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# SCIENTIFIC ARTICLE

## Childhood Typhoid Fever Diagnosed in an Urban U.S. Setting

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### Abstract

The majority of cases of childhood typhoid fever diagnosed in the United States occur in persons recently returned from travel abroad. We report two childhood cases of typhoid fever acquired in Mexico and India and diagnosed in an urban United States setting. This report describes these cases and provides insights into the pitfalls in recognizing this condition in a nonendemic setting as well as information concerning differential diagnosis and treatment.

### Introduction

In the United States, childhood typhoid fever may occur in the form of occasional epidemics, such as the waterborne typhoid outbreak in Dade County, Florida in 1973<sup>1</sup>, or more commonly, as sporadic cases imported from Mexico, India, and other developing countries, where it is endemic. We present two childhood cases of typhoid fever in an urban United States setting

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(Wilmington, Delaware), whose diagnosis was not initially suspected in a place and time in which typhoid fever was rare.

### Case Presentations

**Patient 1.** A 15-year-old Hispanic male presented to the emergency department with a three-week history of abdominal pain and a one-week history of vomiting, diarrhea, headache, fever, and chills. He was sent home with a diagnosis of a "viral" syndrome. Four days later, the patient returned to the emergency department with a higher fever in addition to his other continuing symptoms. On physical examination, he appeared toxic with a temperature of 40°C, pulse of 90/min., and a blood pressure of 100/80 mm Hg. He was estimated to be approximately 10 percent dehydrated. Significant positive findings on this examination included hyperemic pharynx with tonsillar exudate, tender anterior cervical lymphadenopathy, and clear lungs. Abdominal examination revealed periumbilical tenderness, a tender liver palpable two to three centimeters below the right costal margin and a palpable spleen tip. The patient had focal areas of erythema on the right lower thorax. Initial laboratory studies revealed a white blood cell count of 6300 mm<sup>3</sup> with 69 percent polys, 4 percent bands, 20 percent lymphocytes, 4 percent monocytes, and 3 percent eosinophils.

He was admitted to the hospital with a diagnosis of nonspecific gastroenteritis and dehydration. Subsequent history revealed that

the patient had recently traveled by foot and bus from the Mexican border to the United States, often drinking water from rivers and streams along the way. During this journey, he became anorectic and developed abdominal pain.

The diagnosis of typhoid fever was made when blood and stool cultures were reported to be growing *Salmonella typhi*. After eight days of therapy with trimethoprim-sulfamethoxazole (TMP-SMX), the patient had improved considerably and treatment was changed to oral TMP-SMX. Repeat blood and stool cultures were negative for *Salmonella typhi*, and he was discharged on the 15th day after having received TMP-SMX for a total of two weeks. The patient was lost to follow-up.

**Patient 2.** A 16-year-old Indian female, a resident of Wilmington, Delaware, presented to her private physician's office eight days after returning from India. She had a five or six day history of fevers to 40°C, nausea, several bouts of emesis per day, and anorexia as well as intermittent nonproductive cough. The patient was initially treated with oral ampicillin for three days but was subsequently hospitalized because of deterioration in her condition. On admission, she was noted to be mildly dehydrated with a temperature of 40°C, respiratory rate of 20/min., pulse of 84/min., and a blood pressure of 90/64 mm Hg. Physical examination demonstrated erythema of her pharynx without exudate, clear lungs, and no lymphadenopathy. Abdominal examination revealed moderate right upper quadrant tenderness but liver and spleen were not enlarged. Laboratory studies revealed a white blood cell count of 4300 mm<sup>3</sup>, with 53 percent lymphocytes, 31 percent polymorphs, 1 percent monocytes, and 15 percent band forms. Liver function tests revealed an alkaline phosphatase of 289 IU/L, SGOT 285 IU/L, and GGTP 382 IU/L with a total bilirubin value of 0.7 mg/dL. Hepatitis B surface antigen and antibody, anti-HBc (both IgG and IgM) and anti-HAV antibodies were negative. Chest roentgenogram was normal. Stool cultures at this time were reported negative for *Salmonella*, *Shigella*, *Yersinia*, and *Campylobacter*.

