


CASE REPORT

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Typhoid fever presenting with gastric ulcer bleeding

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Abstract

Background: Enteric fever is a systemic disease caused by *Salmonella enterica* serovar Typhi or *Salmonella enterica* serovar Paratyphi, characterized by high fever and abdominal pain. Most patients with enteric fever improve within a few days after antibiotic treatment. However, some patients do not recover as easily and develop fatal life-threatening complications, including intestinal hemorrhage. Lower gastrointestinal bleeding has been reported in 10% of cases. However, upper gastrointestinal bleeding has rarely been reported in patients with enteric fever. We present a case of gastric ulcer hemorrhage caused by enteric fever.

Case presentation: A 32-year-old woman, complaining of fever lasting four days and right upper quadrant pain and melena that started one day before admission, consulted our hospital. Abdominal computed tomography revealed mild hepatomegaly and gastroscopy revealed multiple active gastric ulcers with flat black hemorrhagic spots. The melena of the patient stopped on the third day. On the fifth admission day, she developed hematochezia. At that time, *Salmonella enterica* serovar Typhi was isolated from the blood culture. The antibiotic regimen was switched to ceftriaxone. Her hematochezia spontaneously resolved the following day. Finally, the patient was discharged on the 12th admission day without clinical symptoms. However, her fever recurred one month after discharge, and she was readmitted and *Salmonella enterica* serovar Typhi was confirmed again via blood culture. She was treated with ceftriaxone for one month, and was discharged without complications.

Conclusion: Our case showed that although rare, active gastric ulcers can develop in patients with enteric fever. Therefore, upper and lower gastrointestinal bleeding should be suspected in patients with enteric fever, especially showing relapsing bacteremia.

Keywords: Typhoid fevers, *Salmonella enterica* serovar Typhi, Gastrointestinal hemorrhages, Gastric ulcer, Case report

Background

Enteric fever is a systemic disease caused by *Salmonella enterica* serovar Typhi or *Salmonella enterica* serovar Paratyphi. The bacteria usually invade the small

intestinal mucosa, where they infect and multiply via the lymphatic/blood vessels. Typical symptoms include febrile symptom, whole abdominal pain and tenderness, diarrhea, anorexia, and weight loss [1, 2]. Most people diagnosed with enteric fever improve a few days after empirical antibiotic treatment. However, some patients develop complications [1, 3, 4]. The complications of enteric fever can affect any organ system. The important gastrointestinal manifestations of enteric fever include hepatosplenomegaly, jaundice, lower gastrointestinal hemorrhage, intestinal perforation, and acalculous

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cholecystitis [5]. Intestinal hemorrhage or perforation is the most serious complication of enteric fever [5–7]. Occurring in 10% of cases, lower gastrointestinal bleeding most commonly affects the terminal ileum and ileocecal valve [5, 8]. Meanwhile, upper gastrointestinal bleeding has rarely been reported. We present a patient with enteric fever, presenting with gastric ulcer hemorrhage, as a rare complication of disease.

