showed a 7-day course of either ciprofloxacin or ofloxacin was found to be superior.

Current vaccines against typhoid used in the United Kingdom are only around 75% effective, particularly when bacterial numbers are high.¹⁴ Therefore, immunized United Nations staff in endemic areas cannot be excluded from consideration of this infection.

On one hand, our report has some limitations. First, we did not conduct antibiograms even though blood cultures were positive for *S. typhi*. The use of antibiotics is empiric, thus reducing the specificity of treatment. Second, after treatment, we did not survey patients' opinions. However, in the conditions of the field hospital, there was a shortage of human and material resources, so we were unable to carry out the procedure thoroughly. On the other hand, our report has several strengths. First, we used positive cultures for *S. typhi* as the gold standard for typhoid diagnosis. Second, to the best of our knowledge, this is the first study to report a case of fever-free but still slow pulse due to typhoid.

Conclusions

Typhoid fever is a burden in low- and middle-income countries caused by the bacteria *S. typhi*. Typhoid fever is a bacterial disease spread through contact with food or water contaminated by fecal matter or sewage; the diagnosis of typhoid fever was based on travel history, medical symptoms, Widal test, and blood culture.

Typhoid patients sustain high fevers; relative bradycardia could be a practical tool for diagnosing infectious diseases such as typhoid. Typhoid is a recognized yet unusual cause of syncope; enteric fever should be considered as the cause of patients with symptoms of syncope, sudden onset high fever, and relative bradycardia. The patient was treated with third-generation quinolone antibiotic, the preferred typhoid fever treatment.

Through this case, we have a suggestion for the clinical treatment application. In areas at risk of typhoid or a

prominent typhoid endemic, in patients with bradycardia, even without fever, typhoid must be ruled out.

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Author contributions

All authors contributed equally to data analysis, drafting, and revising the article, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Declaration of conflicting interests

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Ethical approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Vietnam Level 2 Hospital in United Nations Mission in South Sudan (No. 128/VNL2H and was approved on 30 May 2020).

Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

ORCID iD

Tuan Dinh Le  <https://orcid.org/0000-0003-2633-583X>

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