

## Massive small bowel bleeding caused by scrub typhus in Korea

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**Author contributions:** Hong KH organized the study and operated on this case; Bae KB assisted with the operation and wrote the manuscript; Youn WH assisted with the operation and conducted the literature review; Lee YJ diagnosed this case and evaluated the patient preoperatively; Jung SJ confirmed the diagnosis by pathologic findings; and all authors approved the final manuscript.

Supported by A grant from Inje University, 2008

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Received: September 22, 2009 Revised: November 4, 2009

Accepted: November 11, 2009

Published online: February 27, 2010

### Abstract

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.

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**Key words:** Hematochezia; Small bowel bleeding; Scrub typhus; Vasculitis; Multiple small bowel ulcerations

**Peer reviewer:** Dottor Fabrizio Luca, MD, Division of Abdomino-Pelvic Surgery, Via Ripamonti, Milano 435-20141, Italy

Bae KB, Youn WH, Lee YJ, Jung SJ, Hong KH. Massive small bowel bleeding caused by scrub typhus in Korea. *World J Gastrointest Surg* 2010; 2(2): 47-50 Available from: URL: <http://www.wjgnet.com/1948-9366/full/v2/i2/47.htm> DOI: <http://dx.doi.org/10.4240/wjgs.v2.i2.47>

### INTRODUCTION

Scrub typhus, or tsutsugamushi disease, is an acute febrile illness caused by infection with (*O. tsutsugamushi*)<sup>[1]</sup>, an obligate intracellular bacterium transmitted by the bite of larval trombiculid mites (chiggers)<sup>[2]</sup>. 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 elderly<sup>[1]</sup>.

Scrub typhus is a public health problem in Asia where about one million new cases are identified annually and one billion people may be at risk for this disease<sup>[3]</sup>. In addition, reports of infection are becoming increasingly common in travelers returning from Asia to their home countries<sup>[4,5]</sup>.

Scrub typhus is characterized by focal or disseminated vasculitis and perivasculitis which may involve the lungs, heart, liver, spleen, and central nervous system<sup>[1,6,7]</sup>. 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<sup>[8,9]</sup>. 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 accompanied by low attenuation in the periportal areas and inhomogeneous enhancement of the liver (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 feces 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 <sup>3</sup> )	18990
Hemoglobin (g/dL)	8.7
Hematocrit (%)	25.8
Platelets (mm <sup>3</sup> )	94000
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
Hantaan virus antibody	Negative
Leptospira antibody	Negative
<i>O. tsutsugamushi</i> antibody	Positive (1:1280)
HBs Ag	Negative
HBs Ab	Negative
HCV Ab	Negative
HBc Ab IgM	Negative
HAV IgM	Negative
CRP	5.19 (normal < 0.5)

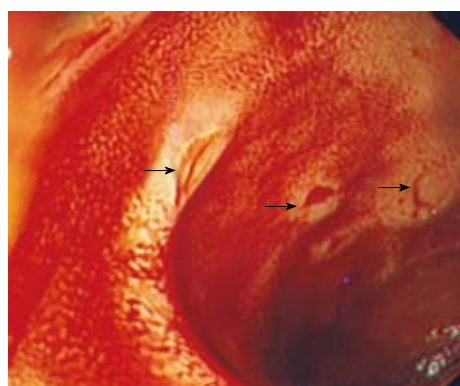
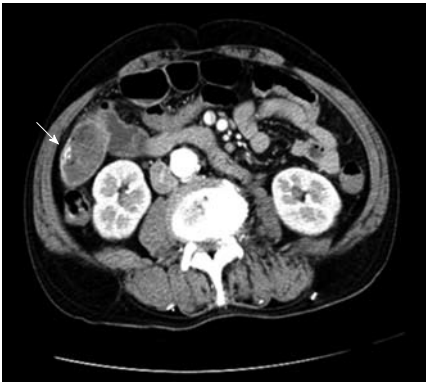


