Spectrum of Chest Radiographic Findings of Influenza A (H1N1) 2009 Virus Infection in Hospitalized Pediatric Patients in Siriraj Hospital

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ABSTRACT

Objective: To evaluate chest radiographic findings of hospitalized pediatric patients with laboratory-confirmed influenza A (H1N1) 2009 virus infection in Siriraj Hospital, during June to August 2009.

Methods: A total of 43 hospitalized pediatric patients with pandemic influenza A (H1N1) 2009 virus infection between June and August 2009 were included. Initial and follow up chest radiographs were retrospectively reviewed by two pediatric radiologists. Radiographic abnormalities were evaluated in pattern, distribution, and extension. Associated pleural abnormality, pneumothorax, pneumomediastinum and hilar lymphadenopathy were also reviewed.

Results: Of 43 included cases, 22 were males and 21 were females, whose age ranged from 6-168 months (mean 75.58, median 74). Negative chest radiograph were found in 3 of 43 cases (6.98%). Most common radiographic abnormalities were peribronchial opacification (93.02%), patchy opacification (79.07%) and confluent opacification (13.95%). These lesions tended to be multifocal (73.42%), bilateral (74.83%) and centrally located (43.36%). Most of the cases improved clinically after medical treatment although, one of our cases died from superimposed ARDS. Most of the cases had clinical improvement after medical treatment with an average length of stay 10.8 days, although, one of them died from acute respiratory distress syndrome (ARDS).

Conclusion: Most of hospitalized pediatric patients with H1N1 influenza virus infection had abnormal chest radiographs. The most common pattern was peribronchial opacification followed by patchy opacification and confluent opacification which trended to be multifocal, bilateral and centrally located.

Keywords: H1N1, virus, pneumonia, influenza, influenza A

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INTRODUCTION

In March 2009, there was an outbreak of pandemic H1N1 2009 influenza virus in Mexico, which quickly spread into other countries. Until October 2009, there was a total of 375,000 confirmed cases over 170 countries and 4,500 deaths worldwide.[1] On June 11, 2009, the World Health Organization (WHO) raised the level of pandemic alert from phase 5 to 6 which is defined as a new virus causing sustained community level outbreaks in more than one WHO region.[2]

Between April 28 and October 17, 2009, there were 28,057 confirmed cases in Thailand and 176 died. Most of the cases had mild symptoms and recovered completely without need for hospitalization.[3] However most of the dead victims had other associated conditions including chronic diseases, low immunity, obesity, advanced age, age younger than 5 year old and pregnancy. The presenting symptoms, mode of transmission and disease prevention of H1N1 2009 influenza virus are quite similar to those of seasonal influenza.[4] The purpose of this study was to describe chest radiographic findings in hospitalized pediatric patients with H1N1 2009 influenza virus infection in Siriraj Hospital.

MATERIALS AND METHODS

This study was approved by the ethics committee of the Faculty of Medicine Siriraj Hospital, Mahidol University (Si.143/2010), in which the informed patient consent was waived due to its retrospective study.

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Patients

All of the patients with laboratory-confirmed influenza A (H1N1) 2009 virus infection who were admitted into the pediatric inpatient department of Siriraj Hospital between June 27, 2009 and August 28, 2009 were included in this study. The patients whose chest radiographs were unavailable and age greater than 15 year old were excluded from this study.

Laboratory confirmation

Specimens from nasopharyngeal swabs were collected at the emergency department or wards. Reverse transcriptase polymerase-chain-reaction (RT-PCR) tests were performed in accordance with published guidelines from the WHO in all patients.[5]

Individual patient data collection

The collected data included a) clinical features including initial symptoms and progressing symptoms during treatment b) past medical history including underlying diseases and previous medical treatments c) laboratory findings.

Radiologic examinations

All postero-anterior upright chest radiographs were performed by digital radiography equipment (Quantum x-ray; QUEST FS series with FCR velocity detector, Philips Optimus 50) with a standard technique (110 kV, 2 mAs, and a 180 cm. film focus distance for the postero-anterior views). The antero-posterior portable chest radiographs were performed with computed radiography machines (DYNARAD HF-110 CM (D1) and KELEX 50 mA (K3)). All chest radiographs including initial and follow up studies were reviewed digitally by two experienced pediatric radiologists using a picture archiving and communication systems (PACS) viewer. Decisions were reached by consensus. The two primary reviewers were blinded to the clinical data and the patient's outcomes.

