A Patient with Dengue Fever Presenting with Rhabdomyolysis

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Abstract

A 16-year-old boy stayed in Tokyo near Yoyogi Park for extracurricular high school activities. After returning home, he experienced an episode of fever and visited our emergency outpatient unit. He initially exhibited symptoms of leukopenia, thrombocytopenia and concomitant rhabdomyolysis and after admission simultaneously developed a biphasic fever and systemic erythema. Based on the results of reverse transcription polymerase chain reaction testing, he was finally diagnosed with dengue fever. After an absence of 70 years, dengue fever has reemerged as a domestic infection. Awareness of this trend led to our diagnosis.

Key words: dengue fever, rhabdomyolysis

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Introduction

Dengue fever is a viral infection spread by mosquitoes in tropical and subtropical regions. It is caused by a single-stranded RNA virus that belongs to the Flavivirus genus, and its main vector is Aedes aegypti (1). The dengue virus can be classified into four serotypes: DENV-1, DENV-2, DENV-3 and DENV-4 (2). Infections exhibit a wide clinical spectrum, including severe and non-severe clinical manifestations in three phases (febrile, critical, and recovery) (3). With the expansion of outbreaks into new countries, with no domestic cases of dengue fever, the number of infected persons has increased by 30× in the past 50 years, with approximately 40-130 million infected persons reported each year (4). However, there have been no recent reports of individuals infected in Japan, and the main cause of dengue fever is thought to be contact with a vector in a foreign location (5, 6). After 70 years of without a domestic dengue case, a patient with domestic dengue fever was first reported in Japan in 2014, after which >150 cases were subsequently documented. We herein report a case of dengue fever diagnosed based on the initial symptoms of rhabdomyolysis.

Case Report

A 16-year-old boy stayed in Tokyo for the first two weeks in August 2014 in order to participate in extracurricular high school activities. He returned to his home in the Ehime prefecture in mid-August and subsequently complained of fever, with a body temperature of 40°C and general prostration at 23:00. At 1:00 the next day, he visited our emergency outpatient unit, presenting with non-bilious vomiting, a headache with postorbital aching pain, fatigue of the lower extremities and sputum production. However, he did not have a sore throat, cough, abdominal pain or skin rash and did not recall being bitten by a mosquito. His abdomen was soft and flat, without muscular defense or tenderness, and no other abnormalities were observed during the physical examination. He was alert, without anemia or jaundice, and his blood pressure (132/63 mm Hg), pulse (92 bpm) and respirations (20/min) were all normal. However, his temperature was 40.3°C, and the laboratory findings revealed mild liver function abnormalities (total bilirubin: 1.3 mg/dL; lactate dehydrogenase: 230 IU/L), as well as mild elevation of the levels of creatine kinase, muscle enzymes...
moderate dehydration. As the patient was young and able to
veloped after the extracurricular activities, we suspected
were detected. Given that the high fever and fatigue had de-
aminotransferase: 16 IU/L), and no electrolyte abnormalities
levels were normal, although his serum potassium level was
and creatinine. Interestingly, the transaminase level was nor-
mental (aspartate aminotransferase: 29 IU/L; alanine
aminotransferase: 16 IU/L), and no electrolyte abnormalities
veloped after the extracurricular activities, we suspected
moderate dehydration. As the patient was young and able to
tolerate the oral intake of food and water, he was discharged
after receiving a single 500-mL infusion of saline.

After returning home, the patient’s fever did not subside,
and he became unable to maintain his oral intake due to re-
peated vomiting. He visited our hospital again at approxi-
mately 13:00 three days after his first visit to the emergency
department due to a persistent fever. Although he was ob-
tunded and exhibited systemic flushing and hyperemia of
the bulbar conjunctiva, he did not have anemia, jaundice,
cyano sis or ecchymosis. His temperature was 40.0°C, and he
exhibited signs of hypotension (96/78 mm Hg) and tachy-
cardia (126 bpm). Interestingly, while his abdomen was soft
and flat without muscular defense or tenderness, his bowel
sounds were slightly sluggish and an enlarged liver was pal-
pable 3 cm below the costal arch. Splenomegaly was also
observed, although no other abnormalities were noted during
this physical examination. Based on these observations, we
suspected an acute febrile illness associated with hypoten-
sion.

The laboratory bloodwork provided the following results:
hemoglobin, 17.4 g/dL; total leukocyte count, 1,810/μL;
platelets, 103,000/μL; red blood cells, 56,500/μL; hema-
tocrit, 48.5%. His hepatic function and pancreatic enzyme
levels were normal, although his serum potassium level was
elevated at 5.2 mEq/L. In addition, laboratory testing re-
vealed elevated levels of aspartate aminotransferase (77 IU/
L), lactate dehydrogenase (443 IU/L), creatine kinase (1,549
IU/L), urinary myoglobin (105.0 ng/mL) and aldolase (24.2
IU/L) (Fig. 1). The patient’s electrocardiography findings
were normal, although sinus tachycardia was detected, and
hepatosplenomegaly and ascites fluid were noted on thoraco-
dominal computed tomography. Based on the presence of
leukopenia and thrombocytopenia, we assumed that the
patient had contracted a viral infection. As dehydration with
concomitant rhabdomyolysis and hypotension were consid-
ered to be the main clinical features, treatment with saline
infusion (20 mL/hg/h) was initiated for hemodynamic stabi-
lization. One hour after starting the infusion, the patient’s
blood pressure and pulse improved noticeably, and the hy-
perkalemia and elevated creatine phosphokinase level were
gradually ameliorated.

