Massive small bowel bleeding caused by scrub typhus in Korea

Ki Beom Bae, Won Hwa Youn, Youn Jae Lee, Soo Jin Jung, Kwan Hee Hong

A 79-year-old man was diagnosed with scrub typhus based on fever, eschar, skin rash and a markedly elevated serum tsutsugamushi antibody and doxycycline was started. Five days later, hematochezia developed and multiple small bowel ulcerations with hemorrhage were seen on colonoscopy. Despite intensive therapy, the massive hematochezia worsened and the distal small bowel was resected. Multiple ulcerated lesions were identified pathologically as vasculitis caused by scrub typhus. This is the first reported case of pathologically proven small bowel involvement in scrub typhus infection.

INTRODUCTION

Scrub typhus, or tsutsugamushi disease, is an acute febrile illness caused by infection with (O. tsutsugamushi)1, an obligate intracellular bacterium transmitted by the bite of larval trombiculid mites (chiggers)2. Usually its symptoms are similar to a mild influenza-like illness and the clinical course is self-limited with spontaneous recovery after a few days. However, some cases are more severe and protracted and the disease may be fatal, especially in the elderly3.

Scrub typhus is characterized by focal or disseminated vasculitis and perivasculitis which may involve the lungs, heart, liver, spleen, and central nervous system4.5. Gastrointestinal involvement is uncommon and bleeding through the gut is a rare complication of scrub typhus. Hematemesis or melena is a reported complication in 6.25%-7% of scrub typhus cases, especially in septic patients, and the site of bleeding is almost always in the...
stomach\textsuperscript{8,9}. Pathologically proven small bowel involvement caused by scrub typhus has never been reported before. Therefore, we present the first case of massive small bowel bleeding caused by scrub typhus infection with its clinicopathological findings.

**CASE REPORT**

A 79-year-old male farmer was admitted with hematochezia. Seven days earlier, he had been treated with doxycycline for scrub typhus diagnosed at a local clinic based on clinical findings which included a fever of up to 39°C, headache, myalgia, skin rash and eschar. The hematochezia developed 2 d before admission. He complained of general weakness and fatigue but no abdominal pain. He was taking an antihypertensive drug but no other medications such as nonsteroidal anti-inflammatory drugs (NSAIDs). On examination, blood pressure was 110/60 mmHg, heart rate 90/min, respiratory rate 18/min and temperature 36.7°C. He looked acutely ill and was jaundiced with pale conjunctiva. Examination of the abdomen showed normal bowel sounds with no distention, tenderness or rebound tenderness. No generalized or peripheral edema was observed but hematochezia was detected on digital rectal examination. His initial hematological and biochemical results showed leukocytosis, anemia, thrombocytopenia, hypoalbuminemia, hyperbilirubinemia, and elevated liver enzymes (Table 1). Serologic testing using the passive hemagglutination assay was strongly positive for *O. tsutsugamushi*. To identify the cause of the hematochezia, gastrofiberscopy, colonoscopy, and contrast-enhanced abdominopelvic computed tomography (CT) were carried out. At gastrofiberscopy, no abnormal findings except a polyp in the fundus were noted. Colonoscopy revealed multiple ulcerations with bleeding in the terminal ileum (Figure 1), and abdominal CT showed the extravasation of contrast dye in the small bowel lumen (Figure 2). No focal hemorrhagic lesion was detected on sequential angiography. Conservative treatment with doxycycline and transfusion was continued for 3 d but the hematochezia did not cease and amounted to 900-1500 mL/d. His hemoglobin gradually fell and vital signs deteriorated, necessitating emergency surgery. During surgery, multiple small ovoid erythematous lesions were seen on the outside of the small bowel which corresponded to ulcerative lesions inside the small bowel lumen (Figure 3). These were scattered throughout the small intestine, especially in the terminal ileum, and were bleeding actively. The involved small bowel was resected and the healthy gut was re-anastomosed. Microscopically, the small bowel showed multiple flask-shaped ulcers and lymphocytic vasculitis in the ulcer bed (Figure 4). Postoperatively, vital signs were stabilized and no further hematochezia was observed 5 d after the surgery, at which time a normal diet was started. Normal feaces were observed 10 d postoperatively and the laboratory findings, including liver function, normalized.

