

## Nalidixic Acid-Resistant *Salmonella enterica* Serotype Typhi Presenting as a Primary Psoas Abscess: Case Report and Review of the Literature

William A. Shakespeare,<sup>1</sup> Daniel Davie,<sup>2</sup> Claude Tonnerre,<sup>3,4</sup> Michael A. Rubin,<sup>3,4</sup>  
Michael Strong,<sup>3</sup> and Cathy A. Petti<sup>3,4,5\*</sup>

University of Utah School of Medicine<sup>1</sup> and Department of Family Practice,<sup>2</sup> Department of Medicine,<sup>3</sup>  
Division of Infectious Diseases,<sup>4</sup> and Department of Pathology,<sup>5</sup> University of Utah  
Hospitals and Clinics, Salt Lake City, Utah

Received 24 April 2004/Returned for modification 29 May 2004/Accepted 19 October 2004

**We report an unusual case of *Salmonella enterica* serotype Typhi presenting as a primary psoas abscess. The isolate tested susceptible to ciprofloxacin but resistant to nalidixic acid in vitro, a pattern associated with fluoroquinolone therapeutic failures. We review the literature for serovar Typhi psoas abscess in the absence of bacteremia and discuss the importance of identifying isolates with reduced susceptibility to fluoroquinolones.**

### CASE REPORT

The patient was a 32-year-old Peruvian male who worked as a shepherd in the mountains near Salt Lake City, Utah. He presented to an urgent care clinic with the chief complaint of gradually worsening left lower back and left inguinal pain following a traumatic fall from a horse 5 months earlier. He reported no history of fever, chills, or abdominal symptoms on presentation or in the preceding 6 months. He also denied a personal or family history of typhoid fever. The clinical symptoms and an elevated white blood cell count of 20,000/mm<sup>3</sup> led the outpatient clinician to order a magnetic resonance imaging study, which showed a left psoas mass consistent with an abscess or a hematoma. This prompted an outpatient computed tomography (CT)-guided aspiration (Fig. 1). CT visualized the multicystic mass within the left psoas with surrounding inflammatory change and fat stranding. The surrounding lymph nodes were all less than 1 cm in diameter. The aspirated fluid revealed 1+ polymorphonuclear neutrophils and no organisms on the Gram stain. A peripherally inserted central catheter was placed in the clinic and, although afebrile, the patient was started on empirical treatment with intravenous cefazolin, 2 g every 8 h. The following day a preliminary culture of the aspirated material grew multiple organisms including gram-negative diplococci, alpha-hemolytic streptococci, nonhemolytic streptococci, and gram-negative rods. The physician thought that the results likely reflected a contaminated sample and made no alteration in therapy. However, the patient's symptoms worsened despite 2 days of intravenous antibiotic therapy and he was admitted to the hospital.

On admission, the patient was afebrile with stable vital signs. Physical examination revealed tenderness to palpation of the left lumbar paraspinous muscles and the left inguinal region, extending 5 to 6 cm inferiorly to include the left superior

medial thigh. No paraspinous or inguinal masses were palpated. He had a positive psoas sign on the left side. Pertinent laboratory results included an elevated white blood cell count of 16,000/mm<sup>3</sup> with a normal cell differential; hematocrit, 37%; C-reactive protein, 33 mg/dl (reference interval, 0.0 to 0.8 mg/dl); alkaline phosphatase, 297 U/liter (reference interval, 40 to 120 U/liter); alanine aminotransferase, 111 U/liter (reference interval, 13 to 72 U/liter); aspartate aminotransferase, 34 U/liter (reference interval, 15 to 59 U/liter); and total bilirubin, 0.7 mg/dl (reference interval, 0.2 to 1.3 mg/dl). Two sets of blood cultures were obtained. The antibiotic therapy was changed to intravenous cefotaxime (2 g every 4 h) to broaden coverage. The gram-negative rod from the initial CT aspirate was identified as *Salmonella enterica* serotype Typhi by use of Vitek GNI + Card (Bio-Mérieux, Durham, N.C.). In addition, the isolate was tested by slide agglutination in somatic antisera and reacted with group D antigen. The identification of the organism was confirmed as serovar Typhi by the Utah Department of Health Laboratory.

