

Typhoid fever: A rare cause of relative bradycardia in Japan

A 22-year-old woman was referred to our hospital from a primary care clinic due to a fever (>38.5°C) that had persisted for 5 days with shivering chills and mild headache, but without diarrhea, rash, arthralgia, or myalgia. On the day of the onset of these symptoms, she had been prescribed levofloxacin tablets from her physician, but the fever persisted. She had returned travel to southern and southeastern Asia (a 3-month backpacking trip to Thailand, India, Burma, Laos, and Nepal) 25 days before the onset of symptoms and had no history of pre-travel consultation. In every country, she had enjoyed fruit juices at street stalls (Figure 1A). Upon first consultation, the general impression was not bad, instead of being febrile. A dry cough appeared on the day she visited our hospital. Her vital signs were as follows: blood pressure, 107/76 mm Hg; heart rate, 88 beats/min; body temperature, 37.3°C; and, Glasgow Coma Scale, E4V5M6. Her spleen was not palpable. The laboratory data showed a normal white blood cell count (4500/ μ L [Eosinophils: 0.2%]), accompanied by mild elevations of C-reactive protein (3.26 mg/dL), aspartate aminotransferase (33 IU/L), and lactate dehydrogenase (279 IU/L). A chest X-ray examination was normal. A peripheral blood smear test and a malaria rapid diagnostic test (First Response Malaria Ag. (pLDH/HRP2) Combo Rapid Diagnostic Test, Premier Medical Corporation Ltd., US) were negative. On the day following our first consultation, a blood culture was positive for Gram-negative rod (GNR) (Figure 1B), and the relative bradycardia was shown (Day 1) (Figure 1C). Based on her travel history, examinations, and the

relative bradycardia, we suspected a diagnosis of enteric fever. We also considered imported multidrug-resistant GNR bloodstream infection. We initiated treatment with azithromycin 500 mg orally for 3 days and meropenem at a dose of 1 g intravenously every eight hours. Finally, GNR was identified as *Salmonella typhi*. On the 4th hospital day, we changed meropenem to ceftriaxone at a daily dose of 2 g administered intravenously according to the susceptibility tests for *S. typhi* (ceftriaxone: susceptible, levofloxacin: resistant). The patient was discharged after treatment that lasted 20 days. During an entire febrile period (days 1-5), relative bradycardia was documented (Figure 1C).

Nevertheless our patient's incubation period of enteric fever was longer than typical one (<21 days),¹ our first diagnosis was enteric fever. A combination of the patient's history and her nonspecific symptoms led us that we should draw blood cultures for possible enteric fever. A dry cough is a well-known symptom of patients with typhoid fever (sensitivity: 40%).² Relative bradycardia was also famous among typhoid fever patients,³ although the sensitivity was low (15%-20%).⁴ Relative bradycardia is also seen in patients with drug fever, *Legionella* infection, lymphomas, and some tropical diseases (malaria, dengue fever, leptospirosis, and typhoid fever).⁵ Relative bradycardia caused by typhoid fever is rare in Japan; however, this symptom might be clinically relevant to a suspicion of typhoid fever, among partially treated culture-negative cases. In this era of globalization, general practitioners should know the typical characteristics of imported infectious

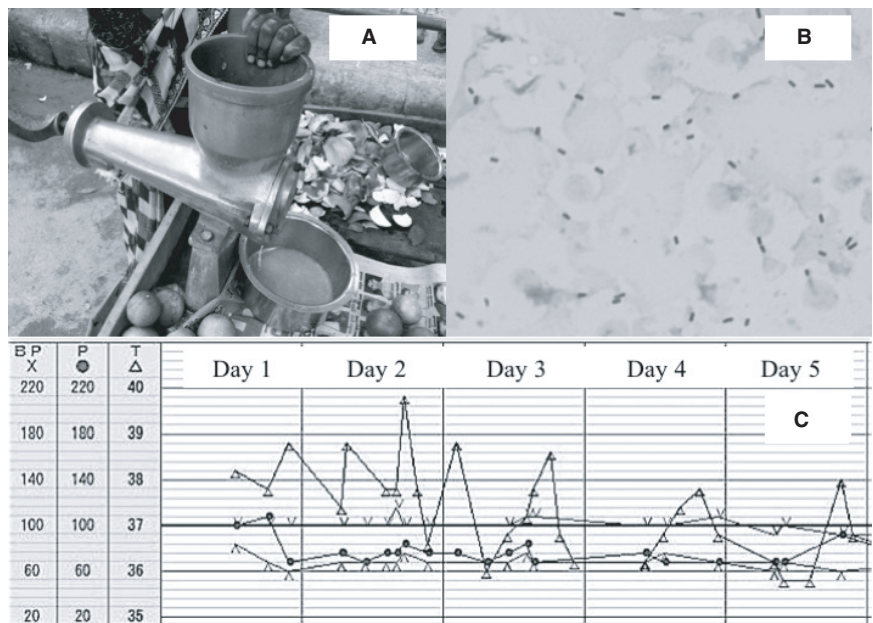


FIGURE 1 A fruit juice maker at street in India. (This photograph was taken by our patient) (A). The blood culture at the first examination was positive for Gram-negative bacilli (B (aerobic bottle)). Relative bradycardia is shown in (C). BP, ×: blood pressure; P, ●: heart rate; T, △: body temperature

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2017 The Authors. *Journal of General and Family Medicine* published by John Wiley & Sons Australia, Ltd on behalf of Japan Primary Care Association.

diseases and should rapidly consult with skilled infectious diseases physicians.

ETHICS STATEMENT

Informed consent was obtained from the patient.

ACKNOWLEDGEMENT

The authors thank junior residents, Eriko Hashimoto and Ryo Yano for their vigorous contribution to our practice.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Kenichiro Yaita MD¹

Nana Oyama MT²

Yoshiro Sakai PhD^{1,3}

Jun Iwahashi PhD¹

Kenji Masunaga MD, PhD¹

Nobuyuki Hamada PhD¹

Hiroshi Watanabe MD, PhD¹

¹*Department of Infection Control and Prevention, Kurume University
School of Medicine, Fukuoka, Japan*

²*Department of Clinical Laboratory Medicine, Kurume University
Hospital, Fukuoka, Japan*

³*Department of Pharmacy, Kurume University Hospital, Fukuoka, Japan*

REFERENCES

1. Spira AM. Assessment of travellers who return home ill. *Lancet*. 2003;361:1459–69.
2. Su CP, Chen YC, Chang SC. Changing characteristics of typhoid fever in Taiwan. *J Microbiol Immunol Infect*. 2004;37:109–14.
3. Cunha BA. Fever of unknown origin: clinical overview of classic and current concepts. *Infect Dis Clin North Am*. 2007;21:867–915. vii.
4. Crum NF. Current trends in typhoid Fever. *Curr Gastroenterol Rep*. 2003;5:279–86.
5. Cunha BA. The diagnostic significance of relative bradycardia in infectious disease. *Clin Microbiol Infect*. 2000;6:633–4.