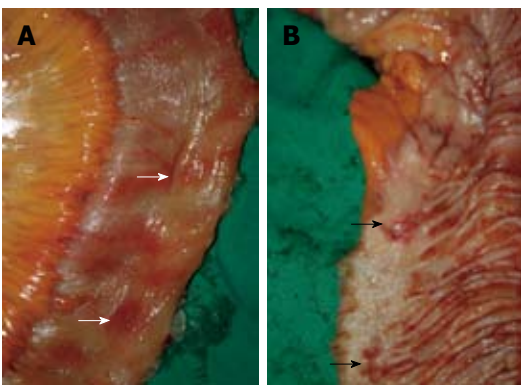
Figure 1 Colonoscopic findings. Multiple ulcerations with bleeding in terminal ileum (arrows).

## 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<sup>[10]</sup>. 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<sup>[3,11]</sup>. 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<sup>[12]</sup>, pneumonitis and acute respiratory distress syndrome<sup>[13]</sup>, hepatitis<sup>[14]</sup>, acute renal failure<sup>[15]</sup>, and upper gastrointestinal bleeding<sup>[8,9]</sup>. These



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

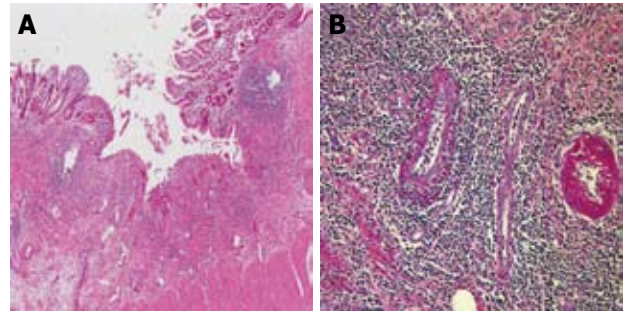


**Figure 3 Operative findings.** A: Multiple erythematous lesions in the serosal surface of small bowel (white arrows) are found; B: Multiple ulcerations in the luminal surface of small bowel (black arrows) are noted.

complications result from vascular injury by vasculitis and perivasculitis in the capillaries or small arterioles<sup>[16]</sup>.

Few studies have reported on the gastrointestinal manifestations of scrub typhus. Kim *et al*<sup>[9]</sup> observed that of all patients with diagnosed scrub typhus, 22.7% have gastrointestinal manifestations usually associated with abdominal pain/tenderness, indigestion, nausea, vomiting, hematemesis, melena, and diarrhea. On gastrofiberscopy, superficial mucosal hemorrhage, multiple erosions and ulcers and unusual vascular bleeding are seen in the stomach. The occurrence of endoscopic features in scrub typhus is associated with the presence of cutaneous lesions and greater clinical severity. Other reported gastrointestinal manifestations include granulomatous hepatitis<sup>[14]</sup>, acalculous cholecystitis<sup>[17]</sup>, pancreatic abscess<sup>[18]</sup>, and gastrointestinal bleeding<sup>[8,9]</sup>. Our patient had more severe complications of scrub typhus, including hypoalbuminemia, hepatitis, jaundice, and acute renal failure, but his most serious complication was hematochezia.

Upper gastrointestinal bleeding associated with scrub typhus is reported in 10.3% of cases and in 3.4%, active bleeding that requires treatment with endoscopic clipping is reported %<sup>[9]</sup>. In contrast, no report has described lower gastrointestinal bleeding associated with scrub typhus with pathologically proven vasculitis. In our patient, mul-



**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).

multiple actively bleeding ulcerative lesions were identified in the terminal ileum at colonoscopy. Pathologically, these lesions consisted of vasculitis and perivasculitis in the affected bowel wall. Although other causes of small bowel bleeding, such as Meckel's diverticulum, angiodysplasia, small bowel tumor, Crohn's disease and NSAID-induced small bowel injury<sup>[19]</sup> 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<sup>[20]</sup> 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 perivasculitis microscopically.

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S- Editor Li LF L- Editor Roemmele A E- Editor Yang C