Case presentation

A 32-year-old woman consulted our hospital for fever lasting four days, and right upper quadrant pain and melena that started the day before admission. Her medical and family histories were unremarkable. She did not drink alcohol and was a nonsmoker. Physical examination revealed moderate right upper quadrant tenderness and a high fever (39.8 °C). Her initial laboratory workup showed an aspartate transaminase (AST) of 106 IU/L, alanine transaminase (ALT) of 97 IU/L, gamma-glutamyl transpeptidase of 108 IU/L, alkaline phosphatase of 123 IU/L, lactate dehydrogenase of 682 IU/L, and C-reactive protein of 14.2 mg/dL. Her hemoglobin level, white blood cell count, and platelet count were within normal range. The serologic markers of viral hepatitis A, B, and C were all negative. Abdominal computed tomography and magnetic resonance cholangiopancreatography revealed mild hepatomegaly and a small benign hepatic cyst measuring 0.8 cm. However, esophagogastroduodenoscopy revealed three gastric ulcers with flat black hemorrhagic spots, which were located from the anterior and posterior walls of the gastric antrum to the greater curvature of the gastric midbody (Fig. 1). The patient did not take medications, such as non-steroidal anti-inflammatory drugs, that could cause gastric ulcers. Histopathological examination of the biopsy specimen, obtained from each ulcer, revealed chronic atrophic gastritis. The patient was treated with antibiotics, hepatotonics, and proton pump inhibitor. The additional serologic tests, performed after admission, showed no evidence of Epstein-Barr virus hepatitis, cytomegalovirus hepatitis, Wilson's disease, autoimmune hepatitis, or other rare type of hepatitis. The patient's melena was relieved by conservative treatment on the third admission day, and her hemoglobin level was maintained at 12.5 g/dL. On the fifth day after admission, she abruptly developed hematochezia, and her hemoglobin dropped from 12.5 to 10.8 g/dL. Her AST and ALT levels increased to 442 IU/L and 248 IU/L, respectively. At a time, *Salmonella enterica* serovar Typhi was isolated from blood cultures. Upper endoscopy and colonoscopy, and liver biopsy were reserved for severe hematochezia or persistent elevation of liver enzymes. The antibiotic regimen was switched from piperacillin-tazobactam plus moxifloxacin to ceftriaxone, according to the antibiotic

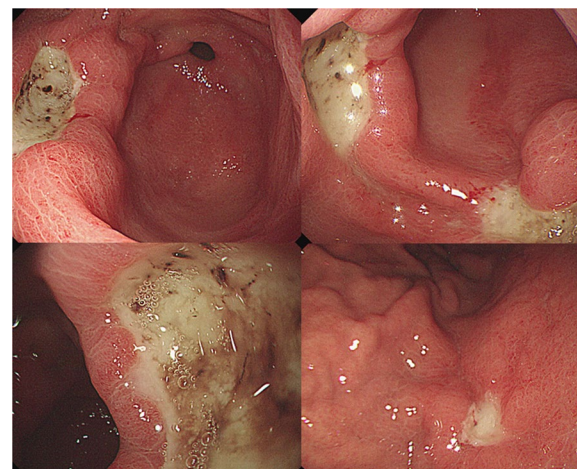


Fig. 1 Esophagogastroduodenoscopy revealed three gastric ulcers with flat black hemorrhagic spots, which were located from the anterior and posterior walls of the gastric antrum to the greater curvature of the gastric midbody

susceptibility test. The next day, the patient's hematochezia stopped, and she started passing loose stools with near-normal color. Her AST and ALT levels gradually decreased, and she was discharged on the 12th day after admission without clinical symptoms. However, her fever recurred one month after her discharge, and she was readmitted and *Salmonella enterica* serovar Typhi was confirmed again via blood culture. Follow-up esophagogastroduodenoscopy (EGD) was performed after 7 weeks of initial EGD and revealed a significantly healed gastric ulcer (Fig. 2). Whole body bone scan and colonoscopy were performed to identify the reservoir for the relapsed infection, however, she had a negative result (Figs. 3, 4). She was treated with ceftriaxone for additional one month and was discharged without complications.

Discussion and conclusions

This is a case of a 32-year-old woman who presented with melena, fever, and right upper quadrant pain, was diagnosed with enteric fever with gastric ulcer bleeding, and treated with antibiotics and proton pump inhibitor. Gastrointestinal bleeding has been reported in 10% of enteric fever patients [5]. However, most of the gastrointestinal bleedings with enteric fever reported in the literature were related to small intestine or colonic lesions. In one study, analyzing the endoscopic findings in patients with enteric fever and gastrointestinal bleeding, the most commonly affected site was the terminal ileum, followed by the ileocecal valve, ascending colon, and transverse colon. Multiple variable-sized punched-out ulcers with slightly elevated margins were representative endoscopic findings [8]. Although there are many studies on lower

