Jpn. J. Infect. Dis., 60, 59-61, 2007

Short Communication

A Case of Japanese Spotted Fever Complicated with Acute Myocarditis

Yasushi Fukuta*, Fumihiko Mahara[1], Tadanori Nakatsu[2], Tetsuya Yoshida[2] and Masaji Nishimura

Department of Emergency and Critical Care Medicine, The University of Tokushima Faculty of Medicine, Tokushima 770-8503; [1]Cardiovascular Surgery and Internal Medicine, Mahara Hospital, Tokushima 779-1510; and [2]Division of Pediatrics, Tokushima Red Cross Hospital, Tokushima 773-8502, Japan

(Received August 11, 2006. Accepted November 13, 2006)

SUMMARY: Japanese spotted fever (JSF) is caused by *Rickettsia japonica*. Although it induces a variety of complications, acute myocarditis has never been reported as a complication of JSF. We treated a JSF patient who developed acute myocarditis. To our knowledge, this is the first case of JSF complicated with acute myocarditis.

A 14-year-old boy with a fever of more 39°C presented at a local clinic. Before the onset of the fever, he had been healthy. Two days after the initial visit, he noticed redness on the skin and went to another hospital. There, a diagnosis of Japanese spotted fever (JSF) was made and treatment with minocycline (MINO) was prescribed. He was referred to a doctor with good knowledge of the disease. An eschar was detected on his right wrist (Fig. 1A), and erythematous blotches were observed over his whole body (Fig. 1B), especially on the palms and soles (Fig. 1C). He did not complain of itching. Neither lymphadenopathy nor hepatosplenomegaly were noted. Table 1 shows the results of the laboratory tests performed on admission. C-reactive protein (CRP) was slightly elevated. The administration of ciprofloxacin hydrochloride (CPFX) failed to lower his temperature. On day 4 after admission, he complained of dry cough and chest oppression.

On day 5, his heart rate was increased to 120 bpm, his blood pressure was 80/40 mmHg, and an electrocardiogram showed a complete right bundle branch block. Chest auscultation revealed cardiac murmur (gallop rhythm). Chest X-ray images showed no pulmonary congestion and the cardio thoracic ratio was found to be 50%. Oxygen saturation was 97% and creatine kinase (CK) was elevated to 1,327 U/l (normal range, 200-400) and CK-MB to 98.3 U/l (normal range, 0.0-3.8). The levels of aspartate aminotransferase, alanine aminotransferase and lactate dehydrogenase were also elevated (Table 1). Diagnosed with acute myocarditis, the patient was transferred to a hospital in which he could be treated by cardiologists.

Transthoracic echocardiography showed an ejection fraction of 69%, mild mitral regurgitation, and mild pericardial effusion (Fig. 2). Ventricular premature contractions were recognized (5 or 6 per min). Symptoms improved with the administration of MINO and globulin (0.8 g/kg of body weight per day, total 37.5g within 2 days). On day 17 after admission, the patient was discharged without any complications.

While indirect immunoperoxidase antibody tests for *Orientia tsutsugamushi* and *Rickettsia japonica* were negative on admission and on day 3, on day 11 a test for *R. japonica* showed the IgG value to be 160 times and the IgM value to be 640 times. Antibody tests for *O. tsutsugamushi* were negative. Serological tests for enterovirus (coxsackie A4, B2, B3 and B4) and adenovirus were both performed on days 5 and 11, and all results were negative.

JSF is a new rickettsial disease discovered in 1984 (1,2). This disease is an infectious disease with acute fever, but most antibiotics are ineffective against it, and JSF may become a fatal illness unless it is carefully treated (3).

