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Short Communication

A Case of Dengue Fever Imported from Burkina Faso to Japan in October 2016

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SUMMARY: Dengue fever remains underreported in Africa due to a lack of awareness among healthcare providers, the presence of other febrile illnesses, and insufficient laboratory testing. We present a case of dengue fever imported from Burkina Faso to Japan, where an outbreak of dengue was reported on October 18, 2016. Phylogenetic analysis revealed that the isolate from our patient belonged to a distinct cluster of sylvatic dengue viruses, suggesting that dengue viruses have been maintained in mosquitoes and human cycles in Burkina Faso for more than 30 years.

Dengue fever is a febrile illness caused by the dengue virus (DENV), which mainly spreads via bites from infected mosquitoes. DENV is a member of the family *Flaviviridae*, which also includes the Zika and yellow fever viruses (1). Currently, the World Health Organization (WHO) reports that dengue is distributed throughout 128 countries (2), with recent models suggesting that as many as 390 million infections occur annually (3). Although the incidence of dengue in Africa remains unknown, outbreaks have been reported in 22 countries since 2013, including Angola, Mauritius, Mozambique, and the United Republic of Tanzania (2). In November 2016, the WHO reported a total of 1,266 suspected cases of DENV infection in Ouagadougou, the capital of Burkina Faso, between August and November of 2016 (4). The present report discusses a case of imported dengue fever from Burkina Faso to Japan, where an outbreak of dengue began in August 2016.

A 44-year-old Japanese woman presented to our hospital with fever and arthralgia in October 2016. She had travelled to Ouagadougou at the beginning of the same month on business, where she stayed for 13 days. On the day after her return to Japan, she began to experience fever and arthralgia, so she presented to our hospital the same day. She was not taking any medication and had no past medical history of note. Physical examination revealed no rash or conjunctivitis. She was unsure whether she had been bitten by mosquitoes during her stay in Burkina Faso. Laboratory analysis revealed normal white blood cell count ($4{,}930 \times 10^6$/L; normal range: $3{,}500–8{,}500 \times 10^6$/L), platelet count ($20{,}800 \times 10^6$/L; normal range: $15{,}000–35{,}000 \times 10^6$/L), and normal liver enzymes (AST 25 U/L and ALT 26 U/L; normal ranges: 13–33 U/L for AST and 6–27 U/L for ALT). The results of rapid flu testing (ESPLINE Influenza A & B-N; Fujirebio, Tokyo, Japan) were negative, and rapid malaria testing (BinaxNOW Malaria; Binax Inc., Scarborough, ME, USA) results were negative for T1 and T2. No malaria-carrying parasites were observed on the blood smear. The patient's fever and arthralgia persisted for 5 days. Six days from the onset of her condition, she again visited our hospital due to the appearance of a rash on her legs. Physical examination revealed petechiae on both lower legs. Laboratory tests revealed normal white blood cell count ($3{,}690 \times 10^6$/L), thrombocytopenia ($2{,}600 \times 10^6$/L), and elevated liver enzymes (AST 145 U/L and ALT 112 U/L). Rapid dengue testing (SD BIOLINE Dengue Duo NS1 Ag + Ab Combo, Standard Diagnostics, Inc., Yongin,Korea) results were positive for non-structural protein 1 (NS1), immunoglobulin M (IgM), and IgG. For further analysis of DENV, viral RNA was extracted from a patient serum sample obtained at the time of her first presentation to our hospital. Real-time reverse transcription polymerase chain reaction (RT-PCR) was performed with DENV 1-4 primers and probes. The sample was positive for DENV-2 (cycle threshold value = 24.2); DENV was then isolated from her blood sample. The patient was diagnosed with dengue fever caused by DENV-2. Her platelet levels and liver enzymes returned to normal ranges within 9 and 12 days, following her initial presentation to our hospital, respectively.

To analyze the isolate in greater detail, the envelope protein-coding region (1,485 bases; GenBank accession number: LC206003) of the DENV-2 genome was amplified using RT-PCR and subsequently sequenced. The result revealed that the isolate belonged to the Cosmopolitan genotype (5), sharing 99% identity with 2 DENV strains isolated from Burkina Faso in 2016 (GenBank accession numbers: KY622762 and KY622763) and 97% identity with one strain isolated from Burkina Faso in 1983 (GenBank accession number: HM234642). The phylogenetic tree also revealed that the isolate belonged to a distinct cluster of sylvatic dengue viruses detected in Burkina Faso in 1980 (Fig.1) (6).

