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A Case of Scrub Typhus Imported from South Korea to Yamagata, Japan

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Scrub typhus, also called tsutsugamushi disease, is a rickettsiosis clinically characterized by fever, rash, and eschar (1). This disease is caused by *Orientia tsutsugamushi*, which is transmitted to humans by larval trombiculid mites (1). The disease is endemic across much of Oceania and the Asia-Pacific region (1). Recently, the numbers of cases of this disease have been increasing in some Asian countries: 3.8-fold in 13 years in South Korea (2), 8.3-fold in 8 years in China (3), and 1.4-fold in 6 years in Taiwan (4).

Early diagnosis and appropriate treatment are important for scrub typhus. One million cases of this disease occur in the endemic region annually (5). This disease is treatable with antibiotics (5), but a delay in antibiotic treatment increases the risk of severe complications (6). Furthermore, the mortality rate of untreated patients is estimated to be 10% (5).

Scrub typhus is transmitted by multiple trombiculid mites harboring different subtypes of *O. tsutsugamushi* (1). In northern Japan, including Yamagata, the Gilliam and Karp types are the major causes of scrub typhus and are transmitted by *Leptotrombidium pallidum* (7). However, in the Kyushu region, which is in southern Japan, the Kawasaki and Kuroki types are the major types and are transmitted by *L. scutellare* (7). Similarly,

in South Korea, which is located close to the Kyushu region, Boryong is the major type and is considered identical to the Kuroki type based on its 56-kDa antigen gene sequence (8).

So far, there are few reports on imported cases of scrub typhus in Japan (9,10). Here, we reported a case of scrub typhus imported from South Korea to Yamagata, Japan; the clinical course of the patient and subtyping result strongly suggested that it was imported.

A 52-year-old woman, who resides in Yamagata, visited Incheon, South Korea from late September to early November in 2015 and worked in the fields during her stay. On October 31, she recognized redness on her left precordium and, on November 1, she experienced a fever of over 38°C. On November 2 (1 day from the onset of fever), she visited a hospital in Incheon. She received antispasmodics and nonsteroidal antiinflammatory drugs, but no antibiotics were administered. On November 4 (3 days from the onset of fever), she returned to Japan and visited Yamagata Prefectural Shinjo Hospital with a fever of 39.2°C. Macular rashes were observed on her face, trunk, and extremities. Furthermore, an ulcerative eschar (7 mm in diameter) with an erythematous halo was found on her left precordium (Fig. 1). Laboratory testing revealed high levels of aspartate aminotransferase (149 IU/μL), alanine aminotransferase (177 IU/μL), lactate dehydrogenase (408 IU/μL), and C-reactive protein (8.1 mg/dL). She was suspected of having scrub typhus and was hospitalized for treatment. She was administered minocycline (200 mg/day) on the day of hospitalization; her rash improved the next day and her fever resolved 2 days after hospitalization. She was eventually discharged 6 days after hospitalization.

Blood samples taken 3 days from the onset of fever

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Table 1. Serum antibody titers from IFAs against 6 *Orientia tsutsugamushi* strains

day ¹⁾	Serum IgG antibody titer against:						Serum IgM antibody titer against:					
	Gilliam	Karp	Kato	Kawasaki	Kuroki	Shimokoshi	Gilliam	Karp	Kato	Kawasaki	Kuroki	Shimokoshi
3	<20	<20	<20	<20	<20	<20	<20	320	<20	<20	640	<20
15	80	160	<20	<20	1,280	<20	320	2,560	<20	<20	10,240	<20

¹⁾: Days from onset of fever.



Fig. 1. Eschar on the left precordial region.

(the day of hospitalization) were positive for the *O. tsutsugamushi* genome using polymerase chain reaction (PCR) with nested primer pairs targeting the 56-kDa antigen gene (11). Moreover, PCR direct sequence analysis of the 440-bp product of the 56-kDa antigen gene (GenBank accession no.: LC127113) revealed 100% nucleotide similarities to the reference sequences of both the Kuroki type strain (GenBank accession no.: M63380) and Boryong type strain (GenBank accession no.: AM494475). To detect *O. tsutsugamushi*-specific antibodies against 6 antigens (Gilliam, Karp, Kato, Kawasaki, Kuroki, and Shimokoshi), immunofluorescence assays were carried out on paired serum samples as previously described (Table 1) (12). The IgG titer against the Kuroki type antigen increased to 1,280 in the convalescent serum. Similarly, a comparison of the paired serum samples showed that the serum IgM titer against the Kuroki type antigen had markedly increased.

