Brief Report

Clinical analysis of 150 cases with the novel influenza A (H1N1) virus infection in Shanghai, China

Qiang Ou[1,2], Yunfei Lu[2], Qin Huang[2], Xunjia Cheng[1,*]

[1] *Department of Microbiology and Parasitology, Shanghai Medical College of Fudan University, Shanghai, China;*
[2] *Shanghai Public Health Clinical Center, Shanghai, China.*

Summary **The aim of the present research was to analyze the epidemiological and clinical characteristics of the novel influenza A (H1N1) in China. We retrospectively analyzed the epidemiological information and clinical characteristics of 150 patients with the novel influenza A (H1N1) virus infection by descriptive epidemiology. There were 82 males and 68 females in this group. The median age of the 150 patients was 34.4 years (range, 4 to 77 years). There were 145 imported cases among the patients and most of these cases came from Australia, America and Canada. The main symptoms included fever, cough and sore throat. Other symptoms included: expectoration, runny nose, throat itching, sniffles, dry pharynx, headache, muscular ache, *etc*. $CD4^+$ T cell counts of 48% of the patients were lower than normal. Computed tomography (CT) of the chest in 32 cases was abnormal, including: increased bronchovascular shadows, pneumonia, pleural thickening and pleurisy, *etc*. Oseltamivir was the first choice for treatment of A (H1N1) influenza and it was safe and well tolerated. The symptoms were minor and the prognosis was good. All patients recovered fully after treatment. Considering the fact that the flu is highly infectious and can be carried through human to human contact rapidly, local Centers for Disease Control and Prevention (CDC) should strengthen monitoring and take some measures in view of an influenza A (H1N1) onslaught.**

Keywords: Influenza A (H1N1), epidemiology, clinical characteristics, oseltamivir

1. Introduction

The Influenza A (H1N1) outbreak recently is an acute respiratory infectious disease caused by a novel strain of influenza A (H1N1) virus. Fever, cough, sore throat, runny or stuffy nose, headache and diarrhea are among the most common clinical features observed in infected patients (*1*). Since influenza A (H1N1) was first found in the United States and Mexico in March 2009 (*2*), the epidemic has been spreading at an extremely high speed in the following 5 months. It has currently affected over 160 nations in the five continents. By August 13, 2009, the World Health Organization (WHO) has announced as many as 182,166 confirmed cases and a death toll of 1,799 with a mortality rate of 0.99% (*3*).

In Mainland China, the Centers for Disease Control reported 2,861 cases of the flu and 2,513 cured cases without dead cases by August 19, 2009. Considering the fact that the flu is highly infectious and can be carried through human to human contact at a high speed, the Chinese Ministry of Health announced on April 30 that influenza A (H1N1) was a Category B contagious disease and that measures for dealing with a Category A contagious disease would be applied to prevent its spread according to *Prevention and Control Law for infectious disease of People's Republic of China*.

In this study, we retrospectively analyzed the epidemiological information and clinical characteristics

**Address correspondence to:*
Dr. Xunjia Cheng, Department of Microbiology and Parasitology, Shanghai Medical College of Fudan University, Shanghai 200032, China.
e-mail: xjcheng@shmu.edu.cn

of 150 confirmed cases received in Shanghai, China in order to enhance the understanding of this new type of influenza.

2. Materials and Methods

2.1. *Case selection and definite diagnosis standards*

The 150 cases of influenza A (H1N1) were from the Shanghai Public Health Clinical Center (SPHCC) between May 23 and July 5, 2009. Definitive diagnosis standards were signs of influenza-like illness including: fever, runny nose, sore throat, cough and headache. The diagnosis was also based on one or several of the following laboratory results: 1) novel influenza A (H1N1) viral RNA from nasopharyngeal specimens was confirmed positive (real-time RT-PCR and RT-PCR) and 2) H1N1 flu virus was separated.