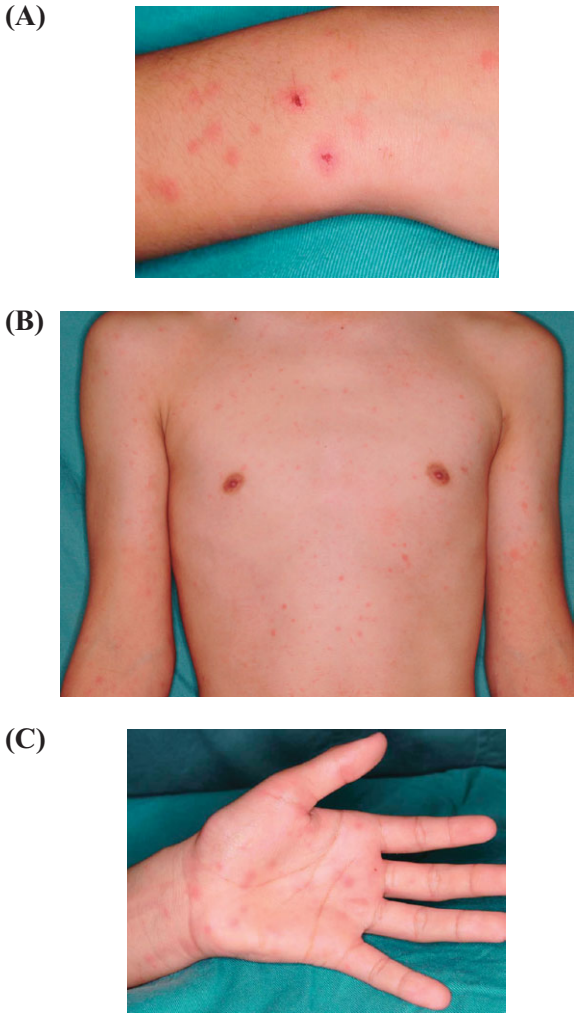

Fig. 1. Eschar on the right wrist (A), erythematous blotches on the whole body (B), and exanthema on the palm (C).

*Corresponding author: Mailing address: Department of Emergency and Critical Care Medicine, The University of Tokushima Faculty of Medicine, 3-18-15 Kuramoto, Tokushima 770-8503, Japan. Tel: +81-88-633-9347, Fax: +81-88-633-9339, E-mail: fukuta@clin.med.tokushima-u.ac.jp

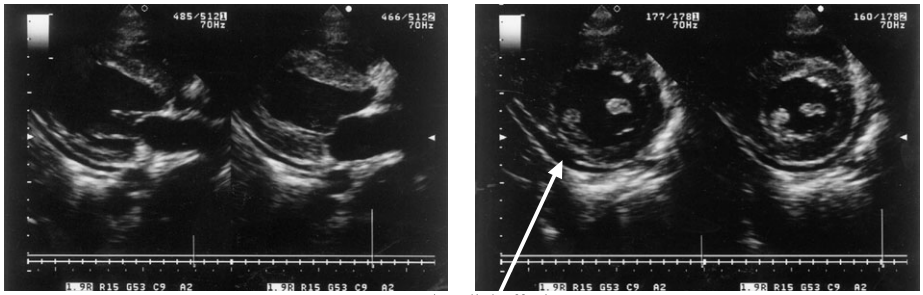

Fig. 2. Transthoracic echocardiography. Echocardiogram showed mild degradation of the ejection fraction and mild pericardial effusion on hospital day 5.

Table 1. Laboratory tests at admission and on day 5

	At admission	Day 5
WBC (/μl)	5,000	8,090
Hemoglobin (g/dl)	14.3	12.5
AST (IU/l)	48	173
ALT (IU/l)	37	58
ALP (IU/l)	464	398
LDH (IU/l)	398	670
γGTP (IU/l)	15	30
CRP (mg/dl)	1.8	1.1

WBC, white blood cells; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; γGTP, gamma glutamyltransferase; CRP, C-reactive protein.

Myocarditis can develop as a complication of various infectious diseases. While enterovirus infections are most commonly complicated with myocarditis, they have rarely been associated with rickettsial disease (4). Myocardial disease in Rocky Mountain spotted fever has been reported (5). But acute myocarditis has never been reported as a complication of JSF, and to our knowledge, this is the first case of JSF complicated with acute myocarditis. Systemic manifestations of a viral, bacterial, rickettsial, fungal or parasitic infection may be attended by a novel onset of cardiac dysfunction. When a patient presents with an episode of cardiac failure, myocardial infarction, cardiac arrhythmias, or conduction disturbances, acute myocarditis is a likely condition. After our patient complained of chest discomfort and cough, chest auscultation revealed a gallop rhythm, which is a sign of ventricular dysfunction. Subsequent electrocardiogram showed a complete right bundle branch block and premature ventricular beats, while transthoracic echocardiography revealed mitral regurgitation and pericardial effusion, and the ejection fraction was maintained at 69%. A definitive diagnosis of myocarditis can be made only by endomyocardial biopsy, an invasive procedure that, even if it is carried out by an experienced practitioner, carries the risk of lethal complications. Moreover, multiple small samples may be required before an accurate diagnosis can be made. Consequently, we did not request endomyocardial biopsy to confirm the diagnosis. The clinical signs and measurements described above, together with the results of laboratory tests, provided strong evidence, however, of acute myocarditis. Although acute myocarditis was previously unknown as a complication of JSF, we believe that acute myocarditis was present in this case.