### Table 1 Initial laboratory findings

| Laboratory test                  | Initial value |
|----------------------------------|---------------|
| White cell count (mm\(^3\))      | 18,990        |
| Hemoglobin (g/dL)                | 8.7           |
| Hematocrit (%)                   | 25.8          |
| Platelets (mm\(^3\))             | 94,000        |
| Protein (g/dL)                   | 4.5           |
| Albumin (g/dL)                   | 2.7           |
| Bilirubin (mg/dL)                | 5.2           |
| Aspartate aminotransferase (IU/L)| 70            |
| Alanine aminotransferase (IU/L)  | 73            |
| Alkaline phosphatase (IU/L)      | 784           |
| Blood urea nitrogen (mg/dL)      | 24            |
| Serum creatinine (mg/dL)         | 1.4           |
| Hantian virus antibody           | Negative      |
| Leptosira antibody               | Negative      |
| *O. tsutsugamushi* antibody      | Positive (1:280) |
| HBs Ag                           | Negative      |
| HBs Ab                           | Negative      |
| HCV Ab                           | Negative      |
| HBo Ab IgM                       | Negative      |
| HAV IgM                          | Negative      |
| CRP                              | 5.19 (normal < 0.5) |

![Figure 1: Colonoscopic findings. Multiple ulcerations with bleeding in terminal ileum (arrows).](image)

**DISCUSSION**

*O. tsutsugamushi* is transmitted by chiggers of the genus *Leptotrombidium* and causes scrub typhus in Southeast Asia, the former Soviet Union, Japan, and Australia. New foci of scrub typhus have recently been described in Australia, Japan, Thailand, and Korea\textsuperscript{[10]}. The activity of the infected mite is influenced by temperature and humidity and transmission occurs all year in tropical areas. In Korea, transmission is seasonal, and peaks in October and November\textsuperscript{[11,12]}. After an incubation period of 10-21 d, the disease is characterized by fever, headache, myalgia, eschar with skin rash, and gastrointestinal symptoms. It is usually treated with doxycycline. Some cases are more severe and protracted and the disease may be fatal, especially in the elderly. The reported severe complications of scrub typhus include meningoencephalitis\textsuperscript{[13]}, pneumonitis and acute respiratory distress syndrome\textsuperscript{[14]}, hepatitis\textsuperscript{[15]}, acute renal failure\textsuperscript{[16]}, and upper gastrointestinal bleeding\textsuperscript{[8,9]}. These
A: Multifocal flask-shaped ulcers are noted [1994; 1]. A: Multiple erythematous lesions in the serosal surface of small bowel (white arrows) are found; B: Multiple ulcerations in the luminal surface of small bowel (black arrows) are noted.

Figure 2  Abdominal CT findings. Extravasation of contrast dye in small bowel (arrow).

Figure 3  Operative findings. A: Multiple erythematous lesions in the serosal surface of small bowel (white arrows) are found; B: Multiple ulcerations in the luminal surface of small bowel (black arrows) are noted.

tiple actively bleeding ulcerative lesions were identified in the terminal ileum at colonoscopy. Pathologically, these lesions consisted of vasculitis and perivascularitis in the affected bowel wall. Although other causes of small bowel bleeding, such as Meckel's diverticulum, angiodyplasia, small bowel tumor, Crohn's disease and NSAID-induced small bowel injury, should be considered, our patient had no history of illness other than hypertension and was not taking any medications such as NSAIDs. Therefore, the cause of his small bowel bleeding was considered to be infection-induced immune-complex vasculitis associated with scrub typhus.

We report the first case of massive small bowel bleeding in scrub typhus with clinical and histopathological findings. The affected small intestine showed multiple actively bleeding ulcerations identified as vasculitis and perivascularitis microscopically.

Figure 4 Microscopic Features. A: Multifocal flask-shaped ulcers are noted (HE × 40); B: Vasculitis is noted with dense infiltration of lymphocytes within the vessel walls in submucosal layer (PAS × 200).

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