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A hospital-associated measles outbreak in health workers in Beijing: Implications for measles elimination in China, 2018

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ABSTRACT

Background: Since the National Action Plan for Measles Elimination 2006–2012 was released in 2006, China has entered into an era of accelerated measles elimination. Despite substantial decline, measles outbreak continued to occur mainly in a non-targeted population, in particular health workers due to occupational exposure. We investigated a measles outbreak in a Chinese medicine hospital, Beijing, in March 2018.

Methods: Descriptive analysis was performed on epidemiology of the outbreak, clinical and laboratory evaluations, vaccination status of cases, and public health response. A case-control study was also conducted to identify the associated risk factors for measles.

Results: From March 13, 2018, through March 27, 2018, a total of 11 measles cases in health workers were reported in Hospital X, Beijing. The median age of cases was 26 years (range, 21–53) and 4 (36.4%) were male. Of the 11 cases, ten had not been vaccinated or had unknown vaccination status; two occurred in emergency departments. No inpatients became infected, 141 (83.9%) of whom in affected departments were 55 years of age or older. The outbreak was confirmed by laboratory testing; the virus strain was genotype H1. The response activities included isolation of cases, and enhanced health surveillance of health workers and inpatients, particularly in affected departments. A total of 2234 doses of measles-containing vaccines (MCVs) were administered, covering 93.3% of susceptible health workers, in addition to 973 doses to the susceptible individuals in household and community. Lack of documentation of MCV vaccination before the outbreak was identified as a risk factor for measles (odd ratio: 3.333, 95% confidence interval: 1.295–8.621).

Conclusions: High coverage of outbreak response immunization activities contributed largely to limit the spread of measles and might provide an indirect protection for inpatients. 2-Dose measles-containing vaccination of personnel in healthcare settings is warranted to prevent potential nosocomial transmission of measles.

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Introduction

Measles, a highly contagious disease caused by measles virus infection, can lead to severe complications, including pneumonia and encephalitis, even death. In the absence of vaccination, more than 95% of individuals were infected by 15 years of age (World Health Organization, 2018a). In 1980, before widespread use of measles vaccine, an estimated 2.6 million measles-related deaths occurred worldwide (World Health Organization, 2018a). With implementation of a routine immunization program and increasingly improving 2-dose measles-containing vaccine (MCV) coverage, measles morbidity and mortality have dramatically declined globally (World Health Organization, 2018a). In 2016, a total of 132,137 measles cases and an estimated 89,780 measles-related deaths were reported worldwide according to the World Health Organization (WHO), decreasing by 85% and 84%, respectively, compared with that in 2000 (World Health Organization, 2017b).

The epidemiological characteristics of measles and effectiveness of vaccine made it possible to eliminate the disease with the high 2-dose MCV coverage and implementation of combined public health interventions (Strebel et al., 2013; World Health

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Organization, 2017a). In 2000, elimination of endemic measles was declared in the United States (Orenstein et al., 2004). In 2005, the Regional Committee of the WHO Western Pacific Region established a goal for measles elimination in the region by 2012 (Regional Committee of World Health Organization Western Pacific Region, 2008). To achieve this goal, the Chinese Ministry of Health released the National Action Plan for Measles Elimination 2006–2012 in 2006 (Chinese Ministry of Health, 2006). Since then, China has entered into an era of accelerated measles elimination and made huge progress towards this target, with annual reported incidence of measles as cases per million population declining from 76.2 in 2006 to 4.6 in 2012 and further to 4.3 in 2017, a historic low (Ministry of Health et al., 2010; Ma et al., 2014, 2015; Hagan et al., 2018; Su et al., 2018). The decline was attributed to high-level 2-dose MCV coverage achieved by routine childhood immunization and supplementary immunization activities (SIAs) in the targeted population, combined with multiple interventions implemented (the evolution of measles vaccination policy and measles surveillance in China is shown in Figure 1).