This was considered a case of scrub typhus imported from South Korea to Yamagata. The patient had stayed in South Korea for more than a month and developed

the symptoms of scrub typhus during her stay. Since the incubation period of the disease is about 5 to 20 days after the initial bite (1), it was speculated that she was infected with the disease in South Korea and not in Japan.

Confirmation of the *O. tsutsugamushi* subtype of imported cases of scrub typhus is important. In this case, the patient harbored Kuroki (Boryong) type *O. tsutsugamushi*, which had not been reported in Yamagata so far. The Kuroki (Boryong) type accounts for about 70% of scrub typhus cases in South Korea (8) and its geographic distribution suggests that this case of the disease was imported from South Korea to Yamagata.

In this case, the patient was treated immediately on returning to Japan and recovered from the disease without any complications. However, in general, early diagnosis and treatment of imported infectious diseases tends to be difficult (13). Therefore, imported scrub typhus may cause severe complications due to delays in diagnosis (6). Recently, the number of scrub typhus cases is increasing in Asian countries (2–4) and these countries are now closely connected with the rest of the world through globalization. Hence, an increase in imported scrub typhus cases is a health concern not only in Asia, but also worldwide. The early diagnosis and appropriate treatment of imported scrub typhus on a global scale is necessary.

In summary, we reported a case of scrub typhus imported to Yamagata, Japan from South Korea. In this case, identification of the *O. tsutsugamushi* subtype was helpful in determining where the patient was infected. It may also be useful in identifying imported cases of scrub typhus because the geographic distribution of *O. tsutsugamushi* subtypes varies among countries and regions.

Conflict of interest None to declare.

REFERENCES

1. Kawamura A Jr., Tanaka H, Tamura A, editors. *Tsutsugamushi Disease*. Tokyo: University of Tokyo Press; 1995.
2. Lee HW, Cho PY, Moon SU, et al. Current situation of scrub typhus in South Korea from 2001–2013. *Parasit Vectors*. 2015;8: 238.
3. De W, Jing K, Huan Z, et al. Scrub typhus, a disease with increasing threat in Guangdong, China. *PLoS One*. 2015;10:e0113968.
4. Centers for Disease Control, R.O.C. (Taiwan). *Disease Surveillance Express*. Available at <<http://www.cdc.gov.tw/english/submenu.aspx?treeid=00ed75d6c887bb27&nowtreeid=6f3d3f9a03083009>>. Accessed February 15, 2016.
5. Paris DH, Shelite TR, Day NP, et al. Unresolved problems related to scrub typhus: a seriously neglected life-threatening disease. *Am J Trop Med Hyg*. 2013;89:301-7.
6. Yasunaga H, Horiguchi H, Kuwabara K, et al. Delay in tetracycline treatment increases the risk of complications in tsutsugamushi disease: data from the Japanese diagnosis procedure

- combination database. Intern Med. 2011;50:37-42.
7. Urakami H, Tamura A. Symbiotic relationship between *Orientia tsutsugamushi* and vector mites. Nihon Saikingaku Zasshi. 1996; 51:497-511. Japanese.
 8. Park SW, Lee CK, Kwak YG, et al. Antigenic drift of *Orientia tsutsugamushi* in South Korea as identified by the sequence analysis of a 56-kDa protein-encoding gene. Am J Trop Med Hyg. 2010;83:930-5.
 9. Ueda S, Yumisashi T, Yoshida K, et al. A case of Tsutsuganushi disease as an imported infection. Kansenshogaku Zasshi. 1997; 71:464-7. Japanese.
 10. Matsumura Y, Shimizu T. Case of imported scrub typhus contracted in Myanmar. Kansenshogaku Zasshi. 2009;83:256-60. Japanese.
 11. Furuya Y, Yoshida Y, Katayama T, et al. Specific amplification of *Rickettsia tsutsugamushi* DNA from clinical specimens by polymerase chain reaction. J Clin Microbiol. 1991;29:2628-30.
 12. Seto J, Suzuki Y, Otani K, et al. Proposed vector candidate: *Leptotrombidium palpale* for Shimokoshi type *Orientia tsutsugamushi*. Microbiol Immunol. 2013;57:111-7.
 13. Taniguchi K, Yoshida M, Sunagawa T, et al. Imported infectious disease and surveillance in Japan. Travel Med Infect Dis. 2008;6: 349-54.