Clinical features of cases of influenza A (H1N1)v in Osaka prefecture, Japan, May 2009

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This report describes the clinical characteristics of influenza A(H1N1)v virus infection in Osaka. By the end of May, 171 cases had been reported in Osaka. Most patients were from one school. No patient had a serious underlying medical condition.Clinical symptoms were mild and resembled those of seasonal influenza. The sensitivity of the rapid antigen test was 77%. Antivirals were given to the majority of the cases. Early antiviral treatment may have shortened the duration of fever.

Background

In Japan, the first case of influenza A (H1N1)v was found at Narita International Airport quarantine station on 9 May. The patient was a high school student who had traveled to Canada [1]. The first non-travel case was detected on 16 May in Kobe. On the same day, subsequent cases were found in Osaka prefecture, about 30 km from Kobe [2]. In the beginning, the authorities decided to hospitalise all patients for the purpose of isolation, based on the infection control law [3,4]; consequently 18 patients were hospitalised in Osaka. On 18 May, Osaka prefecture revised its hospitalisation policy based on clinical severity because of the rapid increase of the number of cases. Patients with mild symptoms were treated as outpatients and placed under medical observation at home. By 20 July, 847 cases had been reported in Osaka. Among them, 171 cases had been reported by the end of May. Most patients were adolescents. Of the 171 cases (including 13 who resided in other prefectures) 105 were from one school. This paper summarises the clinical characteristics of influenza A(H1N1)v cases reported in Osaka by the end of May.

Investigation in Osaka

The National Institute of Infectious Diseases (NIID) in Japan started an investigation on 17 May. By then, two clusters had been found in Osaka. One was the previously mentioned school and the other was a nearby elementary school. Although the numbers of cases were increasing day by day, most cases were linked to these two clusters. We focused the NIID investigation on these clusters; the remaining cases were investigated by the local health center.

Case definition

A case of influenza A (H1N1)v is defined as a person with influenza A(H1N1)v virus infection confirmed by real-time RT-PCR.

Cluster 1

- Secondary school: 1,934 students and 143 employees.
- Study population: 105 cases (103 students, 2 teachers), male: 83, female: 22
- Median age: 16 years (range: 13 to 53 years)
- One patient had mild asthma. No patient had a serious underlying medical condition.

Data collection

Direct face-to-face interviews were carried out by the NIID with 17 hospitalised patients, and telephone interviews were performed with 88 home-quarantined patients by school teachers with our technical assistance.

Cluster 2

- Elementary school: 624 pupils (no information on employees).
- Study population: 7 cases (pupils only), male: 2 , female: 5
- Median age: 11 years. (range: 9 to 12 years)
- One patient had asthma. No patient had a serious underlying medical condition.

Data collection

Direct face-to-face interviews with the patients and their parents were conducted by the NIID or the local health center.

Other cases

- Study population: 59 cases (31 secondary school students, 7 elementary school pupils, 21 other), male: 33, female: 33
- Median age: 15 years (range: 6 to 48 years)
- No patient had a serious underlying medical condition.

Data collection

Direct face-to-face interviews with the patients (or their parents) were conducted by the NIID or the local health center.

Clinical findings

Symptoms and laboratory data

Fever, cough and sore throat were most frequently observed (Table 1, 2). Most of the cases had clinical features similar to seasonal influenza [5]. 19.8% of cluster 1 and 14% of cluster 2 cases had diarrhoea, while usually fewer (approximately 10%) patients have diarrhoea with seasonal influenza in Japan [6]. Standard blood test results of 12 hospitalised patients showed no results specific to this virus. Cluster 2 included the first cases of the outbreak of influenza A (H1N1)v in children in Japan. No

significant differences were found between age groups in symptoms or severity of illness.

Rapid antigen test

Rapid antigen tests were conducted in the majority of cases. However, information on when this was performed was available for 35 cases only. The sensitivity of the rapid antigen test depended on when the kit was used; it was highest on day 1 (82.4%) and was relatively low on days 0 (75%) and 2 (60%) (Table 3). It is difficult to determine the accuracy of the rapid antigen test kit from the data presented here because of insufficient information (e.g. type of kit used). However, we conclude that the rapid antigen test cannot be used to rule out the possibility of influenza A(H1N1)v virus infections.