Despite the success achieved in reducing measles incidence, there still remain many challenges to measles elimination in China, such as prevention and control of healthcare-associated measles. Due to occupational exposure, susceptible healthcare personnel are at higher risk of acquiring measles than the general population (Botelho-Neversa et al., 2012; Fiebelkorn et al., 2014). In addition, as policy of MCV vaccination for healthcare personnel has not yet been established in China to date, measles outbreaks can occur and have occurred in healthcare personnel in China in recent years (Zhang et al., 2016; Jia et al., 2018; Yu et al., 2018). In March 2018, the Beijing Haidian Center for Disease Control and Prevention (Haidian CDC) was notified of a suspected measles outbreak in a Chinese medicine hospital (Hospital X). The Haidian CDC investigated the outbreak and conducted control measures in response to the outbreak, along with the corresponding jurisdiction community health center and Hospital X. In this report, we described the epidemiology of the outbreak and evaluated the control measures to make implications for measles elimination in China.

Methods

Definitions

A suspected measles case was defined as any case with fever, maculopapular rash, and either cough, coryza, or conjunctivitis, or any case for which a clinician suspected measles infection; a confirmed measles case was defined as any case that met a definition of a suspected measles case confirmed by laboratory testing (Chinese Center for Disease Control and Prevention, 2015). A measles outbreak was defined as two or more measles cases that occurred within 10 days in Hospital X from March 13 through April 18, 2018. When the index case was reported on March 13, 2018, health workers in the same department and household of the case were defined as contacts; after the outbreak was declared, health workers and inpatients in the affected department and household of the cases were all considered as contacts.

Investigation and control measures

Investigation and data collection

Field investigation was conducted and demographic information, clinical symptoms, outcomes, vaccination status, and epidemiological information of cases were collected by using a standardized measles case investigation form. Only written documentation of the date of vaccine administered was considered to be valid. The vaccination status of a person for whom vaccination status could not be verified was classified as unknown.

Control measures

Measles cases were isolated at least 5 days after rash onset or 14 days for cases with respiratory complications. After the outbreak was detected, enhanced surveillance of health workers and inpatients was conducted particularly in affected departments. Contacts were traced and followed up to 21 days after the last exposure to measles cases. Health workers present in Hospital X during the outbreak were encouraged to supply their measles history based on their recall without laboratory confirmation and have their documentation of MCV vaccination recorded. Outbreak response immunizations activities (ORIs) with MCV were implemented for those with no prior measles or without documented 2-dose MCV vaccination before the outbreak. The inpatients were not vaccinated because of their underlying medical conditions.

Investigation of source of infection

We conducted a face-to-face interview with the measles cases for potential exposure to measles 7–21 days before rash onset. We also reviewed the electronic records of inpatients and outpatients with fever and rash, who sought medical care in Hospital X from February 19 through March 5, 2018 (i.e., 7–21 days prior to rash onset in the index case). In addition, we conducted a case-control study to identify associated risk factors for measles. In the case-control study, all the first-generation cases were recruited. Each case was matched to controls 1:2 by age and by those who were working in the same department. Potential controls that had

