Clinical and epidemiological characteristics of a young child infected with avian influenza A (H9N2) virus in China

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Abstract
Three cases of the avian influenza A (H9N2) virus have been documented in Changsha, which is a large city that has nine districts and a population of 7.04 million in central South China. Among these patients, one was a girl and two were boys. The ages of the patients were 9 months, 2 years, and 15 years. Two cases of H9N2 were detected in September, 2015 and one was detected in 2017. Two patients were children who had not reached the age for kindergarten and one was a student. These three cases were all mild and were detected in a sentinel hospital of the Chinese Influenza Surveillance System. We describe the clinical and epidemiological features of the youngest patient with H9N2 in 2017 and the surveillance results of the H9N2 virus in live poultry markets in Changsha. From January 2014 to December 2017, 4212 samples were collected in live poultry markets in Changsha, among which 25.81% (1087/4212) were H9N2-positive. Public health concerns should be addressed for emerging H9N2 virus infection, and more strategies should be performed before this virus mutates to be more transmissible and highly pathogenic.

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Introduction

Owing to mutability of influenza virus and improving sensibility of the influenza surveillance system, human infection of novel avian influenza viruses, including H5N1, H5N6, H7N9, and H10N8, are emerging, especially in China.\(^1\)\(^-\)\(^5\) H9N2 virus has also become more frequent.\(^6\) There are three documented H9N2 cases in Changsha (a large city that has nine districts and a population of 7.04 million) in central South China. Among these cases, one patient was a girl and two were boys. The ages of these patients were 9 months, 2 years, and 15 years. Two cases were detected in September, 2015 and one was detected in 2017. Two of the patients were scattered children and one was a student. These three cases were all mild and detected in a sentinel hospital of the Chinese Influenza Surveillance System (CISS). We report here the epidemiological features of the youngest patient with H9N2 in 2017 and the surveillance results of the H9N2 virus in live poultry markets in Changsha.

Case report

The patient, who lives in a six-person family in District A in Changsha, was a 9-month-old boy with no vaccination history of influenza vaccine and no other disease history. The boy had symptoms of fever (no temperature measurement was taken at this time) and was sneezing at 4:00 h on 18 September, 2017. Several hours later, with an auxiliary temperature of 39.5°C, he was sent to the paediatric emergency department of a sentinel hospital of the CISS system. A routine blood examination showed that the white blood cell count was 10.31 \(\times\) 10\(^9\)/L and neutrophils represented 45.9% of blood cells. A throat swab sample was collected at the emergency department for pathogenic detection. Influenza virus antigen detection showed a positive result for influenza A. Consequently, he was diagnosed with influenza and treated with oseltamivir and ibuprofen. However, the patient’s symptoms did not improve after treatment. He returned to hospital three times since 16:00 h on 18 September to 15:00 h on 20 September. Besides oseltamivir and ibuprofen, he was then prescribed oral medicine, including Bifidobacterium and a Chinese traditional medicine (Xiao’er Chiqiao Qingre Keli), as well as intravenous medicine, including andrographolide injection, vitamin C, amino acids, potassium chloride, and a paediatric electrolyte supplements injection. No symptoms were observed after 15:00 h on 20 September. The result of a throat swab sample (collected on 18 September) was H9N2-positive by using polymerase chain reaction, which was performed in the influenza surveillance network laboratory in Changsha Center for Disease Control and Prevention on 22 September. Another throat swab sample that was collected on 23 September was H9N2-negative when tested on 24 September.

The data were obtained from the CISS and a field epidemiological survey. Written informed consent was given by patient’s
guardian for their clinical information. This study was approved by the Medical Ethics Committee of Changsha Center for Disease Control and Prevention.

**Poultry exposure history and close contact tracing**

The patient’s elder sister developed a mild fever, which rapidly disappeared between 16 and 17 September. She did not receive any medical treatment during these days. The patient’s father had mild nasal obstruction, which rapidly disappeared on 18 September. The other family members did not have any symptoms of the upper respiratory tract or influenza-like illness before the patient’s illness onset date.

Close contacts were defined as individuals who had provided care to, had been living with, or had potentially been directly exposed to respiratory secretions or body fluids of the patient after onset of illness of the patient. After close contact tracing, 36 close contacts were confirmed, including five family members of the patients, and 31 medical workers and other patients who were in the same observation room of the hospital. During the following 7 days, no close contact developed an influenza-like illness. Blood samples, which were collected from the patient’s elder sister and father on 23 September, were H9N2-negative when tested on 24 September.

No live poultry exposure history had been reported since 10 days before the patient’s illness onset date. There was no live poultry market or scattered live poultry around the child’s community. The patient’s parents worked in a retail market 10 km away (in District B in Changsha) where live poultry was traded, but they did not provide the name and address of this market. The boy might have been infected through mechanical transmission from his parents. However, no details about the market were provided by his parents.

