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An Outbreak of Measles Classified as Genotype H1 in 2008 in Osaka Prefecture

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Despite the availability of highly effective vaccines, measles has remained endemic in Japan (1,2). From February to March in 2008, seven patients from two families were clinically diagnosed with measles in the southern region of Osaka Prefecture. The two families had no apparent contact with each other. We examined clinical specimens from three of seven patients and detected three measles viruses, which were classified as genotype H1. This report summarizes the results of this investigation.

Case 1

Patient 1: The index patient was a 36-year-old man and a resident of Osaka Prefecture. He presented with a fever (39.3°C), nasal discharge, and conjunctivitis on February 15. On February 19, he had developed a rash and was clinically diagnosed with measles.

Patient 2: The index patient's child was a 9-month-old girl. She was vaccinated against measles on February 20, one day after her father was diagnosed with measles. However, on February 26, she developed a fever (38.8°C), pharyngitis, and a cough, which were followed by a rash on February 29. This patient's throat swab and blood sample were collected on March 7 and were subjected to viral detection using measles virus-specific reverse transcription (RT)-nested polymerase chain reaction (PCR).

Patient 3: The index patient's wife was a 34-year-old woman who had an unknown vaccination history against measles. She had a fever, cough, headache, and nausea on February 27, followed by a rash on March 3. The patient's serum was initially negative for measles-specific immunoglobulin M (IgM) and G antibodies on February 27 and 29, respectively; however, she subsequently seroconverted (IgM 5.8, enzyme immuno-assay; cut-off > 0.8) on March 7. A throat swab and blood sample were also collected on March 7 and were subjected to viral detection.

Patient 4: A 38-year-old woman, a sister of Patient 3, presented on March 8 with a fever that was followed by a rash, and she was subsequently also clinically diagnosed with measles. On March 17, this patient's serum was positive for measles IgM (6.2).

Case 2

Patient 5: The index patient was an unvaccinated 27-month-old boy with a fever (38.3°C), cough, pharyngitis, and nasal discharge on March 8, followed by development of a rash on

March 12. A throat swab was collected for examination on March 13, by which time the rash and fever faded. On March 15, the patient's serum was positive for measles IgM (9.8).

Patient 6: The brother of Patient 5 was an unvaccinated 3-year-old boy who developed a fever and cough on March 15, followed by a rash on March 19. This patient was clinically diagnosed with measles.

Patient 7: The sister of Patient 5 was an 8-month-old girl who developed a fever and cough on March 16, followed by a rash on March 20. This patient was also clinically diagnosed with measles.

Throat swabs and blood specimens were collected from three patients (Patients 2, 3, and 5). To detect the measles virus, patients' samples were tested by measles virus-specific RT-nested PCR, and viral isolation was carried out by sample inoculation onto B95a cells. The virus-specific hemagglutinin (H) and nucleocapsid (N) protein genes were amplified in all samples, whereas the virus was isolated in B95a cells from a blood sample from Patient 2. For genotyping, 520-bp fragments including the 3' terminus of the N gene were sequenced directly using an ABI PRISM 3130 DNA sequencer (Applied Biosystems, Foster City, Calif., USA), and the 3' terminal 456-nt sequence of the N gene was determined. All of the nucleotide sequences were identical to each other. Surprisingly, these sequences were identical to that of another strain detected in China (MVs/Hong Kong.CHN/36.07/1) [EU368828]. Phylogenetic analysis showed that the sequences detected in the patients belonged to genotype H1 (Fig. 1), represented by Hunan.CHN/93/7 (N gene accession no. AF045212). The detected viruses were designated as MVs/Osaka.JPN/10.08/4 in the case of Patient 2, MVs/Osaka.JPN/10.08/6 for Patient 3, and MVs/Osaka.JPN/11.08 for Patient 5, according to the WHO nomenclature. The sequence data generated in the present report were submitted to the DNA Data Bank of Japan and were given the accession nos. AB457180, AB457181, and AB457182, respectively.

