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Short Communication

Epidemiologic report and serologic findings for household contacts of three cases of influenza A (H7N9) virus infection



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ABSTRACT

Background and objective: We conducted epidemiologic investigations and serologic assays on household contacts that were extensively exposed to three influenza A (H7N9) virus infected case-patients before infection-control practices were implemented.

Study design: Data on the early clinical course of each patient and the exposure history for each patient's household contacts were obtained by interviewing household members and by reviewing medical records. Viral RNA in patient samples was tested using real-time reverse transcriptase polymerase chain reaction assay. Antibodies against H7N9 virus in serum samples were tested using hemagglutination inhibition and pseudovirus based neutralization assays.

Results: All household contacts were extensively exposed to the case-patients without the use of measures to protect against infection. Viral RNA was detected in the specimens from case-patients for approximately 7–11 days after confirmation of infection. However, the results of the analyses of serum specimens taken from the household contacts 15–26 days post exposure revealed no evidence of transmission of H7N9 virus from the case-patients to the contacts.

Conclusion: Despite ample unprotected exposures to case-patients during the virus shedding period, household members in this report were not infected by the H7N9 virus.

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1. Background and objective

A novel H7N9 influenza virus that causes human infections was identified in China early in 2013 [1]. Being frequently exposed to case-patients during the contagious phase, household contacts are at a high risk for infection. Similar to infection with seasonal and pandemic influenza viruses, a substantial number of H7N9 virus infected individuals are estimated to manifest mild to moderate symptoms [2,3]. Case ascertainment among most of the contacts in previous large epidemiologic reports has been mostly based on clinical symptoms and detection of virus using real-time reverse

transcriptase polymerase chain reaction (RT-PCR) assay [3,4]. This approach may not detect the asymptomatic cases or the individuals that have cleared the virus. Detection of antibodies to H7N9 virus in serum specimens may reveal these undetected cases and may provide new information that aids in the understanding of the transmission of this novel influenza virus among humans. Here we report the results of epidemiologic investigations and serologic findings on household contacts for three H7N9 infected patients hospitalized at the Shanghai Public Health Clinical Center (SHAPHC), China [5].

1.1. Study design

The patients were diagnosed with H7N9 virus infection confirmed by the means of real-time RT-PCR assay. The infections with seasonal (H1 and H3) and 2009 pandemic H1N1 influenza viruses, and severe acute respiratory syndrome (SARS-CoV) were excluded using the RT-PCR assay [5].

The household contacts had not received any medications (including anti-influenza virus treatment), nor had they used any

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Table 1
H7N9 serologic results for case-patients and household contacts.

Subject	Age (year)	Days after symptom onset in case-patients when serum samples were collected	HI titer	PBN titer
Case-patient 1	79	8	40	20
		14	80	40
		20	160	80
Case-patient 2	67	9	40	40
		12	80	40
		17	640	160
Case-patient 3	88	15	80	40
		19	640	160
		16	<10	<20
Son of case-patient 1	51	16	<10	<20
Wife of case-patient 2	67	15	<10	<20
Son of case-patient 2	42	26	<10	<20
Elder daughter of case-patient 3	Not available	18	<10	<20
Younger daughter of case-patient 3	Not available	18	<10	<20

infection protection measures before confirmation of infection of the case-patients. We interviewed eight eligible contacts from three households. Five of the contacts voluntarily provided post-exposure serum samples. Written informed consent was obtained from the each participant. The study was reviewed and approved by the SHAPHC Ethics Committee.

Information on the early clinical disease course for each case-patient and the history of exposure to the case-patient for each contact was obtained from medical records and from interviews with household contacts and doctors. A standardized form was used during each interview and the information was partially validated by interviewing other relatives of the patient and by examining medical records.

Specimens (throat swab, sputum, urine and stool) from patients were daily collected and promptly transported to the laboratory. Real-time RT-PCR assays were used for detection of RNA segments (hemagglutinin and neuraminidase) of H7N9 virus as previous report [5]. Antibodies against the H7N9 virus were determined using hemagglutination inhibition (HI) assay with live virus (A/Shanghai/4664T/2013 (H7N9)) and horse red blood cells in a biosafety level 3 (BSL-3) laboratory as the protocol developed by Chinese Center for Disease Control and Prevention [6,7]. Pseudovirus based neutralization (PBN) assay was performed in a routine BSL-2 setting according to previous reported method [8].