On the second day of hospitalization, the patient developed fever to 39.9°C. Although blood cultures remained negative, the patient's fever and the psoas pain failed to resolve. On day 5 of the patient's hospitalization, a repeat aspiration and drainage of the psoas fluid collection were performed. The culture of this aspirated material grew serovar Typhi in pure culture. Cultures of the blood and urine remained negative. Stool could not be obtained for culture. Per 2004 NCCLS guidelines for extraintestinal salmonellosis (11), susceptibility testing was performed by disk diffusion and E-test. Culture tested susceptible to all antimicrobials tested except for nalidixic acid. The zone diameters and MICs of the tested antimicrobial agents were the following: ampicillin, 27 mm, 0.5 µg/ml; cefotaxime, 32 mm, 0.5 µg/ml; trimethoprim-sulfamethoxazole, 36 mm, <6 µg/ml; chloramphenicol, 4 µg/ml; nalidixic acid, 6 mm, ≥32 µg/ml; and ciprofloxacin, 25 mm, 0.5 µg/ml.

The patient was maintained on cefotaxime intravenously, which was continued as outpatient treatment until he had completed 5 weeks of therapy. The patient recovered com-

\* Corresponding author. Mailing address: Department of Pathology, University of Utah Hospitals and Clinics, 500 Chipeta Way, Salt Lake City, UT 84108. Phone: (801) 583-2787, ext. 3174. Fax: (801) 584-5207. E-mail: cathy.petti@aruplab.com.

