

Clinical Presentation of Novel Influenza A (H₁N₁) in Hospitalized Children

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Received: Feb 07, 2010; Final Revision: Jul 28, 2010; Accepted: Oct 24, 2010

Abstract

Objective: Human pandemic influenza H₁N₁ virus as the cause of febrile respiratory infection ranging from self-limited to severe illness has spread globally during 2009. Signs and symptoms of upper and lower respiratory tract involvement, fever, sore throat, rhinitis, myalgia, malaise, headache, chills and fatigue are common. In this article we report the clinical presentation of Influenza A (H₁N₁) in our hospitalized children.

Methods: Between September and October 2009, all children requiring hospitalization for suspected H₁N₁ infection were transferred to Pediatric Infectious Diseases ward. For all patients the throat swab was taken for PCR testing to confirm or exclude the diagnosis of H₁N₁ Influenza A. Case patients consisted of H₁N₁-positive patients. Age, sex, symptoms, signs, laboratory data, CXR changes, details of therapy, duration of admission and patient outcome were documented.

Findings: Twenty patients were H₁N₁ positive. Mean age of the patients was 65.50±9.8 months. Fever and coughs were with 55% the most commonly reported symptoms. Other presentations included vomiting (55%), abdominal pain (25%), cyanosis and dyspnea (5%), body ache (40%), rhinorrhea (80%), sore throat (35%), head stiffness (5%) and loss of consciousness (5%). The median temperature of the patients was 38.5°C. Chest X-Ray changes were noted in 13 out of 20 patients (65%). Mean leukocyte and platelet was 6475 and 169000 respectively. Seventeen (85%) patients were treated with Oseltamivir, 3 patients received adjuvant antibiotics. The mean duration of admission was 3 days. Three patients required intensive care support and all of them expired due to superinfection.

Conclusion: Our data confirm that the presentation of influenza in children is variable and 2009 H₁N₁ influenza may cause leucopenia and thrombocytopenia.

Iranian Journal of Pediatrics, Volume 21 (Number 1), June 2011, Pages: 215-219

Key Words: Influenza; Infectious Diseases; H₁N₁; Oseltamivir

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Introduction

Human Swine Influenza A [H₁N₁] is a highly transmissible infection which has predominantly affected children and young adults^[1]. In the United States to date, most confirmed cases of S-OIV (swine-origin influenza A [H₁N₁] virus) infection have been characterized by self-limited, uncomplicated febrile respiratory illness and symptoms similar to those of seasonal influenza (cough, sore throat, rhinorrhea, headache, and myalgia); approximately 38% of cases have also vomiting or diarrhea, neither of which is typical of seasonal influenza^[2].

As with seasonal influenza, some patients with 2009 H₁N₁ influenza present without fever^[3]. Young children are less likely to have the usual influenza signs and symptoms, such as fever and cough^[4]. Influenza illness in infants and children may present similarly to other respiratory viruses, and symptoms and presentation may be different than its presentation in adults^[3]. Infants may present with fever and lethargy, and may not have cough or other respiratory symptoms.

Symptoms of severe disease in infants and young children may include apnea, tachypnea, dyspnea, cyanosis, dehydration, altered mental status, and extreme irritability^[5]. In addition, infants and young children may experience diarrhea more frequently than older children and adults^[3]. This study describes clinical and laboratory characteristics and outcomes of pediatric patients in Zahedan with 2009 influenza A [H₁N₁] infection.

Subjects and Methods

This is a prospective study. All patients (up to 14 years) who were hospitalized in Pediatric Infectious Diseases ward in Ali ebne Abitaleb hospital, Zahedan, Iran, for suspected H₁N₁ infection (at least 24 hours with an influenza-like illness: fever, cough or sore throat), with history of close contact with infected patients by H₁N₁ virus) between September and October 2009, were considered for the investigation.

For all patients the throat swab was taken for PCR testing (a real-time reverse-transcriptase-

polymerase-chain-reaction assay) to confirm or exclude the diagnosis of H₁N₁ Influenza A. Nasopharyngeal specimens were collected using swabs and placed into Universal Transport Media before transport. The specimen was tested at the Bu Ali infectious disease Laboratory Institute for pandemic [H₁N₁] 2009 virus, using real-time reverse-transcriptase polymerase chain reaction (RT-PCR) reagents. Patients with H₁N₁-negative test were excluded from the study.

