



Nontyphoidal *Salmonella* Hepatitis: A Rare Complication of a Common Enteric Infection

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ABSTRACT

Hepatitis from nontyphoidal *Salmonella* gastroenteritis is rare, especially in immunocompetent patients. We present the case of a 30-year-old woman who was found to have *Salmonella* serotype C2 gastroenteritis and elevated liver function tests concerning for concurrent hepatitis. An extensive workup was negative for other etiologies, making *Salmonella* the likely culprit. The patient was managed with supportive measures as her liver function tests and symptoms were improving before obtaining microbiological data. Since the role of antibiotic therapy in such cases is not well studied, disease severity in accordance with current guidelines should be used to tailor treatment on a case-by-case basis.

KEYWORDS: Bacterial Gastroenteritis; *Salmonella*; Hepatitis

INTRODUCTION

Nontyphoidal *Salmonella* (NTS) is a major cause of diarrhea worldwide with over 150 million cases and 50,000 deaths reported annually.¹ Although transmission of NTS can occur person-to-person, most cases occur due to contaminated food or water.² Symptoms are usually self-limiting and begin around 1–3 days after consumption of an offending agent. Diarrhea, abdominal pain, vomiting, and fever are common, but extraintestinal manifestations such as blood stream infection, osteomyelitis, meningitis, and septic arthritis have been reported in older and immunosuppressed adults.³

Although there has been an increasing concern for the invasive nature of nontyphoidal strains in sub-Saharan Africa⁴, to the best of our knowledge, there have been no case reports detailing acute hepatitis from a nontyphoidal strain of *Salmonella* gastroenteritis in an immunocompetent host in the United States. *Salmonella* hepatitis from the more virulent typhoidal strains has been extensively reported in the literature, and hepatitis is estimated to occur in 21%–60% of cases involving these typhoidal strains.^{5,6}

We present the case of a previously healthy 30-year-old woman with no significant medical history who presented with acute *Salmonella* serotype C2 gastroenteritis and markedly elevated liver function tests concerning for concurrent hepatitis. Extensive workup to rule out other potential causes of hepatitis was negative, supporting NTS as the likely culprit.

CASE REPORT

A 30-year-old woman with a history of asthma was admitted to the hospital with 4 days of right upper quadrant abdominal pain, fever, nausea/vomiting, and nonbloody diarrhea. Symptoms began within 2 days of eating 1-week-old raw sushi and were not exacerbated by oral intake. She denied recent travel, undercooked chicken or raw egg consumption, use of new medications/supplements, or other sick contacts.

On presentation, she was afebrile with stable vitals. Physical examination demonstrated tenderness to palpation in the right upper quadrant of the abdomen but absent Murphy sign. The rest of her examination was unremarkable. Initial labs were notable for

a white blood cell count at 4.9 B/L (3.4–10.8), aspartate transferase (AST) 986 IU/L (0–40 IU/L), alanine aminotransferase (ALT) 946 IU/L (0–32 IU/L), and alkaline phosphatase (ALP) 343 IU/L (44–121 IU/L). Total bilirubin was elevated at 1.3 mg/dL (0–1.2 mg/dL), with a 0.9 mg/dL direct component (0–0.4 mg/dL). The international normalized ratio was 1.27, although this was not checked until hospital day 3.

Computed tomography abdomen and pelvis with contrast showed a mildly thickened gallbladder wall without stones. The common bile duct was dilated at 8 mm. A right upper quadrant ultrasound showed a mildly distended gallbladder and dilated extrahepatic ducts without cholelithiasis or choledocholithiasis.

Further testing was pursued to rule out choledocholithiasis. Magnetic resonance cholangiopancreatography abdomen with and without contrast demonstrated mildly dilated intra- and extrahepatic bile ducts without obstructing lesions. She then underwent endoscopic ultrasonography, which was normal without ductal dilation, stones, or sludge. Liver enzymes started to downtrend on hospital day 2 and her symptoms improved.