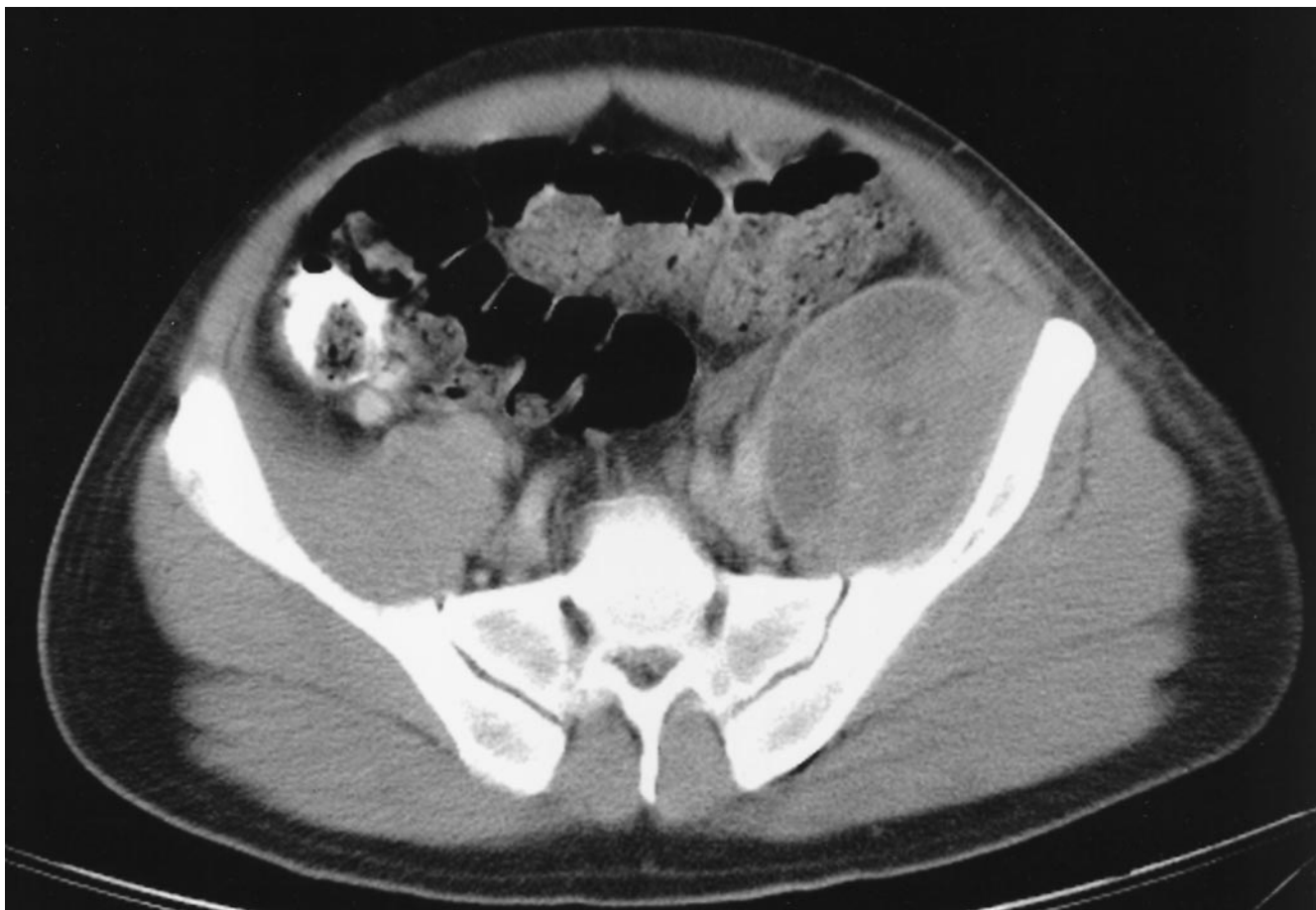


FIG. 1. Computed tomography image demonstrating enlargement of the left psoas muscle with increased density suggestive of abscess. Surrounding inflammatory change and fat stranding are also present. All inguinal lymph nodes are less than 1 cm in diameter.

pletely, remained afebrile, and had no recurrent flank pain. A repeat CT scan demonstrated resolution of the abscess.

Serotype Typhi is a well-known cause of enteric fever, an invasive infection defined as bacteremia with minimal gastrointestinal symptoms. Serotype Typhi bacteremia is commonly associated with extraintestinal disease and can involve the liver, spleen, lymph nodes, skin, bones, joints, endocardium, or central nervous system. Less appreciated is the ability of the organism to penetrate extraintestinal tissues as an isolated finding. A review of the literature shows serovar Typhi to be capable of forming abscesses in various locations including the spleen (8), liver (2), and brain (4). These abscesses, however, were found in patients with known bacteremia. This case report documents the unusual finding of a psoas abscess caused by serovar Typhi in the absence of detectable bacteremia. Also, the susceptibility pattern of the isolated organism highlights the emerging problem of antimicrobial resistance in serovar Typhi and the therapeutic dilemma faced by clinicians regarding the empirical use of fluoroquinolones.

An unusual feature of this case was the localization of the abscess to the psoas muscle. While non-serovar Typhi *Salmonella* psoas abscess has been reviewed previously (5), primary

serovar Typhi-strain psoas abscess is a rare entity. Indeed, we believe this to be only the third report in the worldwide literature of serovar Typhi causing a primary psoas abscess. In 1999, Baccaro described an Argentinean man who developed a serotype Typhi psoas abscess without previous history of typhoid fever (1). In that report, a review of the literature back to the 1930s found no previous mention of serovar Typhi as the cause of a primary psoas abscess. We found an additional case describing a woman in France who developed a serotype Typhi psoas abscess 28 years after a childhood case of typhoid fever. After this lengthy interval of indolence, the infection may arguably be considered a primary psoas abscess (9).