The chest radiographic findings were divided into normal or abnormal group. The abnormalities were described as a) opacification b) atelectasis c) pleural effusion d) air trapping e) nodule f) hilar lymphadenopathy g) pneumothorax h) pneumomediastinum i) ARDS. Peribronchial opacification was defined as coarse linear marking or opacification that radiated from the hilar to the lung which preferentially attenuated the x-ray beam and therefore appeared more opaque than the surrounding area. Ground-glass opacity was defined as an area of hazy increased lung opacity within which definition of lung structures was usually preserved and this opacity was less opaque than consolidation. Consolidation was defined as a homogeneous increased pulmonary parenchymal attenuation that obscured the margins of vessels and airways. Nodular opacity was defined as a rounded opacity measuring less than 3 cm in diameter.[6] Patchy opacity was defined as inhomogeneous airspace consolidation in the anatomic distribution of a bronchial lung segment, such as described in bronchopneumonia.[6-8] Confluent opacity was defined as collection of poorly defined, discrete, or partly confluent opacities. Air trapping was defined as a retention of air in the lung distal to an obstruction which seen as lung hyperinflation with a decrease in parenchymal attenuation.[6]

The anatomic distribution of the lung parenchymal abnormalities was classified as: 1) predominant distribution at (a) central, (b) peripheral, (c) both or (d) negative finding. 2) number of zone abnormalities was classified as (a) focal (a single focus of abnormality) or (b) multifocal (more than one focus of abnormalities), and 3) side of involvement was classified as (a) unilateral or (b) bilateral.

Statistical analysis

Descriptive statistics were use to summarize and displayed all data as the mean, median and standard deviation. All the radiographic findings were described by frequency and percentage. We used Cohen's kappa statistic for determining the inter-observer measure of agreement. Statistical analysis was performed with a statistical software package (SPSS version 13.0).

RESULTS

Of all 48 included cases, 5 cases were excluded due to unavailable chest radiographs (n=4) and age older than 15 years (n=1).

Of the remaining 43 included cases, 22 cases were male and 21 cases were female. The age ranged from 6-168 months (mean 75.58, median 74). Twenty-seven (62.79%) of 43 patients had underlying medical conditions, as shown in Table 1. All 43 hospitalized pediatric patients had initial symptoms of respiratory tract infection. The presenting symptoms of these patients were shown in Table 2. The onset of symptoms before admission was 0.5-10 days (mean 2 days). Their length of stay varied from 2-108 days (median 5 days, average 10.83 days). Most of the cases had favorable clinical outcomes. Three cases (3/43, 6.97%) received intensive care with ventilator support. One case (1/43, 2.33%) died from ARDS and pseudomonas septicemia.

TABLE 1. Underlying medical condition of 27 patients*.

Underlying medical condition	No. of patient
Asthma	3
Allergic rhinitis	3
Down syndrome	1
Apert syndrome	1
Myasthenia gravis	1
HIV infection	1
Lymphoma	1
Leukemia	2
Acquired red cell aplasia	1
Thalassemia	2
Ventricular septal defect (VSD)	1
Total anomalous pulmonary venous return (TAPVR)	1
Atrial septal defect (ASD)	1
Patent ductus arteriosus (PDA)	1
Epilepsy	2
Spastic quadriplegia post meningoencephalitis	1
Focal segmental glomerular lesion	1
Distal renal tubular acidosis	1
Hypertension	1
Nemaline body myopathy	1
Hemangioma at upper eyelid	1
Selective deficiency of IgG3	1
Congenital hydrocephalus and cerebral palsy	1
Bronchopulmonary dysplasia (BPD)	1
Tracheoesophageal fistula post surgical repair	1

*Four cases have more than one underlying medical conditions: one case has leukemia and asthma, one case has BPD and PDA, one case has thalassemia and TAPVR, one case has acquired red cell aplasia, ASD and epilepsy.

TABLE 2. Presenting symptoms of the patient.

