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CASE REPORT

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A pediatric case of imported dengue hemorrhagic fever in Japan

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Abstract

We report a case of imported dengue hemorrhagic fever (DHF) in a 10-year-old Philippine boy. The patient was admitted to the hospital with a 4-day history of high fever, headache, and malaise, and a 2-day history of epistaxis and hematemesis. Symptoms deteriorated after admission, and the patient was subsequently diagnosed with DHF. DHF occurs more frequently among cases of reinfection than among cases of primary infection. Therefore, physicians should recognize the difference in the risk of developing DHF between patients in endemic and nonendemic areas.

KEYWORDS

dengue hemorrhagic fever, imported infectious disease, Japan, pediatrics, tropical disease

1 | INTRODUCTION

Dengue hemorrhagic fever (DHF), which occurs secondary to dengue fever, is characterized by hemorrhagic manifestations and progressive effusions. Although dengue fever is typically a self-limiting disease with a mortality rate of <1%, DHF is a severe, potentially deadly disease.[1] As DHF occurs more frequently among cases of reinfection than among cases of primary infection,[2] DHF seldom occurs in nonendemic areas. Reporting of infectious diseases including dengue fever and DHF is mandatory in Japan; according to a report from the National Institute of Infectious Diseases (NIID), about 10 adult-imported DHF cases are reported annually in Japan, corresponding to 5% of all imported dengue fever cases.[3] However, no pediatric case report has been published since 1989,[4] and only seven cases have been reported in Japanese medical meetings.

2 | CASE DESCRIPTION

In January, a 10-year-old Philippine boy was admitted to the hospital with a 4-day history of high fever, headache, and malaise, and a 2-day history of epistaxis and hematemesis. The patient lived near Manila and visited Japan to meet his family 4 days before he was brought to our hospital. He developed chills and malaise during his flight to Japan. There was an epidemic of dengue fever in the Philippines at that time, although the patient had no recollection of having been bitten by a mosquito. He had no previous history of dengue fever and had taken no protection against mosquito locally. Conjunctival hyperemia and redness of the tongue were noted, while joint pain, splenohepatomegaly, and rashes were not observed. Results from a blood test revealed a white blood cell count of 2500/μL, a platelet cell count of 32 000/μL, and hematocrit levels of 45.2%. Ultrasonography revealed ascites surrounding the liver. The patient was admitted in our hospital, and clinical manifestations of the disease were observed. On the first day of admission, the result of an enzyme-linked immunosorbent assay performed at the Municipal Public Health Institute, using the patient's blood sample obtained at his visit, showed positivity for nonstructural protein 1 of dengue virus. The clinical course after admission is shown in Figure 1. Twelve hours following admission, the patient presented with abdominal pain and hematemesis, positive tourniquet sign (Figure 2), and his hematocrit levels had increased to 52.4%. Because the patient met all the criteria for DHF, including increased vascular permeability, marked thrombocytopenia, a fever