The unique presentation of this case raises a series of questions. First, the source of the patient's infection deserves consideration. There is no known animal host of serovar Typhi; humans are the primary reservoir of the organism. There were no reported local food-borne outbreaks of serovar Typhi during this period. Furthermore, the patient lived and worked alone in a rural area of the mountains with little human contact. This suggests that the patient probably contracted the infection through casual contact, perhaps even years prior to emigrating from his home in Peru, a known region of endemicity. Second, the presence of a serovar Typhi abscess without any history of systemic illness warrants exploration. The

asymptomatic serovar Typhi carrier state is commonly reported, especially in connection with gallstones (7). While this patient was found to have no gallstones on ultrasonic examination, a chronic carrier state should not be excluded. The organism is known to reside within tissue macrophages in the liver and within the spleen and bone marrow (12). In fact, the organisms multiply within the reticuloendothelial system, and infected bile may lead to chronic carriage, thereby serving as a reservoir for future metastatic disease (14). Third, the organism's localization to the psoas muscle is intriguing. The most plausible hypothesis for this finding is that the patient's trauma secondary to being thrown from a horse resulted in a hematoma that was later seeded by serovar Typhi and progressed to abscess formation. There were no lymph nodes proximal to this abscess to suggest an infected lymph node as a source. Based upon our review of the literature, it appears that asymptomatic chronic carriers of the organism can spontaneously seed an organ without concomitant systemic illness.

In addition to the unusual finding of serovar Typhi presenting as a psoas abscess in the absence of bacteremia, this case is notable because it draws attention to an important issue concerning antimicrobial resistance in salmonellae. Management decisions for empirical antimicrobial therapy are becoming increasingly complicated due to the emergence of antimicrobial resistance to commonly used agents, such as ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline. As resistance of serovar Typhi to these classic first-line agents developed worldwide, quinolones became the agents of choice to treat serovar Typhi infections. In the 1990s, resistance to nalidixic acid was reported in Southeast Asia (12). This resistance, most commonly caused by point mutations in the *gyrA* and *parC* genes (6), spread rapidly, and now its distribution is worldwide. For the United States, the Centers for Disease Control and Prevention reported that in the year 2001, 30% of serovar Typhi isolates were nalidixic acid resistant as opposed to 19% in 1999 (10). In the setting of this rising incidence, it is not surprising that the serovar Typhi isolated from our patient's abscess was resistant to nalidixic acid.

Despite the widespread emergence of resistance to nalidixic acid, fluoroquinolones remain an important treatment option for typhoid fever. But over the past decade there have been increasing reports of treatment failures using fluoroquinolones for patients whose serovar Typhi isolates are susceptible to fluoroquinolones and resistant to nalidixic acid in vitro (3, 13, 15). In a study investigating 18 cases of nalidixic acid-resistant, ofloxacin-susceptible serovar Typhi isolates from Vietnam, authors reported that poorer outcomes were associated with fluoroquinolone therapy (15). Last year the Centers for Disease Control and Prevention published a comprehensive report demonstrating that for nalidixic acid-resistant organisms, MICs of ciprofloxacin are typically at the upper range for susceptibility, usually between 0.12 and 0.5  $\mu\text{g}/\text{ml}$  (3). This was also the case with our patient (ciprofloxacin MIC, 0.5  $\mu\text{g}/\text{ml}$ ). The uncertain clinical response of fluoroquinolone-suscepti-

ble, nalidixic-acid resistant strains has prompted debate over changing the established NCCLS breakpoints for fluoroquinolones. Moreover, the clinical effectiveness of fluoroquinolones for serovar Typhi isolates for which MICs of ciprofloxacin were high but which were positive for nalidixic acid susceptibility is unknown.

This case report underscores the necessity of adhering to the recently updated NCCLS guidelines recommending routine screening for nalidixic acid susceptibility with all extraintestinal *Salmonella* isolates to avoid potential treatment failures. Based on our review of the literature and 2004 NCCLS guidelines, we do not recommend the use of fluoroquinolone monotherapy for nalidixic acid-resistant, ciprofloxacin-susceptible serovar Typhi infection, particularly in the case of extraintestinal disease. Further study is needed to better delineate fluoroquinolone MIC breakpoints for salmonellae and to assess the value of these breakpoints in predicting therapeutic response.

