



Another Typhoid Patient From Japan

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DOI: 10.1111/j.1708-8305.2010.00394.x

Typhoid treatment was empirically started in a Japanese patient with undifferentiated fever in Nepal since Japanese tourists, unlike most Americans and Europeans to South Asia, are unable to obtain typhoid vaccination in Japan even for travel to this area of high endemicity. Subsequently, his blood culture grew out *Salmonella typhi*.

Case Report

A 31-year-old Japanese man had a history of abdominal pain and vomiting of 1 day. The pain was in the epigastric region and gradually became intense. It was non-radiating and burning in nature. It was aggravated by food intake. It was associated with nausea and several episodes of vomiting. He also had high fever 1 day earlier which was relieved by paracetamol. Bowel and bladder functions were normal. He had experienced a similar type of pain 2 weeks ago for which he took pantoprazole. He also had recurrent episodes of gastritis in the past. He was not a smoker and did not take alcohol. He had traveled from Australia to South East Asia 5 weeks ago and was in Nepal for the last 20 days before the onset of these symptoms. He had not taken any vaccinations.

His examination was normal except for mild epigastric tenderness. He was treated with domperidone, hyoscine butylbromide, and omeprazole for suspected gastritis. His blood work showed a white blood cell (WBC) count of $8.3 \times 10^9/L$ with 80% neutrophils; liver function tests were normal. Ketones and albumin were present in the urine.

That night he had a severe attack of abdominal pain, vomiting, and fever. When we saw him the next day, the temperature was 102°F, pulse 90/min, blood pressure 150/90 mm Hg, and respiratory rate 30/min. He had epigastric tenderness. Repeat investigations

showed a WBC count of $9.6 \times 10^9/L$ with 85% neutrophils. Malaria parasite was negative on blood film examination. Creatinine, electrolytes, blood sugar, and amylase were normal. Blood was drawn for culture. Chest radiography, ultrasound of the abdomen, and upper GI endoscopy were normal.

He was treated with intravenous fluids, analgesics, omeprazole, and paracetamol. He continued with fever for two more days and was put on azithromycin 1 g a day on the suspicion that this was undifferentiated fever in the tropics, likely enteric fever, typhus, or leptospirosis.^{1,2} The next day blood culture showed profuse growth of *Salmonella typhi* which was sensitive to ciprofloxacin but resistant to nalidixic acid. The fever gradually decreased to normal over another 2 to 3 days.

Discussion

Countries like Nepal in South Asia are areas of high endemicity for enteric fever.³ Travel to the Indian Subcontinent is associated with the highest risk of contracting typhoid fever.⁴ Western travelers to South Asia are routinely recommended vaccination against typhoid by the Centers for Disease Control (CDC), World Health Organization (WHO), and the Health Protection Agency of the UK.⁴ Japanese tourists are not able to obtain typhoid vaccination and therefore are probably more susceptible to acquiring enteric fever while traveling in South Asia. Anecdotally, in recent years, in our clinic we have seen more Japanese travelers with enteric fever than American or European travelers. Previously, it was common for Japanese travelers to

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not receive the hepatitis A vaccine. For this reason, a study from this same clinic showed that the Japanese travelers to Nepal were more predisposed to hepatitis A than other travelers.⁵ The Japanese authorities have indeed now begun to encourage the Japanese travelers to developing countries to obtain the hepatitis A vaccine. Perhaps a similar suggestion needs to be made and typhoid vaccines made available for Japanese travelers to the developing world, especially South Asia, the hub for typhoid fever.

Another reason why this traveler might have been more susceptible to *Salmonella* infection is that he was on the proton pump inhibitor, pantoprazole, which reduces gastric acidity possibly making the individual more prone to acquiring such an infection.⁶

Enteric fever is caused by *S typhi* or *Salmonella paratyphi* and is associated with poor sanitation and contaminated food and water. It can present with a variety of symptoms, the most common being fever, headache, nausea/vomiting, constipation/diarrhea, malaise, and dry cough. If untreated, it can lead to serious systemic complications like intestinal perforation, sepsis, meningitis, hepatic and splenic abscesses, pancreatitis, etc.⁷ An increasing incidence of multidrug resistant and nalidixic acid resistant strains of *S typhi* raises concern as to the choice of antibiotic for the treatment of typhoid fever. Even in the United States, infection with resistant *S typhi* strains is associated with foreign travel, especially the Indian Subcontinent.⁸ The typhoid organism from South Asia is usually reported to be sensitive to ciprofloxacin but resistant to nalidixic acid; importantly, the latter is a truer reflection of ciprofloxacin sensitivity. A recent study showed that an increasing number of typhoid patients in the United States are infected with *S typhi* strains with a decreased susceptibility to fluoroquinolones.⁸ People with suspected enteric fever from South Asia should not be treated with ciprofloxacin. Azithromycin with better intracellular concentrations is an optimal choice.⁹ A similar increasing emergence of infection with strains of *S paratyphi* group A that are resistant to nalidixic acid, coupled with either decreased sensitivity or, in some cases, clinical resistance to fluoroquinolones has been seen.¹⁰

Typhoid is a vaccine-preventable disease. The vaccine is recommended for travelers to the Indian Subcontinent and other developing countries in Central and South America, the Caribbean, Africa, and Asia.¹¹ It may be important to receive the vaccination even for short stays of less than a week to typhoid endemic countries.¹² Two types of typhoid vaccines are available, the inactivated polysaccharide Vi parenteral vaccine and the live oral vaccine. The parenteral vaccine is given as a single injection with a booster recommended every 2 years, whereas the oral Ty21a vaccine is taken as a single capsule every other day for four doses. Booster is recommended every 5 years.¹¹ The oral vaccine should

not be given to severely immunocompromised patients. Although indicated in the traveler to South Asia, these vaccines give only 50% to 80% protection.³ Currently there is no vaccination against *S paratyphi*. One needs to avoid contaminated food and water in conjunction with being vaccinated to try to effectively prevent enteric fever.

Typhoid can still be tricky in its presentation and a high index of suspicion is always required while working in hospitals and clinics in Kathmandu. In this case, the unvaccinated Japanese traveler was a clue to the diagnosis. We conclude that it would probably be in the best interest of Japanese travelers to receive the typhoid vaccine.

Declaration of Interests

The authors state they have no conflicts of interest to declare.

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