Outbreaks of measles in Japan during the past 2 years were primarily caused by D5 genotype viruses (2,4). In Osaka Prefecture, 24 measles viruses were genetically detected in 2007, and all of these belonged to genotype D5. As regards the isolation of genotype H1 measles virus in Japan, isolates of this genotype were reported in Tokyo and Kawasaki City in 2001, followed by isolates in Osaka City and all over Japan in the years 2002 to 2004 (2-4). However, the N gene sequences detected in this study shared little homology with those of other genotype H1 strains isolated in Japan (Fig. 1). Originally, the H1 genotype was considered to be indigenous to China and Korea (3); the measles viruses reported in the

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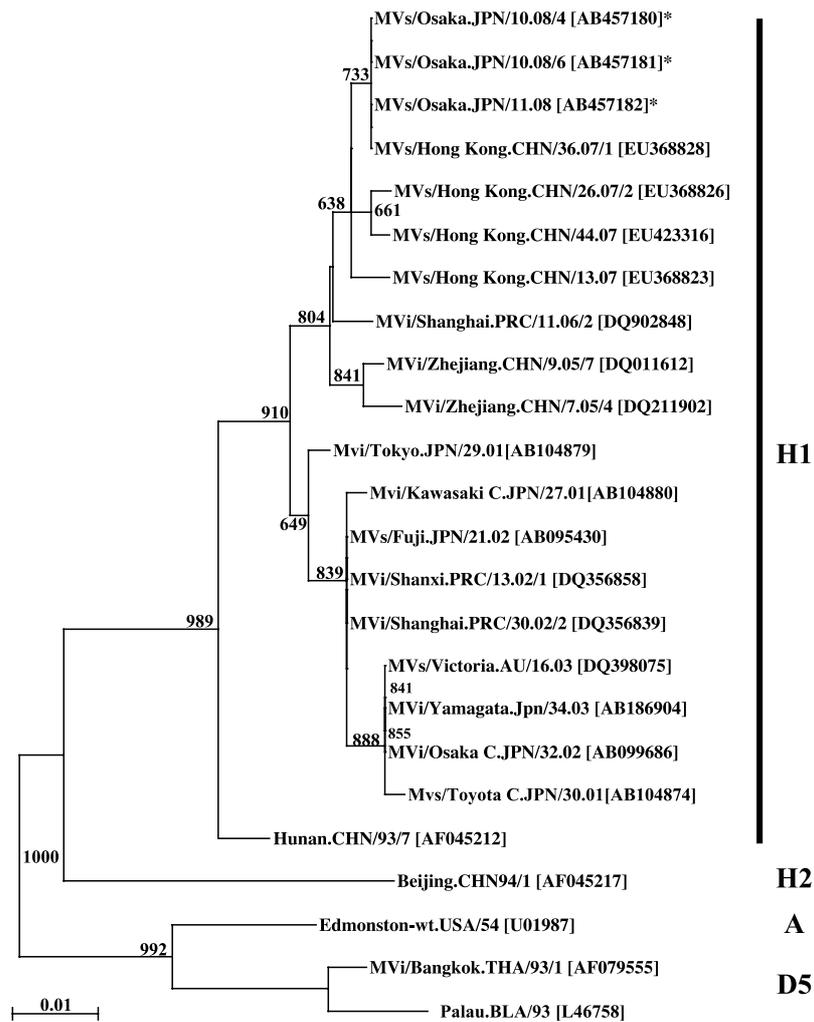


Fig. 1. Phylogenetic tree constructed by the neighbor-joining method with the 3' terminal 456-nt of the *N* gene. The GenBank accession number for each DNA sequence is given in parentheses. The number on each branch indicates the occurrence in 1,000 bootstrap replicates. The scale bar represents 0.01 substitutions per site. The asterisk indicates the sequence originated from this study.

present paper had a sequence identical to that of MVs/Hong Kong.CHN/36.07/1.

Index Patient 1 had no history of overseas travel, but he had sometimes visited Kansai International Airport on business. Thus, his infection with the type H1 measles virus raised the possibility of direct contact between Patient 1 and infected travelers at that international airport who were from measles-endemic countries. Index Patient 5 did not attend a nursery school or kindergarten, nor did he have any contact with the patients in Case 1. Consequently, the source of measles infection in these cases was not identified. However, these findings suggest that the H1 wildtype measles virus was imported from an Asian country to Osaka, Japan in recent years, and that the disease was circulating endemically in the southern region of Osaka Prefecture. Further measles surveillance will reveal the distribution of genotype H1 measles viruses. Careful epidemiological studies of laboratory-diagnosed measles viruses should be carried out on samples collected in the area around

international airports in order to protect against the import and export of measles.

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