Demographic data, underlying medical disease, clinical signs and symptoms, laboratory tests, radiographic changes, details of therapy, duration of admission and disease outcome were documented. The temperature was measured axillary. Three weeks after discharge, patients were followed in outpatient clinic to evaluate general condition and laboratory data.

This study was approved by the ethics committees of Zahedan University of Medical Sciences. Variables were expressed as means (standard deviation). All data analyses were performed using SPSS, version 16.

Findings

Of 132 patients viral swabs was taken. In 20 patients (60% males and 40% females) H₁N₁ test was positive. Mean age of patients was 65.50±9.8 months (range: 6 to 144 months). The most common admission symptoms were fever and cough (n=11). Other common presentations included poor feeding 16 (80%), rhinorrhea 16 (80%), vomiting 11 (55%), body ache 8 (40%), and sore throat 7 (35%). Table 1 shows the clinical characteristics of patients. One of our patients presented with vomiting, high grade fever, body ache and neck stiffness, his cerebrospinal fluid (CSF) analysis was normal without any cells.

The patients were admitted to hospital in average 2 days (range 1 to 5 days) after symptom onset. None of the patients had an underlying medical condition. Table 2 shows the vital signs of patients. Three patients were admitted to the pediatric intensive care unit (PICU), and required mechanical ventilation. Chest X ray changes were noted in 13 out of 20 patients (65%) including 10

Table 1: Clinical characteristics of the patients with confirmed H₁N₁ infection

| Sign or symptom | No. of patients (%) |
|-----------------|---------------------|
| Cough | 19(95) |
| Fever | 18(90) |
| Rhinorrhea | 16(80) |
| Poor feeding | 16(80) |
| Vomiting | 11(55) |
| Fever and cough | 11(55) |
| Body ache | 8(40) |
| Sore throat | 7(35) |
| Abdominal pain | 5(25) |
| Neck stiffness | 1(5) |
| Dyspnea | 1(5) |
| Diarrhea | 0(0) |

(55%) with bilateral infiltrates and 3 (15%) with unilateral involvement on chest radiograph. Among these 13 patients, one patient developed bilateral pleural effusion during her hospital stay and one developed unilateral empyema. Three of the 20 patients had microbiologic evidence of secondary bacterial infection by CSF and blood cultures.

Fourteen (75%) patients received antiviral treatment with Oseltamivir. Two (10%) patients were not treated with antivirals, 1 (5%) treated with antibiotic and 3 (15%) patients received antibiotics and Oseltamivir. None of patients had received seasonal influenza vaccination. Mean length of hospital stay was 4.2±4.6 (range: 1 to 20) days. Patients had not a history of travel to foreign countries prior to admission.

Table 2 shows laboratory findings of the patients. The mean white blood cell count (WBC) was 6475.0 (4.9) and the mean lymphocyte count

was 40.37% (±11.9) (range: 20-58%). Eleven patients (55%) had WBC less than 4000. Three patients had leukocytosis due to superinfection (pneumonia, empyema) that required intensive care support and all of them expired. Ten patients (50%) had platelets less than 150000.

Eighteen patients (90%) were followed 3 weeks after discharge and their cell counts were normal.

Discussion

A novel swine-origin influenza A virus was identified as the cause of outbreaks of febrile respiratory infection ranging from self-limited to severe illness^[2]. The most commonly reported symptoms of influenza A [H₁N₁] virus in different studies include cough, fever, sore throat, malaise and headache ^[6-9].

The signs and symptoms of influenza caused by pandemic H₁N₁ influenza A virus are similar to those of seasonal influenza, although gastrointestinal manifestations appear to be more common with pandemic H₁N₁ influenza^[10]. Vomiting and diarrhea have been reported more often with 2009 H₁N₁ influenza than with seasonal influenza^[1]. Dawood et al mentioned that 25% of their patients had diarrhea, and 25% had vomiting^[2]. In another study, diarrhea or vomiting was reported in 39% of patients, including 42% of children (i.e., patients under the age of 18 years) and 37% of adults (those 18 years)^[11].