2.2. *Data collection and analysis*

Relevant information from the 150 patients was collected, including: gender, age, medical history, exported countries, clinical manifestation, laboratory and imaging examinations, treatment and prognosis. The SPSS 12.0 statistical program was employed during data processing. The study was performed using descriptive epidemiology.

3. Results and Discussion

3.1. *Epidemiological characters*

Among the 150 patients, 82 and 68 were males and females (1:2), respectively. 22.7% were below 18 years old, 111 were between 18-55 years old (74%), 5 were over 55 years old (3.3%); the youngest was only 4 years old, and the oldest 77 years old. The average age of the patients was 34.4 years old. One patient was once diagnosed with hyperthyroidism, 3 with peptic ulcers, 1 with lymphoma, 4 with hypertension, 3 with allergic rhinitis, 4 with asthma, and 1 pregnant. There were 145 imported cases among the patients, including 88 from Australia, 18 from the United States, 14 from Canada, 12 from Britain, 4 from Hong Kong, 2 from Philippines, 2 from Singapore, 1 from Italy, 1 from Mexico, 1 from Thailand, 1 from France, and 1 from Indonesia. Five were second-generation influenza A (H1N1) cases in Mainland China after close contact with confirmed cases.

3.2. *Clinical manifestation*

Major clinical symptoms were listed as follows according to frequency (Table 1): fever (86%), cough (66%), sore throat (10%), expectoration (10%), runny nose (10%), throat itching (6%), snuffle (5%), dry pharynx (4%), headache (3%), muscular ache (2%), and physical signs were throat congestion (92%), swelling of tonsils (30%), and roughness of breath sounds (2%).

Table 1. Clinical manifestation of 150 cases with influenza A (H1N1) virus infection

Symptoms/Signs	Cases number	Percent (%)
Fever	129	86
Cough	99	66
Sore throat	45	30
Expectoration	15	10
Runny nose	15	10
Throat itching	9	6
Snuffle	7	5
Dry pharynx	6	4
Headache	4	3
Muscular ache	3	2
Throat congestion	138	92
Swelling of tonsils	45	30
Roughness in breath sound	3	2

3.3. *Laboratory and imaging examination*

Routine blood tests in 130 cases showed normal or low leukocyte count (86.7%), percentage of neutrophils in 90 cases was higher than normal (60%), $CD4^+$ T cell counts in 72 cases lower than normal (mean 375.9 ± 170.4 cell/μL) (48%). CT of the chest in 32 cases showed to be abnormal, including increased bronchovascular shadows, pneumonia, pleural thickening, and pleurisy.

3.4. *Treatment and prognosis*

Of 150 patients infected with H1N1 virus, 140 of them were treated with oseltamivir. The adult dosage was 75 mg twice a day for five days. The child dosage was determined by weight. Patients with severe illness were given double coptis oral liquid at the same time for antiviral therapy. Patients with both increased absolute neutrophil count (ANC) and white blood cell (WBC) in peripheral blood and CT diagnosis of pneumonia were given an add-on therapy of azithromycin at a dose of 0.5 g each day for three days. Patients with high fever were treated with ice-bags. Because of the side-effects caused by oseltamivir and the fact that her initial symptoms were shown more than 48 h before the treatment, the pregnant patient, together with the other 9 patients with low fever, were given only double coptis oral liquid for antiviral therapy. Through antiviral therapy and symptomatic treatment, clinical manifestations in all patients disappeared and the results of diagnostic testing using nasopharyngeal swabs for H1N1 virus were all negative. All patients recovered fully and the course of disease was 5 to 11 days.

Human history has witnessed three major flu pandemics in 1918, 1957, and 1968. The 1918 pandemic killed at least 40 million people worldwide and pandemics in 1957 and 1968 caused hundreds of thousands of deaths. The origin of the 1918 pandemic virus was poultry. Both the 1957 and 1968 pandemic strains were thought to have originated as reassortants in which one or both human-adapted viral surface proteins were replaced by proteins from avian influenza strains (*4*). H1N1 flu is an acute respiratory infection caused by a new type of influenza virus which infects both humans and poultry. Recent study shows that the virus is a strain of influenza type A in the family orthomyxoviridae that contains gene fragments from avian, swine and human influenza viruses. Human beings are easily infected through interpersonal dissemination.