The patient was hydrated with intravenous fluids and given parenteral ampicillin and gentamicin. Thirty-six hours after starting par-

enteral antibiotics, the patient was still febrile to 40°C. One week after admission, a blood culture obtained in her private physician's office was reported to be growing a gram negative rod, which was subsequently identified as *Salmonella typhi* by the Delaware State Laboratory. The isolate was reported as sensitive to chloramphenicol and ampicillin as determined by the Kirby-Bauer method. During the second week of therapy with ampicillin, the patient defervesced; repeat blood cultures were sterile. The patient was discharged on oral amoxicillin, one gram three times a day, with follow-up by the Department of Public Health.

### Discussion

The incidence of typhoid fever reported by the Centers for Disease Control in the United States fell from one case per 100,000 in 1955 to 0.2 cases per 100,000 in 1966.<sup>2</sup> Since 1978, the annual number of cases reported has stabilized at about 500 cases per year.<sup>3</sup> The percentage of total yearly cases that result from exposure during foreign travel has increased from 33 percent in the interval 1967 to 1972, to 58 percent between 1975 and 1984.<sup>2</sup> Forty-five percent of these imported cases originated in Mexico, while 15 percent resulted from travel to India.<sup>2</sup>

Typhoid fever is a multisystem disease which may involve the central nervous system, lungs, kidneys, and reticuloendothelial system, as well as the gastrointestinal tract<sup>4,5,6</sup> and may encompass many potential differential diagnoses. Therefore, it is possible that during the first week of illness, patients with typhoid fever may present with nonspecific symptoms of fever, malaise, headache, and anorexia which may mimic many viral illnesses including influenza, enteroviral, and adenoviral infections. The presence of an enlarged, tender liver, as well as elevated liver function tests, may lead to a presumptive incorrect diagnosis of viral hepatitis. Typhoid fever may also present with signs and symptoms of simple gastroenteritis mimicking rotaviral infection or bacterial gastroenteritides including nontyphoid *Salmonella*, *Campylobacter*, or *Yersinia*. Patients may also present with signs and symptoms suggesting

meningoencephalitis, bronchopneumonia, acute abdomen, or pelvic inflammatory disease. Late in the course of illness, patients with typhoid fever may undergo evaluation for fever of unknown origin.

The patients described here presented with high fevers and associated findings consistent with, but not diagnostic of, typhoid fever. Both had histories of vomiting, but diarrhea was only present in patient 1. Pharyngitis and liver tenderness were present in each patient. More specific clues found on physical examination were the presence of relative bradycardia in both patients and cutaneous lesions suspicious for rose spots in patient 1. The initial laboratory studies, particularly in patient 2, who had elevated liver function tests and leukopenia, were consistent with the diagnosis of typhoid fever.

The diagnosis of typhoid fever is best established by the isolation of the organism from blood, stool, or bone marrow aspirate. Bone marrow aspirate cultures substantially increase the chances of bacteriological confirmation of typhoid fever, especially when the patient has had prior antibiotic treatment.<sup>7,8</sup> The widespread use of antimicrobials in patients with suspected sepsis may partially treat *S. typhi* infection and possibly inhibit the isolation of the organism from clinical specimens, such as blood and stool.<sup>8</sup> Delay in the diagnosis of typhoid fever usually results from its varied presentations, incomplete patient history, and the physician's lack of experience with this infection.

Worldwide, chloramphenicol has been considered the standard antimicrobial therapy for the treatment of typhoid fever. Trimethoprim-sulfamethoxazole, ampicillin, and amoxicillin however, may also be effective alternatives. Occasional resistance to these antibiotics has been observed among salmonella species isolated in India, Southeast Asia, Korea, Mexico, and central Africa.<sup>9</sup> Third generation cephalosporins, especially cefotaxime and ceftriaxone, have recently been utilized for the therapy of typhoid fever and other salmonellosis with encouraging success.<sup>9,10</sup> While evaluating patients with possible typhoid fever, it may be critical to consider the potential source of the patient's infection. For example, because

chloramphenicol resistance has been reported in Mexico, our first patient from Mexico was treated with TMP-SMX.

Many United States physicians have little personal experience with typhoid fever and may neglect to elicit a timely, pertinent travel history from patients presenting with confusing clinical pictures. Since early treatment of typhoid fever facilitates patients' recovery, physicians must think globally when confronted with foreign travellers.

### Summary

We describe the occurrence of typhoid fever in two adolescents in Wilmington, Delaware. These cases highlight the difficulties often encountered in making this diagnosis in a nonendemic setting and to serve as a reminder that typhoid fever, while often forgotten, is not gone.

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