**H9N2 virus surveillance in live poultry markets**

From January 2014 to December 2017, 4212 samples were collected in live poultry markets in Changsha. Among these samples, 25.81% (1087/4212) were H9N2-positive as tested by polymerase chain reaction performed in the influenza surveillance network laboratory in Changsha Center for Disease Control and Prevention (Table 1). Although this positive rate significantly decreased yearly ($\chi^2 = 49.329, P < 0.001$) as tested by a linear-by-linear association (SPSS 13.0; IBM Corp., Armonk, NY, USA), the yearly positive rate was higher than 20%. Samples from seven categories were collected, among which sewage samples had the highest H9N2-positive rate (36.63%) and live poultry drinking water samples had the second highest rate (35.16%). Faecal dropping swabs had the lowest H9N2-positive rate (0.78%). The H9N2-positive rate was significantly different among the seven categories ($\chi^2 = 462.589, P < 0.001$).

The surveillance data showed that the H9N2 virus had spread widely in the nine districts of Changsha, in which the prevalence of the virus ranged from 5.93% to 58.93% in 2017 (Figure 1). From January to December 2017, 57 samples were collected in live poultry markets in District A where the patient lived, among which 19.30% (11/57) were H9N2-positive. October had the highest positive rate during the whole year. The H9N2 prevalence in District B where the patient’s parents worked was higher than that in District A (Table 2). In District B, 50 samples were collected in live poultry markets and 13 were H9N2-positive, with a positive
rate of 26.0%, which was higher than the rate of the whole city.

**Discussion**

Infection of people with avian influenza A (H9N2) virus was first detected in Guangdong Province, China in 1998. After this time, human H9N2 cases had been occasionally reported from 1998 to 2014. From 2015 to 2017, 23 human cases of H9N2 infection were detected, among which 18 were reported in China. Since 1998, approximately 45 human infections

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**Table 1.** Epidemiological features and results of samples collected in live poultry markets in Changsha, China.

| Year  | Number of samples | H9N2-positive | Positive rate (%) |
|-------|-------------------|---------------|-------------------|
| 2014  | 578               | 178           | 30.80             |
| 2015  | 902               | 337           | 37.36             |
| 2016  | 2141              | 434           | 20.27             |
| 2017  | 591               | 138           | 23.35             |
| Total | 4212              | 1087          | 25.81             |

| Sample types | Number of samples | H9N2-positive | Positive rate (%) |
|--------------|-------------------|---------------|-------------------|
| Faecal dropping swabs | 513               | 4             | 0.78              |
| Poultry cage swabs      | 486               | 15            | 3.09              |
| Drinking water samples  | 1638              | 576           | 35.16             |
| Sewage samples          | 1141              | 418           | 36.63             |
| Chopping board swabs    | 271               | 43            | 15.87             |
| Others                  | 26                | 1             | 3.85              |
| Total                   | 4075              | 1057          | 25.94             |

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**Figure 1.** Location of Changsha, China and the prevalence of H9N2 virus in live poultry markets in nine districts of Changsha in 2017.
with avian influenza A (H9N2) virus have been detected in China, Bangladesh, and Egypt.\textsuperscript{8} The median age of these patients was 4 years (range: 9 months to 84 years), and most of them had only mild illness.\textsuperscript{8,9}

In 2015, we found that symptoms appeared to be mild in children who were infected with H5N6, H5N1, H7N9, and H10N8.\textsuperscript{1} In the current report, we found that symptoms of the youngest patient only lasted 2 days, and that the other two patients only had influenza-like illness. This finding indicates that the symptoms of H9N2 infection appear to be mild in children. The reason and mechanism of this illness remain unclear. Further research is required to examine the mechanism to provide a reference for clinical practice for managing avian influenza infection. Because of the mild symptoms, children infected with H9N2 and other subtypes of avian influenza virus were commonly detected by sentinel hospitals of the CISS system. However, a large amount of hospitals are not covered by this system. In Changsha, there are more than 50 hospitals, excluding private clinics and health care centres, but only two hospitals are included in the CISS system.

Although no environmental surveillance evidence of our case was provided to show a full transmission chain, the positive rates of H9N2 were high in live poultry markets in nine districts of Changsha. Owing to the high prevalence of H9N2 virus in live poultry markets, more H9N2 viral infections might be missed in China. Therefore, public health concerns should be addressed for emerging H9N2 virus infection, and more strategies should be performed before this virus mutates to be more transmissible and highly pathogenic.

### Authors’ contributions

TC designed the research and wrote the article. TC, RL, and BZ performed the data analysis. RL, YL, XZ, and SC performed data collection. The final version was approved by all authors.

### Declaration of conflicting interest

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