In the same way, the most frequent symptoms in our patients were fever, cough, poor feeding, rhinorrhea, vomiting, body ache and Sore throat. None of our patients had diarrhea, but about half

Table 2: Vital signs and Laboratory findings of the patients with H₁N₁

| Parameter | Mean (SD) | Range |
|-----------------------|------------|--------------|
| Pulse rate | 131 (11.1) | 110-150 |
| Respiratory rate | 36.8±7.5 | 25-50 |
| Temperature(axillary) | 38.5±0.91 | 37-41 |
| WBC | 6475±4.9 | 2600-17900 |
| Hemoglobin | 10.8±0.85 | 9.5-12.5 |
| Platelet | 169000±7.9 | 70000-329000 |

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of them complained from vomiting. None of our patients had diarrhea, but about half of them complained from vomiting.

Several severe clinical syndromes associated with influenza A 2009 H₁N₁ infection may be seen^[12]. Other unusual presentations of influenza A [H₁N₁] virus were conjunctivitis, earache, hematemesis, epistaxis, croup, apnea, acute abdomen, spontaneous pneumomediastinum complicating pneumonia, altered mental state^[8,9,13,14].

One of our patients was a 10 year old girl that presented with loss of consciousness (Glassco coma score = 9) and seizure. Her CSF contained white blood cells (segmented: 40%, lymphocyte: 60%). The patient was treated with Oseltamivir. After some days, she had to be intubated because of respiratory failure and acute respiratory distress syndrome and died. An 8 year old boy had empyema and unfortunately two days after thoracotomy expired in pediatric intensive care unit.

Critical illness due to 2009 influenza A [H₁N₁] in Canada occurred rapidly after hospital admission, often in young adults, and was associated with severe hypoxemia, multisystem organ failure, a requirement for prolonged mechanical ventilation, and the frequent use of rescue therapies^[15]. In the same way, our critical ill patients were intubated and because of respiratory failure required mechanical ventilation.

In a study by Jain et al that collected data on 272 patients hospitalized at least 24 hours for influenza-like illness and had positive tests for the 2009 H₁N₁ virus report that a significant proportion of hospitalized patients had findings on chest radiography that in 40% were consistent with pneumonia, and the majority had bilateral infiltrates. They suggested that better studies were needed to correlate radiographic findings with the cause of pneumonia during influenza outbreaks^[11].

In another article that reviewed the chest radiographic and CT findings in patients with presumed/laboratory-confirmed influenza A [H₁N₁] virus infection conclude that the radiographs are normal in more than half of patients with S-OIV [H₁N₁] infection, but manifest as extensive bilateral air-space disease in hospitalized patients requiring advanced

mechanical ventilation. These patients are also at risk for developing plural effusion, which should be carefully sought for on contrast-enhanced CT scans^[16].

In the present study, similar to other studies, bilateral involvement on chest radiograph was the most common presentation. The chest CT scan of one of the patients showed mediastinal adenopathy, ground glass opacity, thickness of interlobular septa, bilateral consolidation with pleural effusion and Non cardiogenic pulmonary edema.

In a large U.S.A. case series of hospitalized patients with 2009 H₁N₁ virus infection during the first 2 months of the pandemic, the following laboratory abnormalities were observed: Leukopenia 20%, leukocytosis 18%, thrombocytopenia 14%, thrombocytosis 9%^[11]. In a study of individuals with probable pandemic H₁N₁ influenza A infection, relative lymphopenia (21 percent of white blood cells) without leukopenia was observed in 23 of 25 adults, but in only 3 of 16 children^[17].

In critically ill children with H₁N₁ influenza of swine origin in the UK lymphopenia and thrombocytopenia was reported in some cases^[8]. In our study about half of patients had leukopenia and/ or thrombocytopenia; their blood cell count was normal after 3 weeks.

Jain et al reported that seventy five percent of their patients received antiviral treatment with Oseltamivir. Data suggest that the use of antiviral drugs was beneficial in hospitalized patients especially when this therapy was initiated early^[11].

As a limitation of this study, some of patients were excluded from the study because they did not want to be admitted in hospital and the group may not be representative of hospitalized patients.

Conclusion

Our data shows that in the H₁N₁ outbreak under study the presentation of influenza in children was variable and H₁N₁ influenza virus caused leukopenia and thrombocytopenia.

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Acknowledgment

The authors thank all colleagues in pediatrics ward and Research Center for Children and Adolescents Health for their help in preparing data.

Conflict of Interest: None

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