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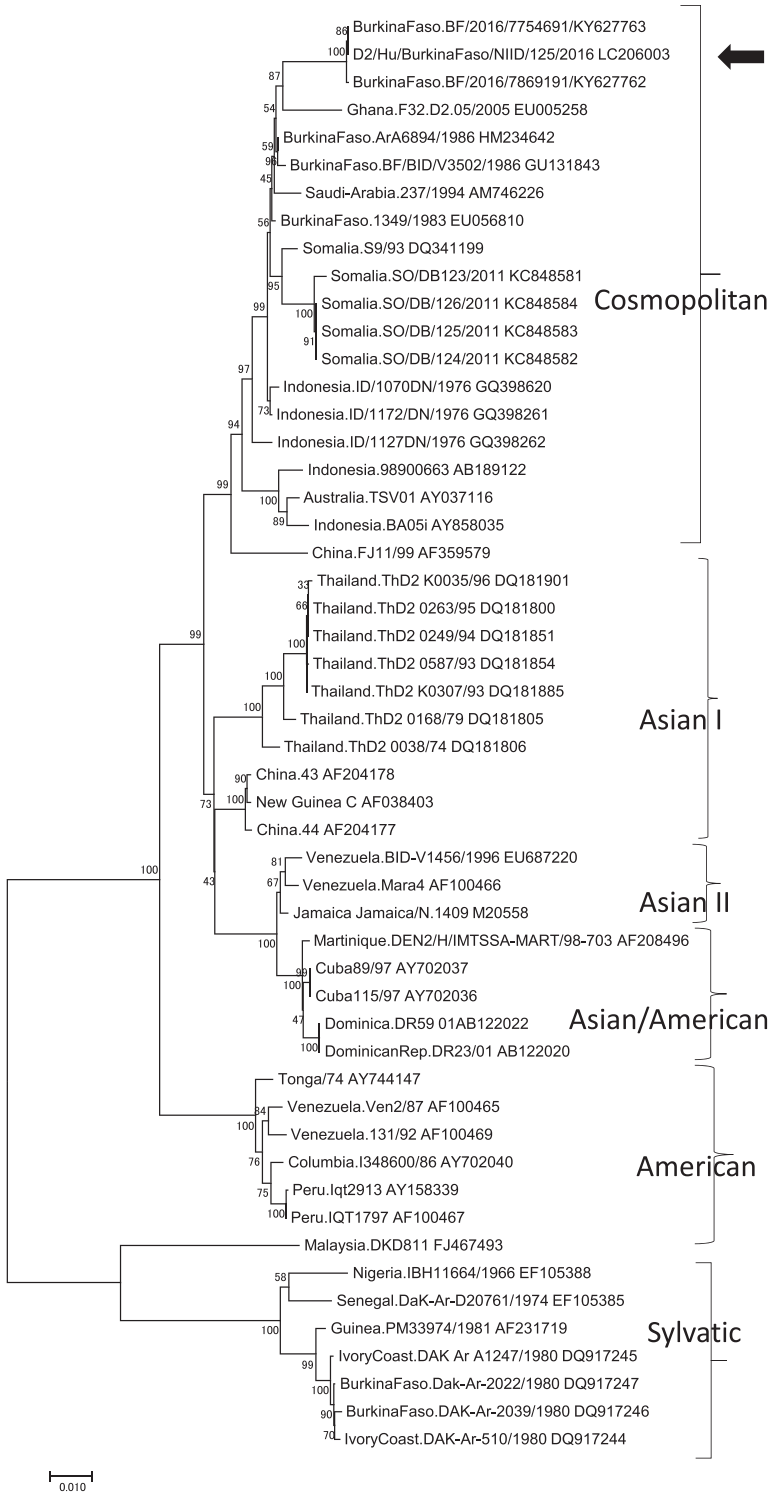

Fig. 1. The phylogenetic tree was based on the E protein coding region and constructed using the neighbour joining method (Molecular Evolutionary Genetics Analysis software; MEGA 7.0). The sequence derived from the patient is indicated with an arrow. The scale bar (0.01) indicates nucleotide substitutions per site.

After the first dengue endemic in Burkina Faso was reported in 1925 (7), no dengue endemics were reported for more than 50 years in the country. In 1982, 6 strains of DENV-2 were isolated from 30 patients with dengue–like symptoms in Ouagadougou (8). In 2007, DENV-1 was identified (9); another outbreak, this time involving DENV-3, occurred in Burkina Faso from October 18 to November 8, 2013 (10). From December 2013 to January 2014, outbreaks of DENV-2, DENV-3, and DENV-4 were reported in the country (11). In the recent outbreak of dengue in 2016, Eldin et al. isolated DENV-2 from a traveler returning from Burkina Faso to France (12).

Our case is one of the first imported cases linked to the dengue outbreak in Burkina Faso that began in late 2016. Our findings indicate that the patient was infected with DENV serotype 2 (DENV-2) of the Cosmopolitan genotype. Phylogenetic analysis revealed that the

isolates in Burkina Faso were found exclusively in the upper branch of the Cosmopolitan genotype, suggesting that DENV-2 in Burkina Faso is not imported but has been circulating in that country for at least 30 years. Therefore, this result can serve to remind us that dengue screening should be performed in malaria-negative travelers with fever who are returning from Burkina Faso.

The phylogenetic analysis also showed that the isolate from our patient belonged to a distinct cluster of sylvatic dengue viruses. Baronti et al. reported the complete coding sequence of 2 DENV-2 strains isolated from travelers to Burkina Faso in November 2016 (13). Those isolates (GenBank accession numbers: KY622762 and KY622763) were almost identical to the isolate from our patient (sharing 99% nucleotide identity). The authors suggested that these strains have been maintained through a sylvatic cycle in Burkina Faso because the isolates share a common ancestor with a DENV-2 strain isolated in the country in 1983 (GenBank accession number: EU056810). However, that strain (EU056810) was isolated from humans (14) and belonged to the Cosmopolitan genotype. In addition, our phylogenetic analysis showed that those strains, including EU056810, formed a cluster distinct from the sylvatic viruses, suggesting that the strains have been maintained in mosquitoes and human cycles in Burkina Faso for more than 30 years.

This report aims to raise awareness among healthcare professionals that dengue fever should be included in the differential diagnosis when patients exhibit fever and arthralgia after returning from dengue-endemic African countries. Furthermore, intensive surveillance efforts and further prevention measures, such as the use of insect repellents, are critical for the control of DENV infection.

Informed consent was obtained, and the study design was approved by the appropriate ethics review board.

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Conflict of interest None to declare.

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