

Short Communication

The First Reported Case of Spotted Fever in Fukui Prefecture, the Northern Part of Central Japan

Yoshihiro Noji^{1,7*}, Nobuhiro Takada², Fubito Ishiguro³, Susumu Fujino¹, Takahiko Aoyama¹, Hiromi Fujita⁴, Yasuhiro Yano², Syunichi Shiomi⁵, Isamu Mitsuto⁶, Keiichiro Takase¹, Toshihiro Haba¹ and Hiroshi Mabuchi⁷

¹Department of Internal Medicine and ⁶Department of Dermatology, Fukui Prefectural Hospital, Fukui 910-8526,

²Department of Pathological Sciences, Faculty of Medical Sciences, University of Fukui, Fukui 910-1193,

³Fukui Prefectural Institute of Public Health, Fukui 910-8551,

⁴Ohara Research Laboratory, Ohara General Hospital, Fukushima 960-0915,

⁵Shiomi Hospital, Fukui 919-0632 and

⁷Molecular Genetics of Cardiovascular Disorders, Division of Cardiovascular Medicine, Graduate School of Medical Science, Kanazawa University, Ishikawa 920-8641, Japan

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SUMMARY: A 53-year-old man visited Mt. Arashima-dake in Fukui Prefecture, and was infested by a tick-like organism. He visited a local clinic on July 12, 2004, complaining of high fever, general fatigue and rash. After several days without definite diagnosis, he was admitted to the Fukui Prefectural Hospital, where he was treated with minocycline hydrochloride for 10 days until recovery. His clinical symptoms on admission were high fever (39.6°C), erythematous eruption, eschar on the right upper arm, and regional lymphadenopathy. The epidemiological status and some clinical findings strongly suggested spotted fever (SF), and SF was confirmed based on the finding that his sera were reactive only to antigens of the SF group rickettsiae in the indirect immunoperoxidase analysis. This case is the first official report of SF rickettsiosis in Fukui Prefecture, the northern part of central Japan.

A 53-year-old man in Awara city, Fukui Prefecture, visited a local clinic on July 12, 2004, complaining of a 3-day history of fever (38-39°C) and general fatigue and a 1-day history of rash. Cefdinir and pranoprofen were administered for several days without effect, and he was then admitted to the Fukui Prefectural Hospital. Physical examination on admission revealed a high fever (39.6°C), generalized macropapular rash that included the palms and soles, eschar on the right upper arm (Fig. 1), and regional lymphadenopathy. Laboratory examinations showed a white blood cell count of 4.3×10^9 /liter (granulocytes, 84.5%; monocytes, 4.5%; lymphocytes, 11%; atypical lymphocytes, 0%), platelet count of 116×10^9 /liter, aspartate aminotransferase of 28 IU/liter, lactate dehydrogenase of 225 IU/liter, and raised levels of C-reactive protein (6.1 mg/dl). The fibrinogen degradation product (FDP) level was normal. At first, the epidemiological status and clinical symptoms indicated tsutsugamushi disease (scrub typhus). However, we strongly suspected that the patient was infected with spotted fever (SF) rickettsia, based on the clinical findings, that the eschar was smaller than those in some reports of tsutsugamushi disease, the rash was present even on the palms and soles, there were no raised atypical lymphocytes, and so on (1). While the Weil-Felix reactions to Proteus OX-19, OX-2 and OX-K were all negative, serodiagnoses of the acute- and convalescent-phase sera by an indirect immunoperoxidase method (2) using antigens of *Orientia tsutsugamushi* (Kato, Karp, Gilliam, Irie/Kawasaki,

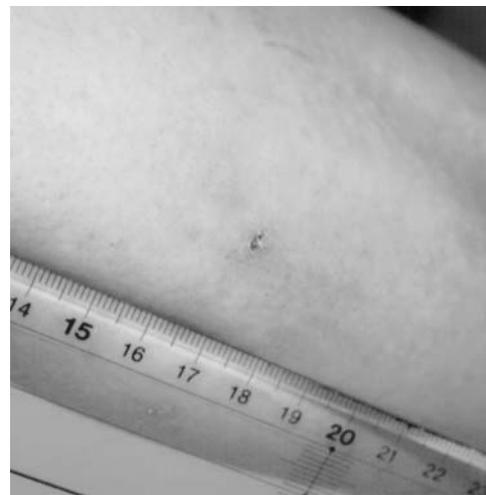


Fig. 1. An eschar on the right upper arm of the patient on admission.