2. Results

2.1. The contact histories

Case-patient 1 was a 79-year-old woman who had been on bed rest for months. She coughed frequently during eating because the anterior branch of her recurrent laryngeal nerve was previously damaged during a thyroidectomy. The H7N9 virus was detectable by real-time RT-PCR assay in her throat swab, sputum, urine, and stool for 10–11 days after she was transferred to the SHAPHC and for 17–18 days after the onset of symptoms. Case-patient 1 lived with her son and his family. Her son provided bedside care, without any infection prevention measures, for at least 4 h/day. After his mother finished eating, her son ate her uneaten food with the same tools. He cleaned her sputum, urine, and stool, and took her underwear to be washed in a washing machine. Other household contacts included a grandson, a daughter-in-law, and a housemaid who declined to provide post-exposure blood. None of the contacts reported any signs of illness. The contacts had cared for the patient for 7 days from the onset of noticeable disease symptoms to the implementation of infection control measures.

Case-patient 2 was a 67-year-old man with diabetes and was in good physical condition. He experienced symptoms for 7 days

before confirmation of infection. H7N9 virus persisted in his laboratory specimens for 7 days after his transfer to the SHAPHC. Case-patient 2 lived with his wife. The wife provided much of his care, which included cleaning his sputum, urine, and stool, washing his clothing, and bathing him without the use of gloves. Their son began to assist with the patient's care 4 days after the onset of symptoms in the patient. He sat at the patient's bedside for at least 6 h/day and provided extensive care that included cleaning urine and sputum. The family ate together and shared the eating utensils. The wife had a reported sore throat and diarrhea when the patient was hospitalized at the SHAPHC, but a real-time RT-PCR assay using a throat swab specimen as the source of template was negative for H7N9. The son reported no symptoms of illness.

Case-patient 3 was an 88-year-old man with severe underlying medical comorbidities. He was admitted to the hospital 7 days after the onset of symptoms. His laboratory specimens were positive for the virus by real-time RT-PCR assay for 11 days after admission to the SHAPHC. Two daughters provided intermittent bedside care, which included cleaning sputum, urine, and stool, and washing the patient's underwear. We did not collect detailed exposure history for the daughters, because they could not be contacted.

2.2. Serologic findings

We collected serum samples from the contacts and the case-patients to determine whether the contacts had acquired the infection. Antibodies against the H7N9 virus were detected using the HI and PBN assays. The antibodies against the H7N9 virus were undetectable in serum samples collected from contacts 15–26 days post exposure, but the reciprocal antibody titer were ≥ 40 in the samples collected from the case-patients 8–20 days after symptoms onset (Table 1).

3. Discussion

The report of family clusters of influenza A (H7N9) infection and a case for probable human-to-human transmission suggest the potential for H7N9 virus spread between close contacts, however, the sustained human-to-human transmission has not been observed with this novel potentially pandemic agent so far [4,9]. Our investigation suggests that for cases reported in this study, the H7N9 virus was not transmitted from the case-patients to their household contacts after prolonged and unprotected exposure. Consistent with the observations in studies of H7N9 virus transmission in animal models, our results indicate that compared with globally disseminated seasonal and pandemic influenza viruses, the H7N9 virus is not readily transmitted in certain household settings [10–13].

Authors' contributions

Chao Qiu and Songhua Yuan conceived and designed the study. Qingguo Chen and Shuihua Lu solicited the contacts. Chao Qiu, Songhua Yuan, Yu Yang, Yanmin Wan and Anli Zhang interviewed the contacts. Di Tian, Zhigang Song, Anli Zhang and Jing He performed the viral load and serologic assays. Songhua Yuan, Yu Yang, Yanmin Wan, Liangzhu Li, Jun Sun, Mingzhe Zhou and Chenli Qiu collected the samples. Zhiyong Zhang, Xiaoyan Zhang, Yunwen Hu and Jianqing Xu supervised the study and provided critical comments. Chao Qiu wrote the manuscript.

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Competing interests

The authors have no conflicts of interest to declare.

Ethical approval

This study was reviewed and approved by the Ethics Committee of SHAPHC.

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