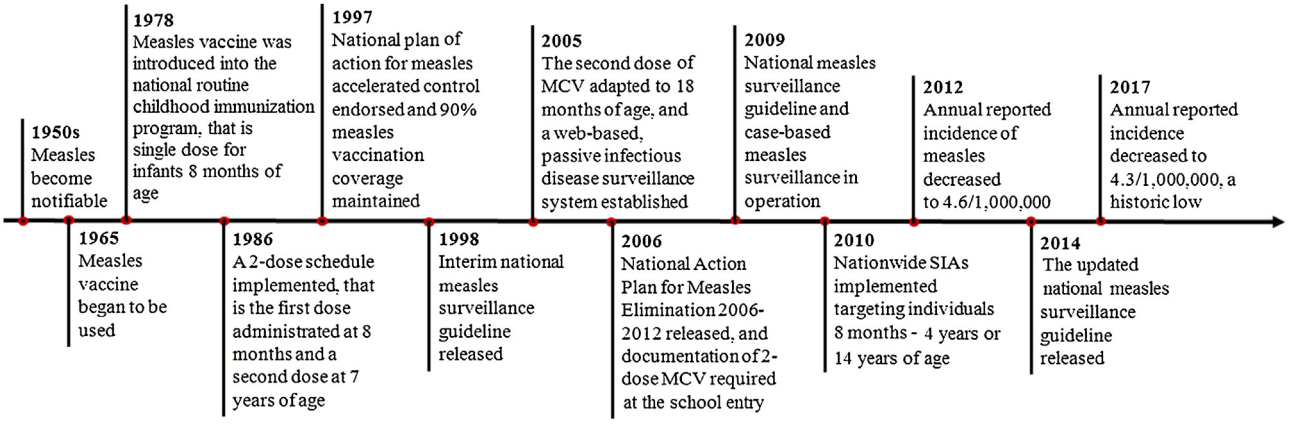

Figure 1. Evolution of measles vaccination policy and measles surveillance and progress toward measles elimination in China, 1950s–2017. Abbreviations: SIAs = supplementary immunization activities; MCV = measles-containing vaccine.

measles before the outbreak, or refused to participate, were excluded. Data, including demographic information, medical care seeking in this hospital and history of travel within the previous 7–21 days, facemask worn during work, travel on scheduled bus to work, MCV vaccination status, and contact history of cases with febrile rash illness, were collected.

Laboratory testing

Serum samples and throat swab specimens were collected and sent to Beijing Measles Networks laboratories, where serological and virological testing was performed. The quantitative results of measles-specific IgM and IG antibodies were obtained by using commercial enzyme linked immunosorbent assay (ELISA) kits (Virion/Serion, Wurzburg, Germany), as previously described (World Health Organization, 2018b). If the initial serum sample that was collected within 4 days after rash onset tested negative for IgM antibody, an additional one was collected at least 5 days after rash onset. Measles virus RNA was detected by using a real-time reverse-transcription PCR (RT-PCR) assay (Jiangsu Bioperfectus Technologies, Jiangsu, China). RT-PCR-positive specimens were genotyped at the Beijing CDC according to the criteria specified by WHO (World Health Organization, 2003); genotype A was considered as vaccine strain and others were wild types. Testing was performed according to the manufacturer's instructions.

Statistical analysis

Descriptive analysis was performed, and the results were reported as frequencies and proportions for categorical variables and as median values and ranges for continuous variables. Demographic characteristics of measles cases were analyzed. The health workers were categorized into three age groups (i.e., <40 years, 40–54 years, and ≥55 years) based on the age when the outbreak occurred on March 14, 2018. Overall and age-specific attack rates were calculated by dividing the number of cases by corresponding aggregate population with no prior measles disease. Pearson chi-square test or Fisher exact test was used to compare proportions or rates; rank-sum test was used to compare medians. In the case-control study, matched odds ratios (mORs) with 95% confidence intervals (CIs) were calculated to measure the associated risk factors for measles. All statistical analyses were performed with SPSS software (version 13.0; SPSS, Inc., Chicago, IL). A two-tailed *P* value was reported with a significant difference of $P < 0.05$.

Results

Setting

Hospital X is a public Chinese medicine hospital located in Haidian District, one of six urban districts of Beijing, involving 2601 health workers in 92 departments including emergency, cardiovascular, and pharmacy department, etc., with an estimated 7100 outpatients daily and 656 beds for inpatients mainly from Beijing. During the outbreak, a total of 2551 health workers were present in the hospital, including 1550 staff members, 568 medical students and 433 other employees (other employees were such health workers that were neither staff members nor students, including environmental service workers, security guards, and care workers, etc.), of whom 32 had prior measles before the outbreak and were excluded when attack rate was calculated. The age distribution of health workers was shown in Table 1. During the past five years, only three measles cases were reported in this hospital (Haidian CDC unpublished data).

Description of the outbreak

During the outbreak, a total of 11 measles cases were reported from March 13 through March 27, 2018, of whom nine were staff members and two were medical students working in nine departments. No deaths occurred. Of the 11 cases, four (36.4%) were male; the median age is 26 years (range, 21–53 years) (Table 2). One (9%) had a documented single-dose measles vaccination approximately 23 years ago, two were unvaccinated, and the remaining had unknown vaccination status. No additional measles cases were detected from March 28 through April 18, 2018-that is 21 days, a maximum incubation period for measles, after the last case being isolated (Figure 2). The overall attack rate was 4.4/1000. Attack rate in health workers <40 years was higher, but not significantly, than that in ≥40 years (5.9/1000 *vs* 2.5/1000, $P = 0.352$). No

Table 1
Number of measles cases and attack rates among health workers, by age, during the March 2018 outbreak in Chinese Hospital X.