Hirano/Kuroki, and Shimokoshi strains), SF group rickettsiae (*R. japonica*, *R. sibirica* and *R. helvetica*), *Rickettsia typhi*, *Coxiella burnetii*, *Francisella tularensis* and *Brucella abortus* revealed him to be positive only for SF group rickettsial antigens (Fig. 2). Almost equal titers of antibodies to all of the SF group rickettsiae used were detected on day 17 and about 1 month post onset. Intravenous minocycline hydrochloride (MINO) (200 mg/day) was started on the day of admission to treat the rickettsial infection, and his fever was reduced on day 3. MINO was tapered to 100 mg/day intravenously on day 6, then transitioned to an additional 3-day treatment with 50 mg/day orally (Fig. 2).

*Corresponding author: Mailing address: Department of Internal Medicine, Fukui Prefectural Hospital, Yotsui 2-8-1, Fukui 910-8526, Japan. Tel: +81-776-54-5151, Fax: +81-776-54-6138, E-mail: nojibon@nifty.com

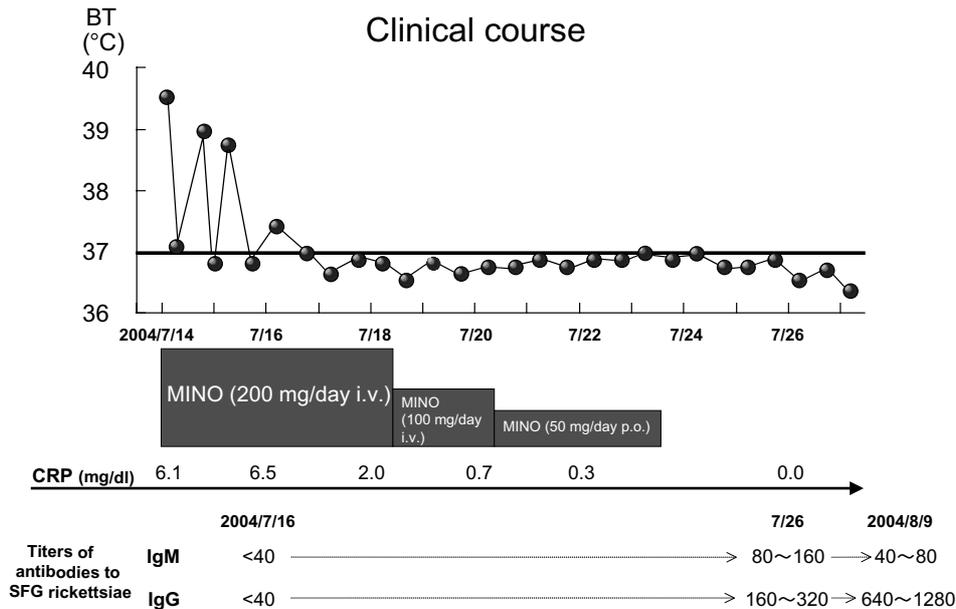


Fig. 2. Clinical course of the present SF patient with serodiagnoses. BT, body temperature; i.v., intravenously; p.o., orally; CRP, C-reactive protein.