Presenting symptoms	No. of patient	Percent (%)
Fever	41/43	95.35
Rhinorrhea	16/43	37.21
Cough	32/43	74.41
Vomiting	1/43	2.32
Diarrhea	2/43	4.65
Sore throat	3/43	6.97
Abdominal pain	1/43	2.32
Other	2/43	4.65

All of the chest radiographs including initial and follow up studies were reviewed (43 cases, 142 images). Three cases had negative initial chest radiographs (3/43, 6.98%). The most common parenchymal and airway abnormalities were peribronchial opacification (93.02%) followed by patchy opacity (79.07%) and confluent consolidation (13.95%). The most common abnormal location was central region (43.36%) and most of the lesions were distributed bilaterally (74.83%) and multifocally (73.42%). The summary of chest radiographic findings has been shown in Tables 3 and 4.

Adult respiratory distress syndrome (ARDS) was found in two cases. The first case was a 7-year-old girl with underlying epilepsy and delayed development who presenting with acute febrile illness and diarrhea. Initially she was admitted in another hospital and referred to our hospital on day 3 with provisional diagnosis of dengue hemorrhagic fever. She was intubated and received ventilator support. Her first chest radiograph performed in our hospital demonstrated diffuse bilateral symmetrical opacities with minimal left pleural effusion. Pneumothorax occurred after she received ventilation support for 31 days, and it was resolved after using chest tube drainage. She was clinically improved after 93 days of treatment with a final diagnosis of H1N1 2009, respiratory failure and septicemia (Fig 1).

The second case was a 6-year-old girl with cerebral palsy and congenital hydrocephalus post VP shunt placement who presented with acute febrile illness for 4 days. Her VP shunt was externally exposed on her first visit and the culture from the tip of her exposed VP shunt demonstrated Methicillin-sensitive *Staphylococcus aureus* and *Pseudomonas aeruginosa*. She developed recurrent aspiration pneumonia during hospitalization. The nasal swab for 2009 H1N1 influenza virus reverse transcriptase polymerase-chain-reaction (RT-PCR) tests showed a positive result. On the third day after of H1N1 influenza virus infection was diagnosed, she died from ARDS with a length of stay of 108 days.

TABLE 3. Summary of chest radiographic findings.

Chest radiographic findings	No. of patient	Percent (%)
Normal	3/43	6.98
Consolidation	4/43	9.30
Ground-glass opacity	2/43	4.65
Patchy opacity	34/43	79.07
Confluent opacity	6/43	13.95
Peribronchial opacity	40/43	93.02
Atelectasis (subsegmental)	4/43	9.30
Pleural effusion (mild, unilateral)	2/43	4.65
Air trapping	5/43	11.63
Nodule	0/43	0
Hilar lymphadenopathy	0/43	0
Pneumothorax	2/43	4.65
Pneumomediastinum	1/43	2.32
ARDS	2/43	4.65

TABLE 4. The location of chest radiographic abnormality.

Descriptive of location	No. of patient	Percent (%)
Distribution		
Central	62/142	43.36
Peripheral	2/142	1.40
Both	48/142	33.57
No. of zone		
Single	5/142	3.49
Multiple	105/142	73.42
Side		
Unilateral	5/142	3.50
Bilateral	197/142	74.83

Pleural effusion was found in two cases. The first case was a 7-year-old girl who had developed ARDS. (Fig 1.) The second case was a 7-year-old boy with underlying epilepsy, atrial septal defeat (ASD) and acquired pure red cell aplasia, who presented with fever and cough. His initial chest radiograph showed peribronchial opacifications with patchy confluent opacities on both perihilar regions and minimal left pleural effusion.

Pneumothoraces were found in two cases. The first case was a 7-year-old girl with ARDS whose pneumothorax was found after using ventilation support for 31 days (Fig 1). The second case was a 7-month-old girl with underlying hemangioma at her left upper eye lid who was admitted for propanolol treatment. She developed fever, cough and lower respiratory tract symptom during hospitalization. Pneumothorax spontaneously occurred on day 18 after admission and pneumomediastinum developed a few hours later which was more obviously seen on follow up images performed on the next day. (Fig 2)