Health workers	Age group	Population	Persons with prior measles	Number of cases	Attack rate (cases per 1000 population)
Students	<40 years	540	0	2	3.7
	40–54 years	7	0	0	0
	≥55 years	1	0	0	0
	Unknown	20	0	0	0
	Total	568	0	2	3.5
Staff members	<40 years	906	14	7	7.8
	40–54 years	496	23	2	4.2
	≥55 years	114	0	0	0
	Unknown	34	0	0	0
	Total	1550	37	9	5.9
Other employees	<40 years	100	0	0	0
	40–54 years	209	0	0	0
	≥55 years	80	0	0	0
	Unknown	44	0	0	0
	Total	433	0	0	0
Overall	<40 years	1546	14	9	5.9
	40–54 years	712	23	2	2.9
	≥55 years	195	0	0	0
	Unknown	98	0	0	0
	Total	2551	37	11	4.4

Table 2
Characteristics of measles cases in March 2018 outbreak in Chinese Hospital X.

Case	Sex	Age (years)	Department	Date of fever	Fever (highest body temperature, °C)	Date of rash onset	Complications	Date of isolation	Days working with rash onset	Measles cases contacted 7–21 days before rash onset	Doses of MCV before the outbreak	Date of last dose
1	F	26	Stomatology	3/9/18	38.5	3/12/18	No	3/13/18	1	Unknown	Unknown	NA
2	F	33	Cashier	3/10/18	38.2	3/14/18	No	3/14/18	0	Unknown	Unknown	NA
3	F	21	Cardiovascular	3/12/18	38.6	3/14/18	No	3/15/18	1	Unknown	Unknown	NA
4	M	25	Emergency	3/7/18	38.7	3/14/18	Pneumonia	3/15/18	1	Unknown	Unknown	NA
5	F	26	Hepatolpathy	3/11/18	39.1	3/14/18	No	3/15/18	1	Unknown	Unknown	NA
6	M	52	Pharmacy	3/23/18	39.0	3/23/18	No	3/24/18	1	Unknown	0	NA
7	F	30	Pharmacy	3/22/18	37.9	3/24/18	No	3/25/18	0	Case 2	Unknown	NA
8	F	22	Spleen	3/23/18	38.7	3/25/18	No	3/26/18	0	Case 5	Unknown	NA
9	F	30	Emergency	3/23/18	39.0	3/26/18	No	3/26/18	0	Case 4	Unknown	NA
10	M	53	Logistics	3/21/18	37.9	3/24/18	No	3/26/18	0	Unknown	0	NA
11	M	24	Endocrinology	3/23/18	38.2	3/26/18	No	3/26/18	0	Case 4	1	9/20/1994

Abbreviations: F = female; M = male; MCV = measles-containing vaccine; NA = not available.