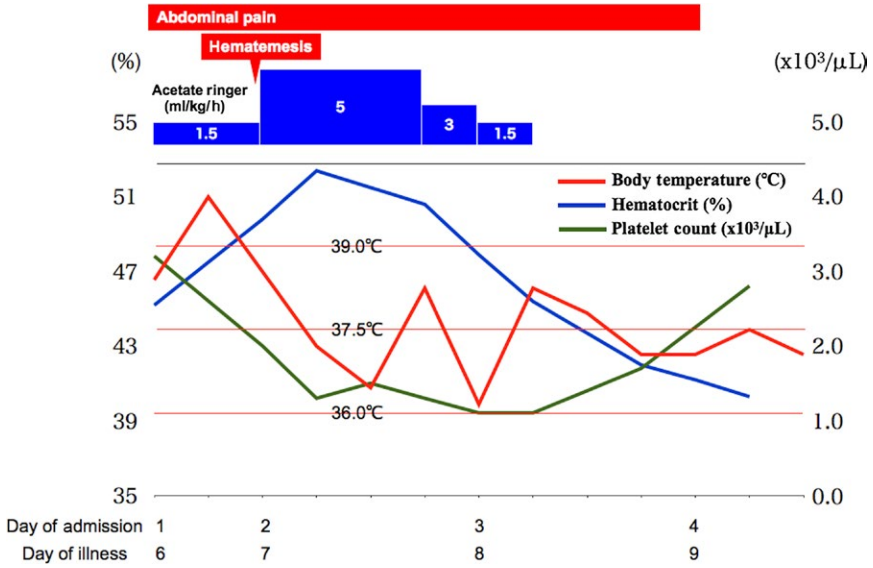

FIGURE 1 Clinical course of the patient

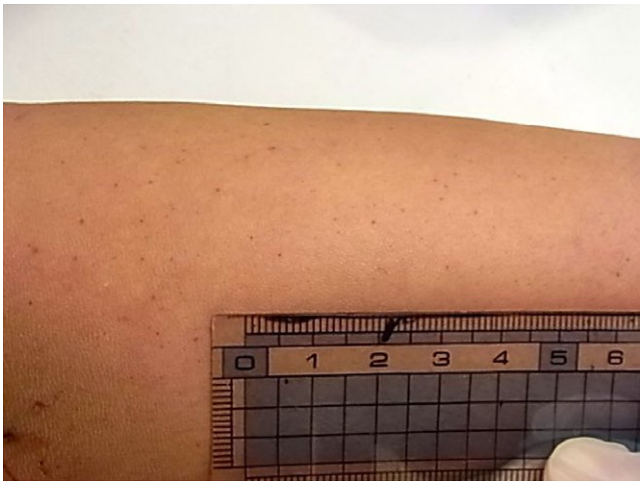

FIGURE 2 Tourniquet sign. The way of tourniquet test is following: Inflate the cuff to a point midway between systolic blood presser and diastolic blood pressure and maintain for 5 minutes. Reduce the cuff, and wait 2 minutes. Count petechiae below antecubital fossa. A positive test is 10 or more petechiae per 2.54 cm square

lasting 2-7 days, and a tendency to bleed, the patient was diagnosed with DHF. Intravascular volume repletion therapy (5 mL kg h^{-1}) with Ringer's lactate was initiated, and the infusion rate was gradually reduced, following the WHO treatment guideline.[5] Although the platelet cell count decreased to 11 000/μL on day 2 following admission, it gradually increased, without the need for a blood transfusion. The patient was discharged on Day 4 following admission. Reverse transcription–polymerase chain reaction analysis of the patient's plasma, performed at the Municipal Public Health Institute, revealed the presence of dengue virus type 1. Dengue virus-specific IgM ELISA (Focus Diagnostics, Inc., Cypress, CA, USA), dengue IgG ELISA (Vircell, Granada, Spain), and genome analysis were performed at NIID. Index values of IgM and IgG levels were 1.02 and 3.74, respectively, on day 5, and 1.81 and 4.48, respectively, on day 11. A genome analysis revealed that the virus detected was of the genotype IV (Figure 3).

3 | DISCUSSION

Approximately 20%-30% of patients with DHF present with shock due to loss of intravascular volume.[6] Although the fatality rate of dengue shock syndrome is 40%-50%, it can be reduced to <1% with early detection and appropriate fluid management.[2] The World Health Organization guidelines recommend attention to clinical warning signs for the development of severe dengue.[3] In this case, symptoms such as abdominal pain, hematemesis, a rising hematocrit, and thrombocytopenia and ascites around liver aided early diagnosis and enabled rapid implementation of fluid replacement therapy. A previous study demonstrated that platelet transfusion was ineffective in preventing bleeding in dengue infection, and that platelet recovery in patients was similar with or without platelet transfusion.[7] Furthermore, platelet transfusion may contribute to fluid overload and prolonged hospitalization.[8] Therefore, we did not perform a platelet transfusion for this patient.

DHF commonly occurs among patients with reinfection. This suggests that viral heterogeneity elicits an immunological response in patients with reinfection.[9] An interview with the patient did not reveal that a previous dengue viral infection had occurred, although a serological test suggested that the patient had a history of dengue viral infection.[2] The genome of dengue virus detected in the patient's plasma was similar to that of the virus that caused an outbreak in Samoa in 2001, which is geographically distant from the Philippines. Thus, we hypothesized that the heterogeneity of these viruses was associated with the development of DHF in this case.

When a dengue virus outbreak occurred in Tokyo, Japan in 2014, only one adult presented with DHF among 162 dengue-infected patients.[10] The following are possible reasons: Few patients who suffered from dengue fever in Japan had a previous dengue viral

