Original Article

Onset and Duration of Symptoms and Timing of Disease Transmission of 2009 Influenza A (H1N1) in an Outbreak in Fukuoka, Japan, June 2009

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SUMMARY: The first confirmed case of 2009 influenza A (H1N1) in Fukuoka, Japan was reported in early-June 2009. The disease rapidly spread through this area, mainly in schools, until there were no new cases detected 3 weeks later. We describe herein the clinical characteristics of this novel infection that came to light through the investigation of this outbreak. The patient records at hospitals and local public health centers were reviewed, and we defined laboratory-confirmed cases as those of a person who had influenza-like symptoms, such as a fever of 37°C or more, cough, sore throat, rhinorrhea, or headache. From May 19 to June 31, 2009, a total of 71 cases were identified. The median age was 11 years, and all the patient took neuraminidase inhibitors and fully recovered. The fevers lasted for 1 to 5 days (median, 2). Cough lasted for 2 to 11 days (median, 7), and in 10 cases (34.5%) cough started before the fever. The incubation period was 2 to 3 days. Infecrors transmitted the disease to another person on the day of or the day before fever onset. The findings regarding the onset and duration of symptoms and the timing of disease transmission of 2009 influenza A (H1N1) may be useful for future response.

INTRODUCTION

The first case of 2009 influenza A (H1N1) not involving travel to the endemic countries was detected in Kobe, Japan on May 16, 2009 (1), and in the following couple of weeks, several small outbreaks occurred in large cities around Japan, such as Kobe, Osaka, Tokyo, Chiba, and Kawasaki.

In Fukuoka City, a 12-year-old boy was first reported to be positive for 2009 influenza A (H1N1) by reverse transcription-polymerase chain reaction (RT-PCR) on June 6. This case was detected by enhanced surveillance systems introduced locally in mid-May 2009. After the patient developed influenza-like symptoms on June 4, his nasopharyngeal specimen was sent from a sentinel clinic to one of the public health laboratories. Fukuoka City is located in the western part of Japan, and its population is around 1.4 million. On June 8, the number of confirmed cases in the city dramatically increased to more than 20. Because we were still in the middle of the containment phase in Japan, a field team consisting of epidemiologists from the Field Epidemiology Training Program and Infectious Disease Surveillance Cen-
developed a fever of 37°C or more.

Three enhanced surveillance systems had been running in the city since mid-May 2009. The first was a telephone triage service managed by local public health centers to guide febrile people to fever clinics. At these clinics, the nasopharyngeal specimens of the patients whom practitioners suspected of having influenza were sent to the Fukuoka City Institute of Hygiene and Environment for confirmation of 2009 influenza A (H1N1). The second was enhanced sentinel surveillance of the influenza virus, in which the number of sentinel sites was increased from 8 to 52 following the occurrence of pandemic influenza. These sentinel sites, which were local clinics other than fever clinics, picked up cases using the same case definition. The third was school absentee surveillance, in which schools where more than 5 students were absent due to fever or influenza-like illnesses were asked to report to the public health center. Then it was judged whether those students should go to fever clinics or not. In addition, once cases were identified, their close contacts were actively monitored by local public health centers by phone every day for a week to assess whether they had developed symptoms or not. Close contacts were defined as those who lived in the same household with a confirmed case at the time of investigation or those who had contact at a school or workplace with a confirmed case and had not taken precautions from 1 day before that case developed symptoms to the time of investigation. If these individuals developed fever or influenza-like symptoms, they were advised to go to fever clinics to be examined.

The patient records held by fever clinics, the information regarding contact tracing by the local public health centers, and laboratory examination results at the Fukuoka City Institute of Hygiene and the Environment were collected in collaboration with the Fukuoka City Government. This investigation was conducted as a public health emergency response according to the Infectious Disease Control Law and supported by the Ministry of Health, Labour and Welfare of Japan.