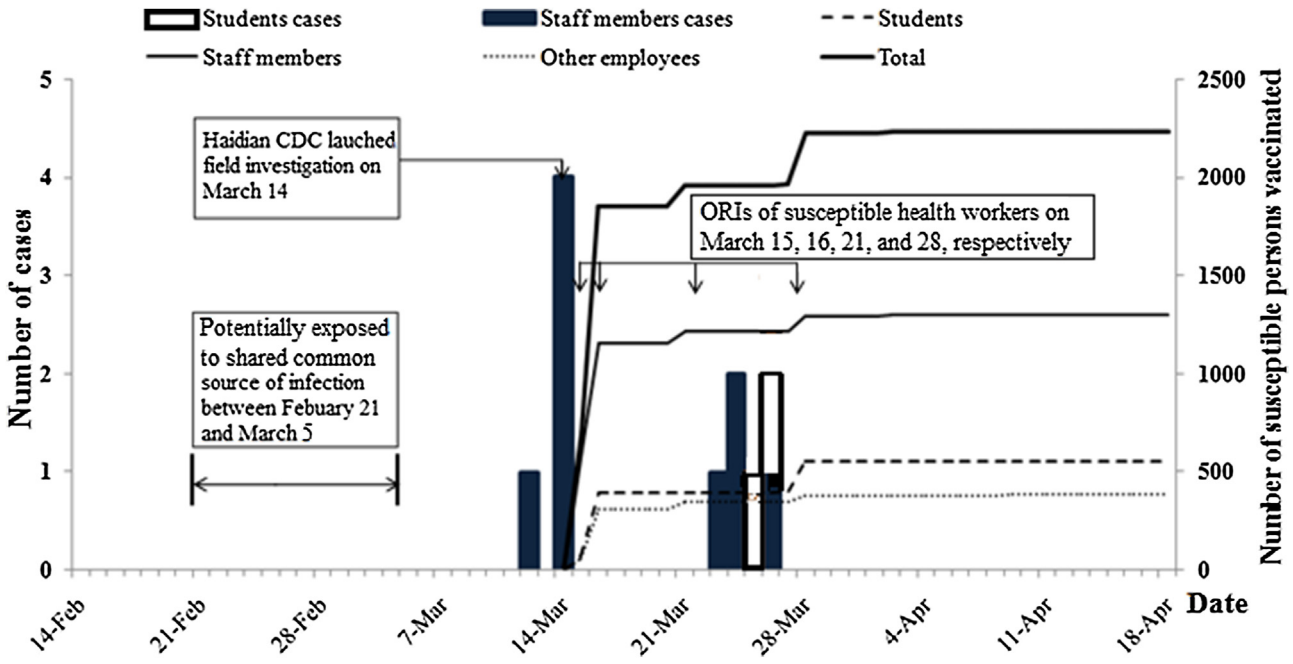

Figure 2. Cases by date of rash onset and cumulative number of susceptible persons vaccinated by date, during the measles outbreak in Hospital X, Beijing, China, from February 17, 2018, through April 18, 2018.
After the two measles cases that occurred in the hospital were reported on March 13 and 14, 2018, the Haidian CDC conducted a field investigation and initiated public health interventions. Due to the time intervals of rash onset in the first five measles cases, they were more likely to share a common source of infection between February 21, 2018, and March 5, 2018. However, no common source of a case patient was identified. During the outbreak, a total of four ORIs with 2234 doses of MCV were implemented to susceptible health workers mainly on March 15, 16, 21, and 28, respectively.
Abbreviations: Haidian CDC = the Beijing Haidian District Center for Disease Control and Prevention; ORIs = outbreak response immunization activities; MCV = measles-containing vaccine.

measles occurred in age group ≥55 years. Attack rate in staff members was higher, but not significantly, than that in medical students (5.9/1000 *vs* 3.5/1000, $P = 0.737$) (Table 1). No inpatients became infected, 83.9% (141) of whom in affected departments were ≥55 years.

Control measures

The response activities included isolation of cases, enhanced health surveillance of health workers and inpatients, particularly in affected departments, and vaccination of susceptible health

workers. During the period of enhanced surveillance, six cases with febrile rash illness were reported among health workers and then confirmed as measles cases (i.e., Case 6–11). In total, 2234 doses of MCVs were administered, covering 93.3% of susceptible health workers, 2217 (94.6%) of which were implemented on March 15, 16, 21, and 28, respectively (Figure 2), in addition to 973 doses to the susceptible individuals in household and community. Educational interventions were also implemented on clinical symptoms, transmission, and prevention of measles.

Laboratory testing

A total of 17 serum samples were collected from the 11 cases, including 11 initial ones and six second ones that were collected 0–2 days and 5–17 days after rash onset, respectively. In addition, 11 throat swab specimens were collected 0–5 days after rash onset. Of the 11 cases, one was positive for IgM antibody alone, six were positive for RT-PCR alone, and three were positive for both IgM antibody and RT-PCR (Table 3). Four PCR-positive specimens were detected as genotype H1, one of which was collected from the case vaccinated 2 days before rash onset. Notably, of the 11 initial serum specimens, two were positive for IgM, both of whom were vaccinated on March 15 and 21, 2018, respectively, one was equivocal, and the remaining eight were negative; of the six second serum specimens collected from the six cases (i.e., Case 1–5, and 11), two were positive, one was negative, and three were equivocal (Table 3). The IgG antibody titers ranged from 1737.6 mIU/ml to >5000 mIU/ml in the nine initial serums, and varied from 3427.7 mIU/ml to 4655.9 mIU/ml in the five second serums (Table 3), all of which were positive according the manufacturer's instructions.