#### REFERENCES

- Baccaro, F. G. 1999. Primary psoas abscess due to *Salmonella typhi*. *Med. Gen. Med.* **10**:E16.
- Ciraj, A. M., D. Reetika, G. K. Bhat, C. G. Pai, and P. G. Shivananda. 2002. Hepatic abscess caused by *Salmonella typhi*. *Trop. Gastroenterol.* **23**:181-182.
- Crump, J. A., T. J. Barrett, J. T. Nelson, and F. J. Angulo. 2003. Reevaluating fluoroquinolone breakpoints for *Salmonella enterica* serotype Typhi and for non-Typhi salmonellae. *Clin. Infect. Dis.* **37**:75-81.
- Hanel, R. A., J. C. Araujo, A. Antoniuk, L. F. da Silva Ditzel, L. T. Flenik Martins, and M. N. Linhares. 2000. Multiple brain abscesses caused by *Salmonella typhi*: case report. *Surg. Neurol.* **53**:86-90.
- Heyd, J., R. Meallem, Y. Schlesinger, B. Rudensky, I. Hadas-Halpern, A. M. Yinnon, and D. Raveh. 2003. Clinical characteristics of patients with psoas abscess due to non-typhi *Salmonella*. *Eur. J. Clin. Microbiol. Infect. Dis.* **22**:770-773.
- Hirose, K., A. Hashimoto, K. Tamura, Y. Kawamura, T. Ezaki, H. Sagara, and H. Watanabe. 2002. DNA sequence analysis of DNA gyrase and DNA topoisomerase IV quinolone resistance-determining regions of *Salmonella enterica* serovar Typhi and serovar Paratyphi A. *Antimicrob. Agents Chemother.* **46**:3249-3252.
- Lai, C. W., R. C. Chan, A. F. Cheng, J. Y. Sung, and J. W. Leung. 1992. Common bile duct stones: a cause of chronic salmonellosis. *Am. J. Gastroenterol.* **87**:1198-1199.
- Lambotte, O., T. Debord, C. Castagne, and R. Roue. 2001. Unusual presentation of typhoid fever: cutaneous vasculitis, pancreatitis, and splenic abscess. *J. Infect.* **42**:161-162.
- Lortholary, O., B. Jarrousse, P. Attali, J. M. Hoang, M. Brauner, and L. Guillevin. 1995. Psoas pyomyositis as a late complication of typhoid fever. *Clin. Infect. Dis.* **21**:1049-1050.
- McClellan, J., M. Reller, K. Joyce, C. Polyak, E. Mintz, F. Angulo, and the NARMS Working Group. 2002. Emerging resistance to quinolones among *Salmonella* Typhi isolates in the United States, 1999-2001. National Antimicrobial Resistance Monitoring System Annual Scientific Meeting, Hilton Head, S.C., 19 to 22 November 2002.
- NCCLS. 2004. Performance standards for antimicrobial susceptibility testing: 14th informational supplement. NCCLS document M100-S14. NCCLS, Wayne, Pa.
- Parry, C. M., T. T. Hien, G. Dougan, N. J. White, and J. J. Farrar. 2002. Typhoid fever. *N. Engl. J. Med.* **347**:1770-1782.
- Threlfall, E. J., L. R. Ward, J. A. Skinner, H. R. Smith, and S. Lacey. 1999. Ciprofloxacin resistant *Salmonella typhi* and treatment failure. *Lancet* **353**:1590-1591.
- Tynes, B. S., and J. P. Utz. 1962. Factors influencing the cure of *Salmonella* carriers. *Ann. Int. Med.* **57**:871-882.
- Wain, J., N. T. Hoa, N. T. Chinh, H. Vinh, M. J. Everett, T. S. Diep, N. P. Day, T. Solomon, N. J. White, L. J. Piddock, and C. M. Parry. 1997. Quinolone-resistant *Salmonella typhi* in Viet Nam: molecular basis of resistance and clinical response to treatment. *Clin. Infect. Dis.* **25**:1404-1410.