According to the information from the 150 patients, the characteristics of the influenza can be summarized as follows. 1) The novel H1N1 virus preferentially infects healthy and younger people. Most of the patients are students and employees abroad. The target group contained 111 patients aged between 18 to 55 years old (74%), and 90 patients without any special medical history, which is different from seasonal influenza infections in which the old and weak are easily infected. 2) Most of the cases were imported. The group contained 145 imported cases, among which 85.4% of them are from the United States, Canada, and Australia. Only 5 second-generation A/H1N1 cases have been found in these patients. 3) There has been a surge in the number of cases. Since the first confirmed H1N1 case in Shanghai on May 23, 50 cases had an interval of 28 days; the 51st to 100th case an interval of 8 days; 101st to 150th an interval of 6 days.

The transmission of influenza A (H1N1) is mainly through the spread of aerosol or droplets from the respiratory secretions of infected individuals. Symptoms of influenza A (H1N1) are similar to the symptoms of regular influenza. According to the reports in recent literature, H1N1 virus may also result in abnormal appearance of nervous system, including hieronosus, altered mental status, abnormal electroencephalogram and so on (*5*). The symptoms were arranged according to frequency as follows: cough, sore throat, expectoration, runny nose, pharynx itching, snuffle, dry pharynx, headache, muscular stiffness and so on. The physical signs are throat congestion, swelling of tonsil, roughness of breath sounds and so on. All of the cases show minor clinical presentation, without severe illness or deaths. It should be noted that clinical manifestation of imported H1N1 flu cases in Mainland China mainly show minor symptoms, so there is no need for panic.

86.7% of cases show normal or low WBC counts in peripheral blood, while 60% show higher ANC percentages, which is one of the features of the novel influenza A/H1N1 virus. $CD4^+$ T cell counts of 48% of the patients were lower than normal. This suggests that H1N1 virus is capable of inhibiting cellular immune function, which is probably related to the induction of excessive apoptosis of lymphocytes (*6*). The detailed mechanism requires further research.

Research shows that neuraminidase (NA) inhibitors oseltamivir can effectively relieve clinical symptoms (*7*). Therefore, patients should be treated with oseltamivir as soon as possible after confirmation. However, oseltamivir resistance may develop during antiviral treatment among immunosuppressed patients. Therefore, it was very important to closely monitor those patients for antiviral drug resistance (*8*). The recommended dose for adults is 75 mg twice daily for five days. To be specific, for patients whose weights are less than 15 kg, the dose is 30 mg twice daily, for patients whose weights are between 15 to 23 kg, 45 mg twice daily, between 23-40 kg, 60 mg twice daily, and more than 40 kg, 75 mg twice daily. The Chinese medicine double coptis oral liquid can also be adopted as an antiviral treatment. Patients with bacterial infections were given antibiotics. During treatment with oseltamivir for 140 patients of the group, no adverse reactions were observed. These results suggest that oseltamivir is safe and well tolerated.

All patients were discharged from the hospital after anti-viral and symptomatic treatment with a good prognosis. However, it is worthwhile to note that the main target group of highly contagious H1N1 virus is healthy young and middle-aged persons. As the number of confirmed cases keeps increasing, fatality rates can possibly rise. The pandemic is more serious in nations where there are areas of poor hygiene. Meanwhile, it should also be pointed out that the flu virus is prone to gene rearrangement and strain variation with seasonal changes which may lead to more intensive invasiveness and pathogenicity. Thus, local centers for disease control and prevention should strengthen monitoring and take active measures to manage the influenza A/H1N1 virus pandemic (*9*).

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