Source of infection investigation

Due to the time intervals of rash onset in the first five measles and the incubation period of measles (7–21 days), they were likely to share common source of infection between February 21 and March 5, 2018 (Figure 2).

Interview of the first-generation cases

All five first-generation measles cases (Case 1–5) were interviewed for the source of infection. However, no common source of infection was reported. They did not attend any common activities from February 21 through March 5, 2018, and neither had they had contact with febrile rash illness cases nor had even they known each other before. However, of these five cases, one was a member staff in emergency department and two had visited the emergency room about two weeks before rash onset (one for medical care and the other for visiting friend). None of the 64 remaining health workers in the emergency department, including 49 staff members and 15 medical students, reported that they had febrile rash illness during this period.

Review of patients' electronic records

A total of 5110 patients with fever and/or rash, including inpatients and outpatients, sought medical care in this hospital from February 21 through March 5, 2018, all of whose electronic records were reviewed. Of these, a total of 57 cases with febrile rash illness based on clinical diagnoses without laboratory confirmation were recorded, of whom 49 were herpes zoster cases, four were exanthema subitum cases, two were herpangina cases, and two were herpetica pharyngitis cases. However, no measles cases were recorded.

Case-control study for associated risk factors for measles

Comparing cases and controls, those visiting the emergency room 7–21 days before the outbreak (3/5 for cases vs 0/10 for controls; mOR: 2.500, 95% CI: 0.855–7.314; $P = 0.022$), and without documentation of MCV vaccination before the outbreak (5/5 for cases vs 7/10 for controls; mOR: 3.333, 95% CI: 1.295–8.621; $P = 0.026$) were associated risk factors for measles. No other behaviors or exposures were identified as risk factors (Table 4).

Table 3
Laboratory testing results of the measles cases in March 2018 outbreak in Chinese Hospital X.

Case	ORI	Vaccine type	Date of ORIs	Date of rash onset	Serum No.: days from rash onset to sample collection	IgM	IgG (mIU/mL)	Days from rash onset to throat swabs specimen collection	RT-PCR	Genotype
1	No	NA	NA	3/12/18	Serum 1: 2 Serum 2: 17	Negative Equivocal	>5000 4344.3	2	Positive	H1
2	No	NA	NA	3/14/18	Serum 1: 0 Serum 2: 16	Negative Equivocal	1897.7 3682.2	0	Positive	H1
3	No	NA	NA	3/14/18	Serum 1: 1 Serum 2: 16	Negative Positive	1737.6 3739.5	1	Positive	ND
4	No	NA	NA	3/14/18	Serum 1: 1 Serum 2: 7	Negative Negative	4344.3 3427.7	1	Positive	ND
5	No	NA	NA	3/14/18	Serum 1: 1 Serum 2: 5	Negative Equivocal	4515.3 4655.9	5	Negative	NA
6	Yes	MR	2018/3/21	3/23/18	Serum 1: 1	Negative	2251.3	1	Positive	H1
7	Yes	MR	2018/3/15	3/24/18	Serum 1: 1	Negative	1830.3	1	Positive	ND
8	Yes	MR	2018/3/21	3/25/18	Serum 1: 1	Positive	NA	1	Positive	ND
9	Yes	MR	2018/3/15	3/26/18	Serum 1: 0	Positive	NA	0	Positive	ND
10	No	NA	NA	3/24/18	Serum 1: 2	Equivocal	3768.7	2	Positive	H1
11	No	NA	NA	3/26/18	Serum 1: 1 Serum 2: 7	Negative Positive	2278.5 NA	1	Negative	NA

Abbreviations: ORI = outbreak response immunization activity; RT-PCR = real-time reverse-transcriptase polymerase-chain-reaction; NA = not available; ND = not done; MR = measles-rubella vaccine.

Table 4
Descriptive variables and matched odds ratios for associated risk factors for measles during the March 2018 outbreak in Chines Hospital X.