Infectious stool bio fire panel was positive for *Salmonella* and subsequent stool culture grew a nontyphoidal C2 serotype. Infectious disease was consulted and recommended no antibiotics given clinical improvement. She was subsequently discharged several days later with an AST of 84, ALT 325, and ALP 205. Her symptoms had resolved by the time of discharge. The transaminitis resolved by 2 weeks postdischarge (Table 1). Other workup included: negative antismooth muscle and mitochondrial antibodies, negative for elevation of IgG antibody levels, normal ceruloplasmin levels, and normal ferritin. Hepatitis C antibody and polymerase chain reaction, hepatitis B core and surface antibody, and hepatitis A IgM antibody were negative. HIV 1/2 antibodies were also negative.

DISCUSSION

Although there have been previous reports of NTS hepatitis occurring in the United States, the patients in those cases had either concurrent viral hepatitis or HIV.^{7–9} Outside of the United States, González-Quintela et al did look at hepatic enzyme derangements in 104 patients admitted to their hospital

with enterocolitis due to *S. enteritidis* from 1995 to 2003. In that study, median liver enzymes found during NTS infection were AST 17 UI/L (7–426 UI/L), ALT 16 UI/L (6–617 UI/L), and ALP 115 UI/L (59–641 UI/L). Within their cohort, which adjusted for preexisting liver disease, 23% of patients had abnormal ASTs (upper limit normal [ULN] < 29), 18% had abnormal ALT (ULN < 25), and abnormal ALP was only seen in 6.1% (ULN < 195). No bilirubin elevations were seen, although their reference range was 0.2–2.6 mg/dL. Only 2 patients without preexisting liver disease in the cohort achieved acute hepatitis, which they defined as AST or ALT 10× ULN. Interestingly, those were both seen with AST elevations of 269 and 306 UI/L.¹⁰ Our patient’s liver enzymes were as high as 25× the upper limit of normal with both ALP and bilirubin elevated, indicative of concurrent biliary injury.

Given concern for choledocholithiasis on noninvasive imaging, endoscopic ultrasonography was pursued. No stones or sludge were seen in the gallbladder, and the common bile duct was normal. Given these findings, it is unlikely that the patient passed a gallstone during her hospital course, and this is further supported by the protracted delay in normalization of hepatic function tests across several weeks. In cases of transient liver function test elevation secondary to gallstone passage, a more rapid return to baseline is expected.¹¹

Standard practice for NTS infection isolated to the intestine, without severe disease, is to refrain from antibiotic treatment, as it may lead to increased drug resistance and prolong the carrier state.^{12,13} In our case, the patient was treated with supportive care only. This decision was influenced by lack of early microbiological data and quick improvement of her symptoms. Although our patient recovered on supportive care alone, the role of antibiotics in NTS with liver involvement requires additional investigation.

In summary, this case demonstrates the ability of NTS gastroenteritis to cause hepatobiliary disease in immunocompetent patients. Providers should be aware of patients who present with *Salmonella* gastroenteritis and elevated liver enzymes, as extraintestinal manifestations can occur, even in otherwise healthy individuals. The role of antibiotic therapy is not well defined, and overall disease severity in accordance with current practice guidelines should guide therapy.

Table 1. Liver function test trends

	Initial presentation	Discharge (3 days later)	One week post-discharge	Two weeks post-discharge
AST (0–40 IU/L)	986	84	80	23
ALT (0–32 IU/L)	946	325	305	55
ALP (44–121 IU/L)	343	205	139	81
Tbili (0–1.2 mg/dL)	1.3	0.4	0.3	0.5
Dbili (0–0.4 mg/dL)	0.9	<0.2	<0.2	<0.2

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate transferase.

DISCLOSURES

Author contributions: All authors helped to write the manuscript and were involved in patient care. MJ Bierowski is the article guarantor.

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