The spotted fever group rickettsioses are distributed all over the world (6,7). In Japan, JSF and tsutsugamushi disease have been recognized. JSF was first recognized in 1984 by Mahara et al. (1,2), and *R. japonica* is known to be the cause (8,9). A triad of clinical symptoms is characteristic of JSF: high fever, erythema, and tick-bite eschar. Exanthema on the palms and soles is a specific feature of JSF. Definitive diagnosis is made when indirect immunoperoxidase antibody measurement against *R. japonica* is higher than 40 times (10); besides presenting typical symptoms of JSF, the patient in the present case had IgG values against *R. japonica* that were 160 times and IgM values of 640 times. Serological tests for enterovirus and adenovirus were negative. Therefore we diagnosed this case as JSF.

JSF is associated with central nervous system disorder (11), liver dysfunction, immunodeficiency syndrome, disseminated intravascular coagulation, and shock. If not appropriately treated, it can be fatal (3). While antibiotics, such as penicillins, β-lactams, and aminoglycosides are ineffective, MINO, doxycycline, and new quinolones do act against JSF. A susceptibility study in vitro has demonstrated MINO to be the most potent known antibiotic for JSF (12). The patient received MINO during the early phase of the disease and CPFX later. Seventeen days after admission, he was discharged from the hospital without sequelae. Even though acute myocarditis developed, MINO and CPFX effectively treated the JSF. In severe cases, Iwasaki et al. reported the effectiveness of new quinolones for treating JSF (3).

We experienced JSF complicated with acute myocarditis. It is the first case of acute myocarditis associated with JSF.

REFERENCES

1. Mahara, F. (1984): Three Weil-Felix reaction (OX2) positive cases with skin eruption and high fever. J. Anan. Med., Assoc., 68, 4-7 (in Japanese).
2. Mahara, F., Koga, K., Sawada, S., et al. (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).
3. Iwasaki, I., Mahara, F., Takada, N., et al. (2001): Fulminant Japanese spotted fever associated with hypercytokinemia. J. Clin. Microbiol., 39, 2341-2343.
4. Feldman, A.M. and McNamara, D. (2000): Myocarditis. N. Engl. J. Med., 343, 1388-1397.
5. Marin-Garcia, J. and Mirvis, D.M. (1984): Myocardial disease in Rocky Mountain spotted fever: clinical, functional, and pathologic findings. Pediatr. Cardiol., 5, 149-154.
6. Fournier, P-E., Fujita, H., Takada, N., et al. (2002): Genetic identification of rickettsiae isolated from ticks in Japan. J. Clin. Microbiol., 40, 2176-2181.
7. Jang, W., Kim, J.H., Choi, Y.J., et al. (2004): First serologic evidence of human spotted fever group rickettsioses in Korea. J. Clin. Microbiol., 42, 2310-2313.
8. Mahara, F. (1997): Japanese spotted fever: report of 31 cases and review of the literature. Emerg. Infect. Dis., 3, 105-111.

9. Uchida, T., Uchiyama, T., Kumano, K., et al. (1992): *Rickettsia japonica* sp. nov., the etiological agent of spotted fever group rickettsiosis in Japan. Int. J. Syst. Bacteriol., 42, 303-305.
10. Fujita, H., Watanabe, Y., Takada, N., et al. (1993): Isolation and serological identification of causative rickettsiae from Japanese spotted fever patients. Asian Med. J., 36, 660-665.
11. Araki, M., Takatsuka, K., Kawamura, J., et al. (2002): Japanese spotted fever involving the central nervous system: two case reports and a literature review. J. Clin. Microbiol., 40, 3874-3876.
12. Suto, T., Hatakeyama, H., Ito, R., et al. (1989) In vitro susceptibility of a strain of rickettsia recently isolated from a case of Japanese spotted fever to chemotherapeutic agents. J. Jpn. Assoc. Infect. Dis., 63, 35-38 (in Japanese).