Variables	Cases, No. (proportion) N = 5	Controls, No. (proportion) N = 10	Matched odds ratios (95% CI)	*P*
Male	1 (1/5)	4 (4/10)	0.375 (0.030–4.709)	0.434[a]
Beijing registry (*hukou*)	2 (2/5)	2 (2/10)	6.000 (0.536–63.984)	0.251[a]
Age, median (range), years	25 (21–33)	31.5 (23–37)	NA	0.282[b]
Behaviors and exposures				
Facemask not worn during work	1 (1/5)	0 (0/10)	1.250 (0.806–1.938)	0.724[a]
Visiting emergency room 7–21 days before rash onset	3 (3/5)	0 (0/10)	2.500 (0.855–7.314)	0.022[a]
History of travel within the previous 7–21 days before outbreak	3 (3/5)	5 (5/10)	1.500 (0.170–13.225)	1.000[a]
Travel on schedule bus to work	1 (1/5)	5 (5/10)	0.250 (0.020–3.100)	0.580[a]
Without documentation of MCV vaccination before outbreak	5 (5/5)	7 (7/10)	3.333 (1.295–8.621)	0.026[a]

Abbreviations: CI = confidence interval; NA = not available; MCV = measles-containing vaccine.
[a] Fisher exact test.
[b] Rank-sum test.

Discussion

The outbreak we described here was one of the largest hospital-associated measles outbreaks that occurred in health workers caused by indigenous measles virus (genotype H1) circulating in China since first identified in the 1990s (Xu et al., 2014; Zhang et al., 2007). Most health workers in this hospital had not been vaccinated with 2-dose MCVs before the outbreak, reflecting inadequate population immunity required to interrupt measles transmission (Strebel et al., 2013). The quick public health response triggered by this outbreak, in particular the ORIs that covered 93.3% of susceptible health workers and prompted swift herd immunity against measles, limited the spread of the measles virus only in health workers with 11 cases, indicating that the multiple interventions that were in place have been effective in containing the outbreak.

The first five measles cases were more likely to share a common source of infection due to the date of rash onset. However, no case patient was identified, though we have tried our best to interview all first-generation cases, and reviewed electronic records of outpatients and inpatients. The result of the present study that visiting the emergency room 7–21 days before rash onset was identified as a risk factor for measles was consistent with the data in previous case-control studies (Farizo et al., 1991; Miranda et al., 1994). The patients who sought medical care in the emergency room are more severe cases and usually need urgent intensive treatments, after which they will be transferred to the corresponding ward. The emergency room has become a connected "belt" that links patients and the departments of cardiology, endocrine, etc., and facilitates potential transmission of communicable diseases, including measles. Thus, more attention should be focused on the patients with fever and/or rash who sought medical care in the emergency room. Moreover, it is not always possible to identify patients with measles since early symptoms are not specific. Therefore, it is important that healthcare workers use standard precautions consistently when providing medical care to all patients, regardless of their diagnosis.

Though inpatients, particularly in the affected departments, did not receive MCVs in this outbreak, none became infected, indicating that a high level of ORIs with MCVs in health workers might provide an indirect protection. On the other hand, two factors may contribute to the findings. First, all measles cases were isolated in a timely manner. Second, as most (83.9%) inpatients in the affected departments in Hospital X were $\geq$55 years, they might have acquired measles immunity by natural infection in childhood.

The prior measles of 32 health workers as well as Case 11 were not confirmed by laboratory testing but based on their or parental recall, which may not be reliable. Notably, Case 11 aged 26 years, who was not vaccinated due to prior measles based on parental recall, became infected, verifying the unreliability and highlighting the prior laboratory-confirmed measles as evidence of measles immunity, particularly in outbreak settings. In reality, the prior measles recalled by patient or parents and even documentation of diagnosis by physician but lack of laboratory confirmation have not been considered as an acceptable criterion for evidence of measles immunity in the United States since 2013 (Centers for Disease Control and Prevention, 2013). A similar recommendation in China should be considered for persons at high risk of measles, particularly health workers, in order that these individuals be vaccinated under a potential exposure and be protected.