Six days before the onset of illness, the patient had visited Mt. Arashima-dake near Ono city in the northern part of Fukui Prefecture. Three days before the onset, he found a plump, grey insect biting deeply into his right upper arm. He instantly plucked it off. His illness may have been transmitted by this tick-like insect. Subsequent surveys of ticks confirmed that the species that are abundant in areas of southwestern Japan to which Japanese spotted fever (JSF) is endemic (3-5) are almost entirely absent in the Mt. Arashima-dake region (data not shown). The transmission dynamics of this area must be further surveyed in detail.

JSF, an emerging tick-borne infectious disease, was first reported in Tokushima Prefecture in 1984 (6), and the causative agent was named *R. japonica* (7). According to the epidemiological reviews (8,9) and some personal communications, cases of JSF have been recorded mainly in south-

western and central Japan along the warm climate zone (over 400 cases and 18 different prefectures up to 2003). The present case is the first official report of SF rickettsiosis in Fukui Prefecture, and possibly the first case in the northern half of central Japan (Fig. 3). However, the present case could not be definitively diagnosed as a case of JSF, because of reactivity common to SF group rickettsiae in serotest and geobiology (tick fauna and snowy weather) different from those in the southwestern Japan and also complication of tick-rickettsiae relationships in Japan (5,10).

This rickettsiosis is not commonly recognized by clinicians, because of the sporadic outbreaks. Because SF endemic areas are rather latent, careful monitoring of SF as an emerging rickettsial disease is warranted even in areas not commonly known for the disease which are in tick fauna, especially in summer season which is long and hot out of the ordinary.

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REFERENCES

1. Mahara, F. (1997): Japanese spotted fever: Report of 31 and review of the literature. *Emerg. Infect. Dis.*, 3, 105-111.
2. Suto, T. (1991): A ten years experience on diagnosis of rickettsial disease using the indirect immunoperoxidase method. *Acta Virol.*, 35, 580-586.
3. Takada, N., Fujita, H., Yano, Y., Oikawa, Y. and Mahara, F. (1992): Vectors of Japanese spotted fever. *J. Jpn. Assoc. Infect. Dis.*, 66, 1218-1225.
4. Takada, N., Fujita, H., Yano, Y., Tsuboi, Y. and Mahara, F. (1994): First isolation of a rickettsia closely related to Japanese spotted fever pathogen from a tick in Japan. *J. Med. Entomol.*, 31, 183-185.



Fig. 3. Geographical distribution of JSF cases during 1984-2003 in Japan, including the present SF case. Closed circle: JSF cases; ★: the present case.

5. Fujita, H., Watanabe, Y., Ishikura, M. and Takada, N. (1999): List of all isolates of spotted fever group rickettsiae from ticks in Japan 1993-1998. *Ann. Rep. Ohara Hosp.*, 42, 45-50.
6. Mahara, F., Koga, K., Sawada, S., Taniguti, T., Sigemi, F., Suto, K., Tsuboi, Y., Oya, A., Koyama, H., Uchiyama, T. and Uchida, T. (1985): The first report of the rickettsial infection of spotted fever group in Japan; three clinical cases. *J. Jpn. Assoc. Infect. Dis.*, 59, 1165-1172 (in Japanese).
7. Uchida, T., Yu, X., Uchiyama, T. and Walker, D. H. (1989): Identification of a unique spotted fever group rickettsia from humans in Japan. *J. Infect. Dis.*, 159, 1122-1126.
8. Mahara, F. (1999): Rickettsioses in Japan, p. 233-239. *In* D. Raoult and P. Brouqui (ed.), *Rickettsiae and Rickettsial Disease at the Turn of the Third Millennium*. American Society for Rickettsiology, New York, N.Y.
9. National Institute of Infectious Diseases and Infectious Disease Control Division, Ministry of Health and Welfare (1999): Japanese spotted fever. *Infect. Agents Surveillance Rep.*, 20, 211'-212'.
10. Fournier, P. E., Fujita, H., Takada, N. and Raoult, D. (2002): Genetic identification of rickettsiae isolated from ticks in Japan. *J. Clin. Microbiol.*, 40, 2176-2181.