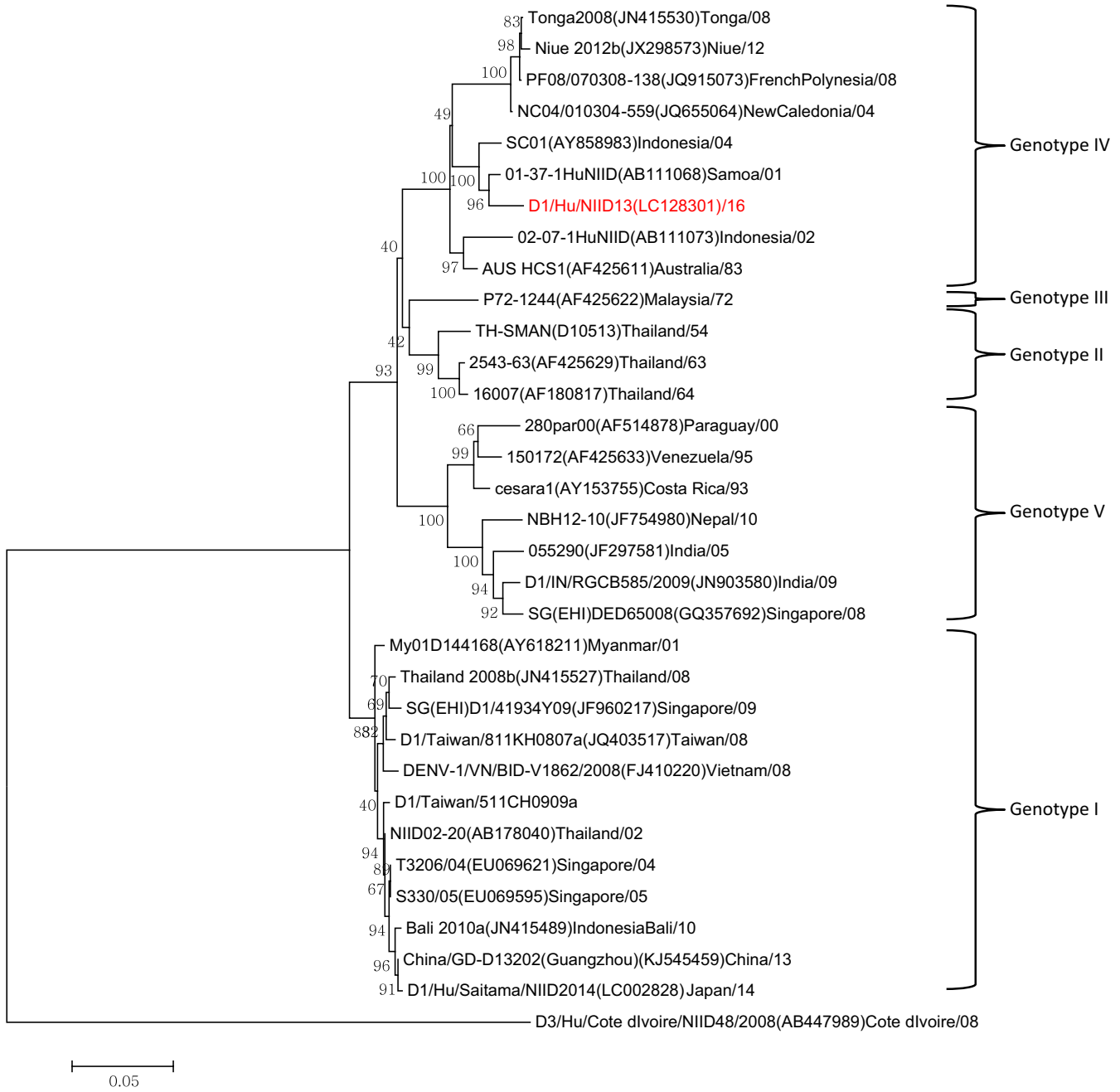

FIGURE 3 Phylogenetic tree of dengue virus type 1 genomes. The virus identified in this study is shown by red color

infection, reports were not revised in spite of patients developing DHF after initially reporting them as dengue-infected patients, or physicians did not correctly diagnose patients who developed DHF. Several facts support the first hypothesis; the only DHF patient had been previously infected with dengue virus,[11] and morbidity due to DHF among imported cases was four times higher than among domestic cases in the year of the outbreak, 2014.[10] On the other hand, a lack of understanding of tropical infectious diseases in nonendemic areas could explain the last hypothesis. Nevertheless, the impression that few dengue fever cases became severe in the Tokyo outbreak in 2014 may lead Japanese physicians to underestimate the severity of dengue fever. However, imported dengue fever cases are more likely to become DHF than domestic cases. Recently, international interactions have increased dramatically. Therefore, even physicians in nonendemic areas should recognize the difference in the risk of developing DHF between patients in endemic and nonendemic areas. Additionally, physicians should have a better understanding of dengue viral infections to prepare themselves for treating patients in the future.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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