In this outbreak, nine cases were born after measles vaccine was introduced into the national immunization program, and seven of these had high-level IgG antibody titers even in the initial serums that were collected 0–2 days after rash onset, indicating that they might have been vaccinated previously. We found that the IgM antibodies with commercial serological tests used remained negative or equivocal even in the secondary serum samples collected 5–17 days after rash onset in Case 1, 2, 4 and 5, coinciding with the results reported by (Hickman et al. (2011). This may be associated with the reinfection of measles that occurred in persons that had been vaccinated previously, led the IgG antibody to increase rapidly but IgM to rise slightly or fleeting, indicating that the negative results of IgM even 4 days after rash onset may not rule out measles infection. This phenomenon highlights that false negative IgM results can occur and make diagnoses of measles more complicated in the vaccine era. However, the fact that RT-PCR was positive for measles virus RNA in nearly all throat swab specimens suggested that when IgM testing was constrained, the RT-PCR test may also be a sensitive method to confirm a measles infection (Rosen et al., 2014).

The MCV immunization strategies have resulted in a dramatic decline in measles incidence in China, particularly in the target population. With changes in epidemiology and implementation of case-based measles surveillance in China, data on source of exposure and occurrence of measles cases in healthcare facilities available can provide key scientific evidence for decision making in vaccine policy (Fiebelkorn et al., 2014). Though policy of vaccination may not be made based only on one outbreak investigation, the findings in this study and in other healthcare-associated outbreaks (Zhang et al., 2016; Jia et al., 2018), as well as other evidence, suggested that 2-dose MCV vaccination of personnel in healthcare facilities in China should be warranted to prevent spread of measles to and from health workers. In addition, the establishment of a vaccination card and immunization registry for personnel in healthcare facilities is needed to promptly identify measles vaccination status and to vaccinate individuals as necessary.

Limitations

There were four limitations in this study. First, the source of infection of the outbreak was not identified. As the source of infection either from healthcare personnel or from patients might be of diverse significance for nosocomial measles transmission control, more efforts are needed for future outbreak investigation. Second, three cases might be misclassified. As RNA detection is more likely successful when the specimens are collected early (usually most successful within three days after rash onset) (World Health Organization, 2018b), the RT-PCR-negative result of Case 5 may be associated with the relative long interval between specimen collection and rash onset. In addition, two specimens collected from cases vaccinated 6–12 days before rash onset were not genotyped. Because MCV-associated reactions can show as fever and rash, these two cases might be misclassified. However, due to epidemiological links to the laboratory-confirmed measles cases, they were more likely to be infected by wild-type virus according to the WHO guideline (World Health Organization, 2003, 2018b). Third, as some febrile rash in cases that sought medical care in this hospital represented similar symptoms to measles, such as exanthema subitum, measles was not ruled out in the absence of laboratory confirmation, though most cases showed transparent symptoms and signs. Finally, the case-control study in measuring associated risk factors was limited by a small sample size, which resulted in wide CIs.

Conclusions

In conclusion, this study indicated that high-level coverage of ORIs with MCV of susceptible health workers contributed largely to limit the spread of measles and might provide an indirect protection for inpatients. Although there was substantial progress towards measles control in China during the past two decades, additional efforts should be made to prevent and control potential nosocomial transmission of measles through 2-dose MCV vaccination of personnel in healthcare facilities in addition to strict adherence to infection control strategy in daily medical activities.

Authors' contributions

JF designed the study, coordinated field epidemiological investigation and data collection, supervised data collection, engaged investigation, did the statistical analysis, and drafted the manuscript.

CJ designed the study, coordinated field epidemiological investigation and data collection, and drafted and reviewed the manuscript.

JW designed the study, engaged investigation, coordinated laboratory tests and data collection, and reviewed the manuscript.

LS performed the measles-specific IgM and IgG antibodies testing and interpreted the results of the laboratory testing.

RC, WC, FZ, and ZX conducted field epidemiological investigation and collected data.

YX coordinated field epidemiological investigation and reviewed the manuscript.

All authors have seen and approved the final version of the manuscript for publication.

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Conflict of interest

None.

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Ethical approval

This study was part of public health response of outbreak, not research. Ethical approval was not required.

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