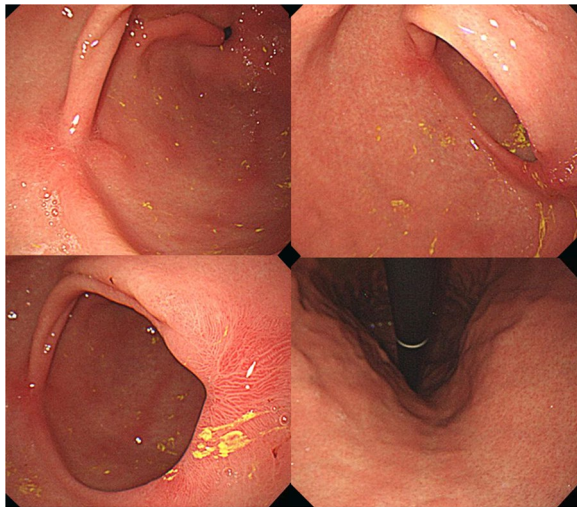


Fig. 2 Follow-up esophagogastroduodenoscopy revealed a significantly healed gastric ulcer

gastrointestinal bleeding in patients with enteric fever, upper gastrointestinal bleeding has rarely been reported in patients with enteric fever. There have been only a few

reports on patients, who presented with melena, diagnosed with aortoduodenal fistula associated with nontyphoidal *Salmonella* aortitis [9, 10]. Harza et al. recently reported the case of a patient with enteric fever, who presented with hematemesis and melena, were diagnosed with primary aortoduodenal fistula due to infected aortic aneurysm with *Salmonella enterica* serovar Typhi infection, and underwent emergency endoaneurysmorrhaphy [11]. However, cases of enteric fever, presenting with gastric ulcer bleeding, have not been reported until now. To the best of our knowledge, this is the first case report of enteric fever presenting with gastric ulcer bleeding. The most common causes of peptic ulcer disease are *Helicobacter pylori* infection and ingestion of nonsteroidal anti-inflammatory drugs (NSAIDs). *Helicobacter pylori* was not identified in gastric biopsy specimens from our patient, and she had no history of taking NSAIDs or other ulcerogenic drugs. Also, she was not taking any proton pump inhibitors, antibiotics, or bismuth compounds that could cause the missed diagnosis of *Helicobacter pylori* infection. Moreover, she was young and no had underlying disease. Therefore, gastric ulcer bleeding in our patient can be presumed to be caused by *Salmonella enterica* serovar Typhi infection. Enteric fever