Treatment

Among 171 cases in Osaka, antivirals were given to 165 (96%); oseltamivir to 95 (56%) and zanamivir to 68 (40%) of the cases. Further two cases took zanamivir at first, and then switched to oseltamivir. Information on the duration of symptoms under treatment was available for 90 cases. Of these 90 cases, 44 received oseltamivir, 45 zanamivir and one switched from zanamivir to oseltamivir in the middle of clinical course. There was no significant difference in the duration of fever between two medications (oseltamivir 2.32 days, zanamivir 2.36 days, P=0.88, t test). Nevertheless, the results indicated that earlier administration of antivirals contributed to a reduction in the duration of fever (Table 4). However, this result is not enough to completely evaluate the effectiveness of antivirals, because we could not compare these groups to a group without prescriptions. Also, we could not assess whether antivirals reduced severity of illness, since the symptoms of all cases were mild.

Outcome

A few patients had underlying medical conditions, such as asthma. All these cases had a relatively quick and uneventful recovery. Because of the infection control law, 18 patients were hospitalised but all had mild symptoms and had no clinical indication for admission.

Conclusions

In Osaka, the majority of influenza A (H1N1)v cases occurred among healthy children and adolescents. The proportion of patients who had diarrhoea was slightly higher compared to that observed in seasonal influenza patients, but other clinical symptoms resembled those of seasonal influenza. No severe cases occurred. The results of the rapid antigen test were not sufficient to diagnose influenza A (H1N1)v virus infections. Antivirals were given to the majority of the cases. The analysis showed that early antiviral treatment shortened the duration of fever. One limitation of our study was that the methods of collection of clinical information were not standardised. Further studies are necessary to determine the accuracy of rapid antigen tests and the effectiveness of antivirals.

Table 1

Clinical symptoms of cases of influenza A(H1N1)v in cluster 1 (secondary school n=105), Osaka, Japan, May 2009

Symptom	Number of cases	Proportion of cases (%)
High fever of or above 38˚C	94/105	89.5%
Cough	86/104	82.7%
Low grade fever below 38˚C, feverish, chills	66/99	66.7%
Sore throat	68/104	65.4%
Nasal discharge, nasal congestion	62/104	59.6%
General fatigue	56/97	57.7%
Headache	50/96	52.1%
Joint pain	32/94	34.0%
Muscle pain	19/96	19.8%
Diarrhoea	19/96	19.8%
Conjunctivitis	6/94	6.4%
Vomiting	5/94	5.3%

Table 2

Clinical symptoms of cases of influenza A(H1N1)v in cluster 2 (elementary school, all ≤12 years old, n=7), Osaka, Japan, May 2009

Symptom	Number of cases	Proportion of cases (%)
High fever of or above 38˚C	7/7	100%
Cough	7/7	100%
Nasal discharge, nasal congestion	6/7	86%
General fatigue	5/6	83%
Headache	5/6	83%
Sore throat	5/7	71%
Low grade fever below 38˚C, feverish, chills	5/7	71%
Joint pain	3/5	60%
Muscle pain	3/5	60%
Diarrhoea	1/7	14%
Conjunctivitis	0/5	0%
Vomiting	0/5	0%

Table 3

Rapid kit test results of RT-PCR positive cases of influenza A(H1N1)v in Osaka, Japan, May 2009 (n=35)

Result of rapid test	Number of days from onset				Total
	Day 0	Day 1	Day 2	Day 3	
Positive	9	14	3	1	27
Negative	3	3	2	0	8
Positive rate (%)	75.0	82.4	60.0	100	77.0

Table 4

Prescription day and duration of fever in confirmed cases of influenza A(H1N1)v in Osaka, Japan, May 2009 (n=90)

Prescription day from onset of fever*	Number of cases	Average duration of fever	Standard deviation (SD)	P-value**
Day 0	39	1.90 days	0.821	P < 0.001
Day 1	39	2.51 days	0.970	
Day 2-5	12	3.42 days	1.379	

* Fever ≥ 38˚C
** One-way ANOVA

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