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An Isolated Incidence of Rubella Outbreak at a Workplace in Hokkaido, Japan

Masahiro Miyoshi[1]*, Rika Komagome[1], Hideki Nagano[1], Kenichi Takahashi[1], Hiroshi Koba[2], Yumiko Kaneko[2], Yasuko Watanabe[2], Fumiaki Suzuki[2], Takashi Hiroshima[2], Ichiro Aida[3], Sayaka Kitamura[4], Naosuke Saji[5], Ryo Yamaguchi[5], and Motohiko Okano[1]

[1]*Center for Infectious Diseases Control, Hokkaido Institute of Public Health, Sapporo 060-0819;*
[2]*Hokkaido Government Shiribeshi General Subprefectural Bureau, Kutchan 044-8588;*
[3]*Hokkaido Government Tokachi General Subprefectural Bureau, Obihiro 080-8588;*
[4]*Hokkaido Government Ishikari General Subprefectural Bureau, Sapporo 060-8558; and*
[5]*Department of Health and Welfare, Hokkaido Government, Sapporo 060-8558, Japan*

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Rubella is an acute and contagious disease that is mainly characterized by fever, rash, and cervical lymphadenopathy (1). Under the Law Concerning Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (the Infectious Diseases Control Law) in Japan, rubella has been classified as a category V infectious disease and requires mandatory reporting instead of sentinel reporting since January 1, 2008 (2). Here, we report an isolated rubella outbreak that occurred among adults in Hokkaido.

On May 14, 2011, some workers reported fever and rash (Table 1). Initially, we tested for the presence of measles antibodies as a part of the process of eliminating measles in Japan. We obtained leukocyte (serum in the case of some patients), throat swab, and/or urine samples from 9 patients (Table 2) and analyzed these samples using enzyme immunoassay (EIA) for measles-

*Corresponding author: Mailing address: Center for Infectious Diseases Control, Hokkaido Institute of Public Health, North 19 West 12, Kita-ku, Sapporo 060-0819, Japan. Tel: +81-11-747-2764, Fax: +81-11-747-2757, E-mail: miyo@iph.pref.hokkaido.jp

Table 1. Epidemiological information of the patients

Patient no.	Age	Date of arrival in Hokkaido	Accommodation	Date of onset[1)]	Date of onset (rash)	Vaccination status
1	20s	2011/4/20	A	5/9	5/13	Unknown
2	30s	4/11	B	5/11	5/13	Unknown
3	50s	—	Own home	5/12	5/18	Unvaccinated
4	40s	4/20	C	5/13	5/13	Unvaccinated
5	20s	—	Own home	5/13	5/14	Unknown
6	40s	4/20	C	5/14	5/15	Unvaccinated
7	30s	4/20	F	5/15	5/15	Unvaccinated
8	40s	3/28	E	5/15	5/16	Unknown
9	30s	4/21	C	5/15	5/18	Unknown
10	30s	4/20	B	5/16	5/17	Unknown
11	40s	4/24	D	5/16	5/17	Unknown
12	30s	4/17	G	5/19	Unclear	Unknown
13	40s	Resident of Hokkaido	H	5/20	5/23	Unknown
14	40s	Resident of Hokkaido	I	5/21	5/21	Unknown
15	30s	4/29	J	5/23	5/23	Unknown
16	30s	4/18	C	5/28	6/2	Once
17	40s	—	Own home	6/1	6/2	Unknown

1): Date indicates the day of onset including two or more of the following symptoms: fever (15), lymphadenopathy (3), headache (4), cough (3), sore throat (5), catarrh (5), malaise (5), arthralgia (4), inertia (1), fundus oculi pain (1), sputum (1), and diarrhea (1). Number in patenthesis indicates the number of cases having symptoms.

Table 2. Specific tests for rubella virus in this outbreak

Patient no.*	Days after onset**	Rubella virus-specific antibodies			RT-PCR		
		Specimen	IgM index value[1)]	IgG index value[2)]	Specimen	NS	E1
1	8	Serum	0.44	0.15	Serum	−	−
3	7	Plasma	0.64	1.07	PBMC	−	−
					Ts	+	+
					U	+	+
7	2	Serum	2.16	0.16	Serum	−	−
8	2	Serum	0.02	0.13	PBMC	+	+
					Ts	+	+
					U	+	+
9	4	Plasma	0.14	0.27	PBMC	+	+
					Ts	+	+
					U	−	−
10	4	Plasma	2.36	0.31	PBMC	−	−
					Ts	+	+
					U	+	−
11	1	Plasma	0.25	0.09	PBMC	+	−
					Ts	+	+
					U	+	+
12	1	Plasma	0.07	0.12	PBMC	−	−
					Ts	+	−
					U	−	−
13	4	Plasma	0.2	0.06	PBMC	−	ND
					Ts	+	+
					U	+	−

* and **: Case number and the date of onset are corresponded with Table 1.
1): IgM index value $\geqq$1.21 is defined as positive.
2): IgG index value $\geqq$1.0 is defined as positive.
PBMC, peripheral blood mononuclear cells; Ts, throat swab; U, urine; −, negative; +, positive; ND, not done.

specific immunoglobulin (IgM) and tests for detecting the genomes of measles virus. However, the results of these tests were negative. Rubella virus may cause the formation of rashes similar to those observed in measles (1). For this reason, we analyzed the collected samples using an EIA kit (Denka Seiken Co., Tokyo, Japan) with rubella virus-specific IgM and IgG antibodies and/or evaluated the presence of both nonstructural