### RESULTS

A total of 71 confirmed cases were identified (Table 1). These included 41 males and 30 females, and the median age was 11 years (range, 2–43 years). Thirty-eight cases were students of 5 elementary schools and 15 were students at one junior high school. Seven cases had well-controlled asthma or a history of asthma, but were otherwise healthy. The epidemic curve showed that the outbreak began almost simultaneously in 2 public schools on June 3, and thereafter spread through the community (Fig. 1). These 2 public schools were a junior high school and an elementary school that are near each other. Almost all the cases lived in or worked

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: Male</td>
<td>41 (56.3)</td>
</tr>
<tr>
<td>Female</td>
<td>30 (43.7)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td></td>
</tr>
<tr>
<td>0–4</td>
<td>2 (2.8)</td>
</tr>
<tr>
<td>5–9</td>
<td>20 (28.2)</td>
</tr>
<tr>
<td>10–19</td>
<td>36 (50.7)</td>
</tr>
<tr>
<td>20–29</td>
<td>9 (12.7)</td>
</tr>
<tr>
<td>30–39</td>
<td>3 (4.2)</td>
</tr>
<tr>
<td>40–49</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Affiliation: Elementary school</td>
<td>38 (53.5)</td>
</tr>
<tr>
<td>Junior high school</td>
<td>15 (21.1)</td>
</tr>
<tr>
<td>Kindergarten</td>
<td>2 (2.8)</td>
</tr>
<tr>
<td>Children &lt;3 years old</td>
<td>2 (2.8)</td>
</tr>
<tr>
<td>Teacher of junior high school</td>
<td>2 (2.8)</td>
</tr>
<tr>
<td>Imported case</td>
<td>4 (5.6)</td>
</tr>
<tr>
<td>Others</td>
<td>8 (11.3)</td>
</tr>
<tr>
<td>Comorbidity: Asthma</td>
<td>7</td>
</tr>
<tr>
<td>Treatment: Oseltamivir</td>
<td>40 (56.3)</td>
</tr>
<tr>
<td>Zanamivir</td>
<td>31 (43.7)</td>
</tr>
</tbody>
</table>

**Fig. 1.** Epidemic curve of 2009 influenza A (H1N1) outbreak in Fukuoka, Japan, May 19–June 31, 2009.
in the same ward (Hakata) of the city’s 9 wards. All had epidemiological linkages except one cluster consisting of 4 office workers and 4 patients who had recently been to endemic countries. The main symptoms of affected individuals were fever, cough, sore throat, general fatigue, and headache (Table 2). All patients had a fever of 37°C or more that lasted for 1 to 5 days with a median of 2 days. Sixty-two patients had a fever of 38°C or more, but 10 of them did not have such a high fever on the day of their first clinic visit. Cough lasted for 2 to 11 days with a median of 7 days. Sore throats lasted for 2 to 7 days with a median of 3 days. Among the 29 cases whose information was available, cough started before the onset of fever in 10 (34.5%), on the day of fever in 9 (31.0%), and after the onset of fever in 10 (34.5%). Throats became sore before the onset of fever in 2 (28.6%), on the day of fever in 2 (28.6%), and after the onset of fever in 3 (42.9%). The maximum time lag from the onset of fever was 3 days for cough and 2 days for sore throats. Abdominal pain or discomfort developed in 8 patients. Among these 8, 7 were of children under 12 years old, and in 5 of them there was no diarrhea or soft stools, nausea, or vomiting. Oseltamivir was prescribed in 2 of them and zanamivir for 6.

All 71 confirmed cases were checked by a rapid antigen test for influenza A, and 68 were positive (95.8%). All cases had mild symptoms and were administered neuraminidase inhibitors. Most cases were prescribed with oseltamivir, but zanamivir was often used for children between 7 to 14 years of age. The time between the onset of fever and the start of medication ranged from 1 to 4 days, with a median of 1 day. There were no significant differences in the proportion or duration of symptoms between cases treated with oseltamivir and those with zanamivir. All cases recovered without any complications. Forty-five cases were hospitalized for the purpose of isolation, but not due to the severity of illness.