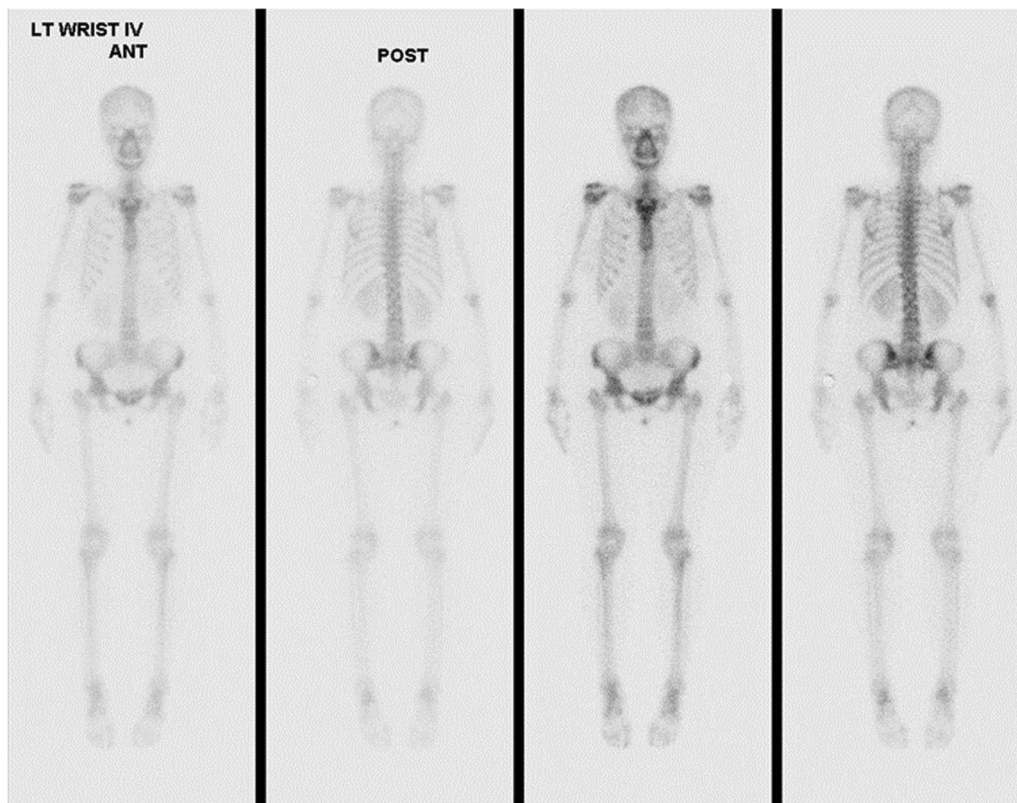


Fig. 3 Whole body bone scan showed no obvious uptake

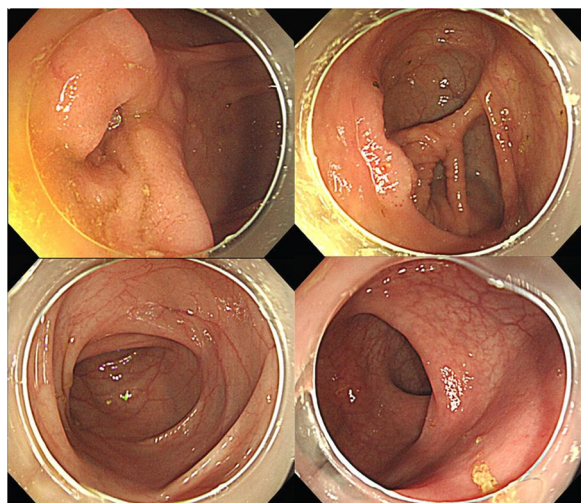


Fig. 4 No lesions were seen at colonoscopy

induces various clinical symptoms by forming typhoid nodules, which indicate lymphoid hyperplasia, in the reticuloendothelial system, including the liver, spleen, and other lymphoid organs. Mucosal ulcer formation or ulcer bleeding occurring in the lower gastrointestinal tract was also associated with mucosal ulceration secondary to hyperplasia of the Peyer's patches or lymphoid follicles. However, the mechanism behind gastric ulcer formation in the present case is unclear. Interestingly, an experimental study involving *Salmonella enterica* serovar Typhimurium-infected mice, frequently used as an animal model for enteric fever, found that *Salmonella enterica* serovar Typhi infection may induce hemorrhagic ulcers by promoting gastric oxidative stress. Ofloxacin, lysozyme chloride, and oxyradical scavengers, including glutathione, allopurinol, and dimethylsulfoxide ameliorated hemorrhagic ulcer formation [12]. Another study using rats reported that *Salmonella enterica* serovar Typhi infection may cause hemorrhagic gastric ulcers by increasing histamine secretion and vascular permeability [13].

Despite these findings, there have been no reported cases or mechanistic studies of enteric fever accompanied by gastric ulcer bleeding. Our patient, who presented with gastric ulcer bleeding, was discharged after her symptoms had improved with antibiotic treatment. However, she was readmitted due to recurrence with a positive blood *Salmonella enterica* serovar Typhi blood culture. Based on this finding, the factors associated with the relapsing enteric fever could be related to the development of gastric ulcer bleeding. Enteric fever can relapse within one month in about 5–10% of patients [3, 4]. Several studies have reported that the gallbladder

or mesenteric lymph node served as niches for persisting *Salmonella*, but the mechanism behind relapsing enteric fever remains unclear [14, 15]. Further studies on the mechanism underlying recurrent enteric fever could explain the cause of gastric ulcer bleeding which is a rare clinical symptom of enteric fever.

In conclusion, our case suggested that, although rare, peptic ulcers could develop in patients with enteric fever. Upper gastrointestinal bleeding as well as lower gastrointestinal bleeding should be suspected in patients exhibiting symptoms suggestive of gastrointestinal bleeding, especially presenting relapsing bacteremia.