On the second day of hospitalization, the patient’s vital
signs were stable, and his fever gradually subsided to
36.6°C at 18:00, although a mild eruption on the precordia
was simultaneously observed. The next day, the patient’s
fever gradually returned, and his temperature reached 39°C
at approximately 1:00, by which time the eruption had spread
to his extremities and face. As his vital signs were stable,
we provided continuous symptomatic treatment, and blood
samples were collected to test for the presence of antibodies

Figure 1. The patient’s clinical course. CK: creatine kinase, Cr: creatine, K: serum potassium,
Ht: hematocrit, PLT: platelet count, WBC: total leukocyte count, DIC score: scored per the Japanese
Ministry of Health, Labour and Welfare disseminated intravascular coagulation diagnostic criteria.
Later that day (the third day after hospitalization), the patient developed a confluent rash covering his entire body (Fig. 1, 2A), as well as purpura on the hard palate. His temperature was 38.3°C, his heart rate was 58 bpm, his respiratory rate was 23/min and his total leukocyte count was 3,670/mL. Therefore, he satisfied three diagnostic criteria for systemic inflammatory response syndrome. In addition, the platelet count was 44,000/mL, the prothrombin time was 0.94 sec, the fibrin degradation product level was 12.9 μg/dL and the fibrinogen level was 233 mg/dL. Interestingly, although he met the diagnostic criteria for acute disseminated intravascular coagulation (DIC) (7), he did not meet the Japanese Ministry of Health, Labour and Welfare DIC diagnostic criteria (8) (Fig. 1). In addition, blood samples (collected every six hours) did not reveal any tendencies toward exacerbation. In addition, while his condition improved during hospitalization, the rash on the dorsal surface of both hands and upper thigh became progressively aggravated, and areas of a confluent rash appeared (Fig. 1, 2B).

On the fifth day of hospitalization, his fever decreased to normal (with no relapses of fever) and his clotting function improved. The laboratory results did not indicate the presence of antibodies to measles, chickenpox, the Epstein-Barr virus or parvovirus. On the eighth day of hospitalization, his erythema completely resolved. On the 10th day of hospitalization, a televised news report described the reemergence of dengue fever after a 70-year absence in Japan. The patient subsequently revealed that he had stayed in a hotel in the neighborhood of Yoyogi Park and jogged in the park. Based on this new information, we suspected that he had dengue fever with signal symptoms (Group B according to the World Health Organization classification). Therefore, we promptly submitted specimens to the National Institute of Infectious Diseases, and the polymerase chain reaction results revealed a positive reaction for DENV-1. The patient was discharged on the ninth day of hospitalization.

**Discussion**

Patients infected with the dengue virus experience the onset of a sudden, high fever during the febrile phase, which persists for 2-7 days, often presenting with a biphasic fever with facial flushing, muscle pain and headache. Vomiting and enlargement of the liver are also common among infected patients. Although it is difficult to distinguish dengue fever from other febrile diseases in the early febrile phase, the presence of leukopenia and a positive tourniquet test may increase the likelihood of a dengue fever diagnosis (9, 10).

Unfortunately, the mechanism responsible for the rhabdomyolysis observed in our patient remains unclear, although various mechanisms (e.g., direct viral invasion or immune-mediated injury of the muscle fibers) have been postulated. Interestingly, the dengue virus has a high efficiency for infecting and replicating inside human muscle cells (11). Therefore, it is possible that direct dengue virus muscle injury and hypovolemia (due to the high fever and enhanced vascular permeability) may have partially contributed to the development of rhabdomyolysis in this case. Fortunately, although the patient was hospitalized for rhabdomyolysis due to dehydration, he met the World Health Organization criteria for dengue fever with warning signs, although he did not meet the diagnostic criteria for severe dengue fever.

In the critical phase, dengue fever is characterized by leukopenia, thrombocytopenia and increased hematocrit caused by plasma leakage (9, 12). In the current patient, the rhabdomyolysis was considered to be the initial finding, and no nonsteroidal anti-inflammatory drugs were administered, as we believed the saline infusion and cooling of the body surface to be sufficient, given our initial diagnosis of dehydration.

Unfortunately, dengue fever has reemerged as a domestic infection in Japan after an absence of 70 years, and many clinicians in Japan are unfamiliar with it. Interestingly, our conclusive diagnosis was inspired by the news of domestic infections. However, given current transportation systems,
patients may develop similar conditions when in foreign
countries, and it is possible that viruses may also spread
throughout the local region when the infected patient re-
turns. Therefore, we conclude that sharing information re-
garding prevalent emerging and reemerging infectious dis-
eases is necessary. In addition, we must develop the means
to easily access related diagnostic procedures and therapies.

The authors state that they have no Conflict of Interest (COI).

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