In Hakata ward, 382 close contacts were followed up, and 173 antiviral prophylaxis were administered, mainly to household and workplace contacts. Oseltamivir was used for 132 people, and zanamivir for 41 children. Among these close contacts, 24 were later identified as probable cases, and 15 of these 24 probable cases were identified as confirmed cases. One confirmed case and 2 probable cases had records of receiving antiviral prophylaxis, but they seemed to have developed symptoms before the prophylaxis. Other cases had not received prophylaxis.

Transmission from a confirmed case to another person was found in 5 cases which were strongly suspected of having had a single opportunity to come into contact with the infected, and the incubation period and the day when an infected had infected another person could be evaluated among them (Table 3). Based on fever onset, the incubation period was from 2 to 3 days. One infected 3 cases, and infection occurred on the day of or the day before the fever onset of the source.

Several control measures were taken by the local government, including strong advice for close contacts to stay home, administration of neuraminidase prophylaxis for close contacts, school closure, and communication to the public about the epidemiological and clinical information of the disease via the Internet, as well as daily press conferences. After the last case was found on June 17, 2009, no indigenous cases were reported for the next 3 weeks in Fukuoka City.

**DISCUSSION**

We have reported herein an outbreak of 2009 influen-
za A (H1N1), which occurred from June 3 through June 29 in Fukuoka, Japan, and an investigation of its 71 cases. This outbreak was controlled successfully as a result of comprehensive control measures by the local government and delayed disease expansion until the next outbreak occurred 3 weeks later. The clinical characteristics of 2009 influenza A (H1N1), such as the timing and duration of symptom development, and the timing of disease transmission, some of which have not been reported, were obtained through the investigation of this outbreak by means of careful and intensive interviews by staff members of fever clinics and local public health centers.

We considered a fever to be a temperature of 37°C or more, although a fever of 38°C or more has been used classically. Some studies have considered a fever to be a temperature of 38°C or less, just feverish (2,3), or have not mentioned criteria for fevers (4) in their case definition, but there were no consistent differences in the characteristics of symptoms among these reports. Furthermore, it was reported that a certain amount of infected people had atypical symptoms (5) or were even asymptomatic (6) in 2009 influenza A (H1N1). So we considered that a fever of 37°C or more, along with laboratory confirmation, was acceptable as a case definition.

The fact that case identification depended on a rapid antigen test for influenza, the sensitivity of which was reported to be 11.1 to 69% (7,8), means that cases may have been missed in this investigation. Furthermore, it was reported that a rapid antigen test cannot detect patients with low viral load (7), such as those who were checked at an early stage of the disease. Because cases of people who were checked shortly after they developed symptoms might have been missed in this investigation, the estimation of the incubation period in this investigation could be biased towards a longer period.

The treatment and prophylaxis of neuraminidase inhibitors might shorten the duration of symptoms or decrease the number of cases, according to the report of seasonal influenza (9,10). The treatment was reported to decrease viral shedding, which wanes 4 days after illness onset (11), so the treatment and prophylaxis may also shorten the time between fever onset of the index case and viral transmission to another person. In this investigation, we could not evaluate the effect of these drugs because all cases received the treatments, and the number of households who received prophylaxis was limited.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (yr)</th>
<th>Infector</th>
<th>Duration of fever</th>
<th>Duration of cough</th>
<th>Date of contact</th>
<th>Timing of virus transmission</th>
<th>Fever onset of secondary case</th>
<th>Incubation period (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>11</td>
<td>June 7–8</td>
<td>June 7–13</td>
<td></td>
<td>June 6</td>
<td>Day −1</td>
<td>June 9</td>
<td>3</td>
</tr>
<tr>
<td>M</td>
<td>23</td>
<td>June 11–12</td>
<td>June 10–NA</td>
<td></td>
<td>June 11</td>
<td>Day 0</td>
<td>June 13</td>
<td>2</td>
</tr>
<tr>
<td>M</td>
<td>26</td>
<td>June 13–16</td>
<td>June 13–15</td>
<td></td>
<td>June 12</td>
<td>Day −1</td>
<td>June 15</td>
<td>3</td>
</tr>
<tr>
<td>F</td>
<td>28</td>
<td>June 13–16</td>
<td>June 13–15</td>
<td></td>
<td>June 12</td>
<td>Day −1</td>
<td>June 14</td>
<td>2</td>
</tr>
<tr>
<td>F</td>
<td>25</td>
<td>June 13–16</td>
<td>June 13–15</td>
<td></td>
<td>June 12</td>
<td>Day −1</td>
<td>June 14</td>
<td>2</td>
</tr>
</tbody>
</table>