Abbreviations

ALT: Alanine transaminase; AST: Aspartate transaminase; NSAIDs: Nonsteroidal anti-inflammatory drugs.

Acknowledgements

Not applicable.

Authors' contributions

HJJ and JSL drafted the manuscript. HSE and Shinye C collected the clinical data and performed follow-up. BSL, SHK, ESL, JKS, HSM, SHK, HSL, Seong-woo C, and HSK reviewed the literature. HSE and Shinye C critically revised the manuscript for intellectual content. All authors have read and approved the final manuscript.

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Availability of data and materials

All data generated during this study are included in this published article.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the Chungnam National University Hospital (IRB number: CNUH 2021-07-068).

Consent for publication

Written informed consent was obtained from the patient before the publication of this case report.

Competing interests

The authors declare that they have no competing interests.

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References

- Harris JB, Brooks WA. Typhoid and paratyphoid (enteric) fever. In: Hunter's tropical medicine and emerging infectious diseases. Elsevier; 2020. p. 608–616.
- Murinello A, Morbey A, Coelho JF, Mendonça P, Pires A, Ramalho VM, Ribeiro NC, Lázaro A, Peres H, Netta J. Typhoid fever-clinical and endoscopic aspects. *Jornal Português de Gastreenterologia*. 2008;15(2):76–82.
- Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. Typhoid fever. *N Engl J Med*. 2002;347(22):1770–82.
- Bhan MK, Bahl R, Bhatnagar S. Typhoid and paratyphoid fever. *Lancet*. 2005;366(9487):749–62.
- Crump JA, Sjölund-Karlsson M, Gordon MA, Parry CM. Epidemiology, clinical presentation, laboratory diagnosis, antimicrobial resistance, and antimicrobial management of invasive *Salmonella* infections. *Clin Microbiol Rev*. 2015;28(4):901–37.
- Chanh NQ, Everest P, Khoa TT, House D, Murch S, Parry C, Connerton P, Van Bay P, Diep TS, Mastroeni P. A clinical, microbiological, and pathological study of intestinal perforation associated with typhoid fever. *Clin Infect Dis*. 2004;39(1):61–7.
- Butler T, Islam A, Kabir I, Jones PK. Patterns of morbidity and mortality in typhoid fever dependent on age and gender: review of 552 hospitalized patients with diarrhea. *Rev Infect Dis*. 1991;13(1):85–90.
- Lee JH, Kim JJ, Jung JH, Lee SY, Bae MH, Kim YH, Son HJ, Rhee PL, Rhee JC. Colonoscopic manifestations of typhoid fever with lower gastrointestinal bleeding. *Dig Liver Dis*. 2004;36(2):141–6.
- Morrow C, Safi H, Beall AC Jr. Primary aortoduodenal fistula caused by *Salmonella* aortitis. *J Vasc Surg*. 1987;6(4):415–8.
- Bardin JA, Collins GM, Devin JB, Halasz NA. Nonaneurysmal suppurative aortitis. *Arch Surg*. 1981;116(7):954–6.
- Hazra D, Kota AA, Agarwal S. *Salmonella* aortitis causing primary aortoenteric fistula. *Indian J Surg*. 2021.
- Hung CR, Wang PS. Gastric oxidative stress and hemorrhagic ulcer in *Salmonella* typhimurium-infected rats. *Eur J Pharmacol*. 2004;491(1):61–8.
- Hung C-R, Wang PS. Role of histamine and acid back-diffusion in modulation of gastric microvascular permeability and hemorrhagic ulcers in *Salmonella* typhimurium-infected rats. *Life Sci*. 2004;74(16):2023–36.
- Griffin AJ, Li L-X, Voedisch S, Pabst O, McSorley SJ. Dissemination of persistent intestinal bacteria via the mesenteric lymph nodes causes typhoid relapse. *Infect Immun*. 2011;79(4):1479–88.
- John ALS, Ang WG, Huang M-N, Kunder CA, Chan EW, Gunn MD, Abraham SN. S1P-Dependent trafficking of intracellular *Yersinia pestis* through lymph nodes establishes Buboes and systemic infection. *Immunity*. 2014;41(3):440–50.

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