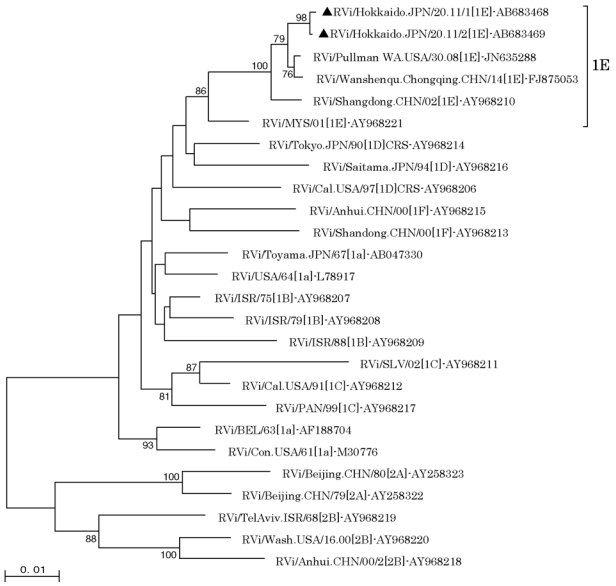

Fig. 1. Phylogenetic tree based on the 739-nucleotide region of E1 gene of rubella virus. Bootstrap values above 75 are shown, and the samples obtained in this outbreak are marked with black triangles.

protein (NS) and envelope protein 1 (E1) genes of rubella virus using reverse-transcriptase polymerase chain reaction (RT-PCR) (3) (Mori Y, personal communication). As shown in Table 2, the rubella virus-specific IgM antibodies were present in 2 patients (Nos. 7 and 10), while the rubella virus-specific IgG antibody was present in only 1 patient (No. 3). In addition, 6 patients (Nos. 3, 8–11, and 13) were positive for both NS and E1 genes and 1 patient (No. 12) was positive only for the NS gene. Phylogenetic analyses using the neighbor-joining method were performed by direct sequencing of 739 nucleotides of E1 gene, which corresponded to the minimum acceptable window defined by the World Health Organization (4). Nucleotide sequences determined in this study have been submitted to the DNA Data Bank of Japan (GenBank accession nos. AB683468 and AB683469). Two groups of the sequence (RVi/Hokkaido.JPN/20.11/1 and RVi/Hokkaido.JPN/20.11/2) were detected, and the genotypes of both the groups were highly homologous to that of the 1E strains of rubella virus. There was only one synonymous substitution between them (Fig. 1). The genotype 1E genome was also reported in an outbreak that occurred in Niigata Prefecture in the same year (5).

From the clinical manifestations and laboratory findings, total of 17 patients (men; age range, 20s–50s) were diagnosed as rubella (Tables 1 and 2). All the patients had no history of travel to foreign countries. Five of the patients were local residents, and the remaining were from areas outside Hokkaido. Fourteen patients, including 2 local residents, had stayed temporarily at accommodation facilities near the workplace. Three patients (Nos. 1, 4, and 11) had arrived possibly during the incubation period of the disease (12–23 days prior to the onset of infection). The earliest case, patient No. 1, showed onset of symptoms on May 9, after which more patients fell ill on every day from May 11 to 16. Additionally, 11 patients showed the onset of symptoms during May 9–16, and they stayed at 8 different accommodation facilities. Therefore, the epidemiological survey suggests that several patients, including Nos. 1, 4, and 11, were most probably exposed to the rubella virus at around the same time.

A person with rubella can generally shed the virus from 7 days before and after the onset of rash (1). Patient No. 1 was considered as the earliest case because the rashes in this patient were first notified on May 13. Patients (Nos. 1–11) who showed onset of the symptoms until May 16 were considered to be initially infected during similar period. Patients (Nos. 12–17) who showed onset of the symptoms after May 19 were considered to have been secondarily infected. Further, since patient No. 16 (onset of symptoms on May 28) had used the same accommodation facility that was used by patient Nos. 4, 6, and 9 (onset of symptoms on May 13, 14, and 15, respectively), he may have contracted the infection from the workplace or the accommodation facility. During and after this outbreak, no sporadic cases of rubella were reported in Hokkaido.

Only patient No. 16 had a history of rubella vaccination, whereas the other patients were not aware of their vaccination statuses (Table 1). Until the Immunization Law in Japan was amended in 1994, routine immunization for rubella virus was performed only for female students of junior high school from 1977; between 1989 and 1993, the measles-mumps-rubella vaccine was optionally administered to infants aged 12–72 months. Therefore, adult men aged 30–40 years are presently considered to be highly susceptible to rubella (6). The present study supports this claim since the rubella virus outbreak, which showed that the rubella virus-specific IgG antibodies were absent in many male patients during the early phase of the infection.

Seven patients were negative for rubella virus-specific IgM antibodies, and clinical specimens from 5 of them were collected on the same day as the onset of rash. During the early phase of the infection, it is difficult to diagnose the disease on the basis of serological findings alone (7). The symptoms of rubella are often mild or subclinical (1). However, rubella virus infection in pregnant women may cause congenital rubella syndrome (CRS) (1,8,9). The occurrence of CRS is most likely to coincide with a rubella epidemic (10). Thus, improved immunization and effective surveillance systems are critical for preventing infection and eliminating rubella.

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Conflict of interest None to declare.

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