1: Timing of virus transmission denotes gap between fever onset of the source case to date of contact, based on fever onset of the source.
2: Incubation period denotes days between date of contact and fever onset of secondary case.
3: The same person.
4: NA, not available.

The proportion of symptoms was found to be similar to those published previously, except for fever and abdominal symptoms (1,2,4,12–19). The proportions of symptoms, however, depended on the case definition, and investigators publishing these reports had employed a variety of case definitions. These reports have mentioned fever, 62.5–95%; cough, 51–97.2%; sore throat, 29–77.9%; rhinorrhea, 32–79%; headache, 13–94%; nausea, 1.9–24.5%; vomiting, 1.9–23.5%; diarrhea/soft stools, 2.8–22%; muscle pain or arthritis, 10.1–74.2%; and conjunctivitis, 1.6–35%. Showing a similarity to the previous reports from Japan (1), China (2), and Colombia (19), gastrointestinal symptoms such as nausea, vomiting, and diarrhea or soft stools were less frequent in this investigation than other reports, even though many patients took oseltamivir, which was reported to induce nausea (9). No fewer than 18% of cases reported abdominal pain or discomfort. Some studies reported that abdominal pain occurred in around 10% of patients (20,21), while others did not even mention these symptoms (2,4). One possible explanation of these differences is that because definitions of nausea, diarrhea, abdominal pain, or discomfort were not clearly defined in this investigation or previous studies, and some of these symptoms may have been misclassified.

The duration of symptoms was found to be similar to those mentioned in previous reports (2,12), except for cough, which persisted longer in our investigation. In some cases, cough continued for as long as 11 days, although the patients did not show signs or symptoms of pneumonia. This recording of long duration of cough may be a result of careful phone calls by health officials conducted every day. One important point is that cough occurred before the onset of fever in around a third of the cases, and this finding poses a big challenge to outbreak response, because cough is considered to play an important role in the transmission of influenza (22,23), and it is quite difficult to identify infected patients with a cough earlier because mild cough might be undetected by others and depends on self-reporting.

The incubation period of 2–3 days observed in this outbreak was similar to that of seasonal influenza (24) and swine influenza (2,25), but shorter than that of avian influenza A (H5N1), which has been reported to have a median of 5 days (26). Recently, Lessler et al. estimated the incubation period of 2009 influenza A (H1N1) using the data of an outbreak at a high school in New York City (4), and reported that the median incu-
bation period was 1.4 days. One reason why incubation periods in our report were longer than their report is that we employed fever as the sole indicator, which is considered to be more objective than other symptoms, but it could delay case identification.

Viral transmission occurred on the day of or 1 day before fever onset; however, Lessler et al. reported that median generation time was 2.7 days (4). The timing of viral transmission in our study tends to be shorter because we defined it as the period between contact with the infecter and the fever onset of the secondary case, while they defined the generation time as the time between successive onsets of symptoms in a chain of transmission. Because in most cases viral shedding occurred in the first 2 to 3 days (27), it seems that the greatest chance of transmission lies in the early days of the illness. Thus, cough etiquette in daily life seems to be more important than control measures after the occurrence of an outbreak.

This investigation provided information regarding the onset and duration of symptoms, and the timing of disease transmission. Although these findings are difficult to generalize because of the small sample size, they may be useful for controlling future outbreaks in communities, schools, or health care settings.

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