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Measles Transmission among Technical Interns from the Philippines in a Training Institute in Toyama Prefecture, Japan, in March 2019

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Measles, an acute and highly contagious disease caused by the measles virus, can be prevented by vaccination (1). Single-dose and 2-dose measles virus-containing vaccines were introduced in 1978 and 2006 in Japan, respectively, in the national immunization program. To achieve high herd immunity levels and to strengthen epidemiological surveillance, Guidelines for the Prevention of Specific Infectious Diseases: Measles was launched in Japan in 2007. Because of these efforts, Japan had eliminated measles in March 2015, and this was confirmed by the World Health Organization (WHO) (2). Though the elimination of measles has significantly progressed worldwide since decades, outbreaks continue to occur, including in Japan (3). As more than 700 cases had been reported in Japan in 2019, measles control has become an important issue (4).

In March 2019, 3 technical interns from the Philippines who were on training were diagnosed with measles in an institute in Toyama, Japan. This study aimed to describe the epidemiologic features of this outbreak.

Cases were defined as patients with measles in Toyama, with the date of onset of symptoms between March 11 and April 20, 2019. The epidemiological study was conducted under the “Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases.” We conducted laboratory examinations such as viral genome detection using real-time reverse transcription polymerase chain reaction (RT-PCR) (5) and measles-specific immunoglobulin M

(IgM) serology (ELISA Kit, Denka Seiken Co., Tokyo, Japan). The patients were classified according to their clinical manifestations as follows: classical measles (characterized by a triad of fever, generalized rash, and catarrh) and modified measles (with manifestations including fever and/or localized rash).

Table 1 and Fig.1 show the characteristics of measles and the training period, clinical course, and examination results of the patients, respectively. Patient A was a 24-year-old woman diagnosed with classical measles on March 29, 2019. Measles virus genotype B3 was detected in the patient. However, rubella virus and IgM antibodies against the virus were not found. Patient A was from the Philippines. She traveled to Japan on February 25, 2019, and attended technical intern training in Toyama for a month. She presented with a rash and fever on March 22, 2019, following which she stayed home according to the doctor’s advice.

Before the diagnosis of patient A was confirmed, 2 trainees (patients B and C) presented with signs of measles. Patient B was a 22-year-old man from the Philippines who traveled to Japan on March 2, 2019, and attended the same training. He developed catarrh and fever as well as rash on March 11 and 12, 2019, respectively. Since the physician suspected a drug eruption, the patient continued to attend the training. Later, the genome of the measles virus was detected in peripheral blood mononuclear cell samples collected on March 30, 2019. However, the patient had recovered at that time. In addition, the genotype of the measles virus could not be analyzed owing to the low viral load. Patient C was a 22-year-old woman from the Philippines who visited Japan on February 25, 2019. She had attended the same training and had shared a room with patient A. She developed a rash on March 24, 2019, but she had no fever. Measles virus genotype B3 was detected in samples collected from her on March 30, 2019. Measles was prevalent in the Philippines from 2018 to 2019, and the genotype of the measles virus

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Table 1. Characteristics of 3 trainees with measles

Patient	Sex	Age	Measles type	Vaccination status (detailed history)	Date of onset	Date of sample collection	Real-time PCR				IgM ELISA (index value)	
							Nasopharyngeal swab	Serum/ plasma	Urine	PBMC		
A	F	24	Classical	Unknown	March 22	March 29	+	+	+	NT ¹⁾	+	(9.94)
B	M	22	Classical	Y (No record)	March 11	March 30	–	–	–	+	+	(5.19)
C	F	22	Modified	Y (No record)	March 24	March 30	+	+	–	+	+	(2.32)

¹⁾: NT, the sample was not tested because it was not collected.

Fig. 1. (Color online) Training period, clinical course and examination results of the patients. MV: measles virus, B3: MV genotype B3.

was B3 type (6,7). Figure 2 shows the phylogenetic tree of the measles virus B3 genotype strains obtained using N gene nucleotide sequences (450 bases). Two strains of this outbreak clustered with other Japanese strains in 2019 and the Filipino strain in 2018 with 100% nucleotide identity. Because no measles cases had been reported in Toyama since 2018 before this outbreak, patient B was considered as the index case. It was thought that he was infected with the measles virus in the Philippines after which he entered Japan during the incubation period.

To prevent measles transmission, 491 individuals (including 32 Filipino technical interns, 21 staff members of the institute, 3 instructors, 7 training organizers, 2 drivers, 38 visitors, 18 staff members of the clinic, and 370 individuals in the institute) were assessed from March 31 to April 20, 2019. Further, the Toyama Prefectural Government provided information about the measles infection to the local medical associations, doctors, and the public. Twenty patients were suspected of having measles on the basis of clinical signs from March 29 to May 9, 2019. Because all cases had negative PCR results, no additional cases were recorded. However, the current study had several limitations. First, mild cases might have been missed in mid-March because patient B was infectious during March 10–16, 2019. Second, the enhanced surveillance of measles might have been insufficient. Third, most vaccination histories were based on patients' memories, and there were no available medical records.

In the Philippines, a 2-dose vaccination for measles (monovalent measles vaccine at 9–11 months old and MMR at 12–15 months old) was implemented in 2009 (8). This indicates that Filipino individuals aged ≥ 10 years might not have received the 2-dose

vaccination. A previous study showed that a rubella outbreak had occurred among Vietnamese technical interns in Saitama, Japan, in 2017 (9). The number of foreign technical interns in Japan is increasing, and it reached approximately 328,360 in 2018 (10). The herd immunity threshold of measles was as high as 95%. In Japan, since 2011, the proportion of individuals aged ≥ 2 years with antibody positivity (with a particle agglutination titer ≥ 16) has been $\geq 95\%$ (4). Though a high herd immunity level was achieved, measles transmission occurred owing to an imported measles strain. Therefore, the measles vaccination status of foreign technical interns must be confirmed prior to their entry into the country. Further, efficient contact tracing of patients with measles should be conducted to control the spread of the infection.

This study was approved by the Ethics Review Committee of the Toyama Institute of Health. The nucleotide sequences determined in this study were deposited in GenBank under accession numbers LC532170 and LC532171.

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Conflict of interest None to declare.

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Fig. 2. Phylogenetic tree of the genotype B3 measles virus strains. The phylogenetic trees were constructed using the maximum-likelihood method based on the N450 nucleotide sequence. Circles indicate strains detected in Toyama, Japan in 2019. Underlined strains are WHO reference strains.

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