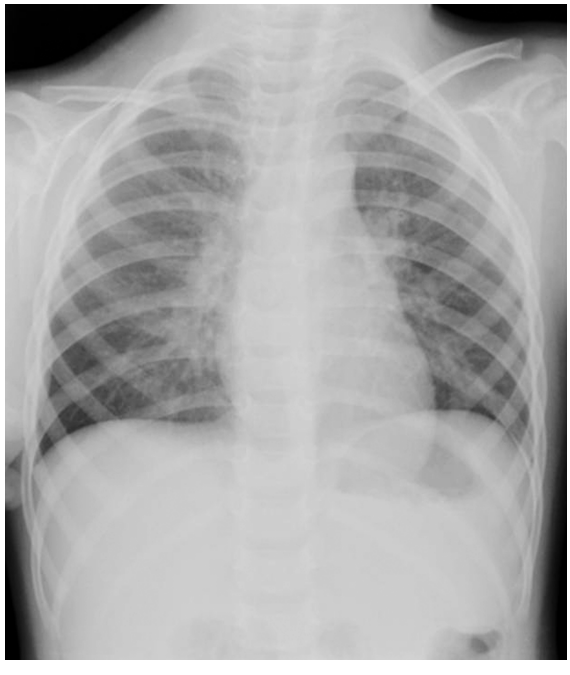

Fig 1. A two-year-old girl presented with fever and cough. The frontal chest radiograph demonstrates bilateral asymmetrical patchy opacities predominately on both perihilar regions which is the most frequent finding in this study.

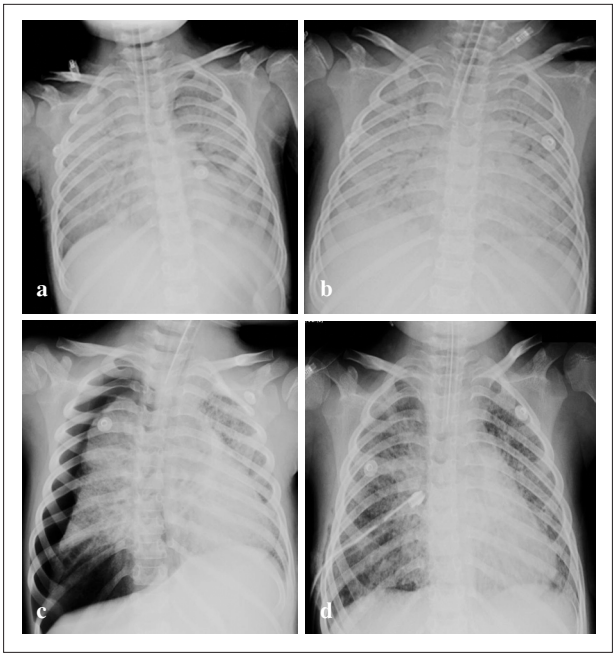

Fig 2. A seven-year-old girl with fever and respiratory failure

a) Initial chest radiograph (day 3) demonstrates diffuse bilateral symmetrical opacities, compatible with ARDS.

b) On day 10, progressive opacities bilaterally due to superimposed infection. Sputum culture done on day 13 revealed Acinetobacter Baumanii.

c) On day 31. Right pneumothorax occurred.

d) Post right chest tube insertion, interval decrease opacities represent improvement of disease.

None of these cases showed nodular opacity or hilar lymphadenopathy.

There was good correlation (kappa value = 0.905) for pleural effusion. Pneumothorax, ARDS, confluent opacity, peribronchial opacity, ground glass opacity and air trapping had fair correlation with kappa value 0.789, 0.612, 0.664, 0.529, 0.470 and 0.454, respectively. We found poor correlation in patchy opacity and atelectasis (kappa value = 0.206 and 0.078 respectively).

DISCUSSION

Our study focused on hospitalized pediatric patients. Most of them had underlying medical illnesses (62.79%) which were the reasons for admission. Common clinical features of hospitalized pediatric patients with laboratory confirmed pandemic H1N1 2009 influenza virus infection include fever with accompanying symptoms of cough, rhinorrhea, sore throat and gastrointestinal symptoms such as vomiting or diarrhea. These results correlate with previous studies done in adult and pediatric populations.[9-11]

Most patients in our study did not have severe illness or unfavorable outcome during hospitalisation by influenza itself. Although two patients had ARDS and needed ventilation support, we though the actual precipitating causes of unfavorable outcomes were co-infection (pseudomonas septicemia) and their underlying central nervous system abnormality that could impair respiratory protective mechanisms leading to increased risk of aspiration. In this study, initial chest radiographs were abnormal in 93.02% of the patients, which was far more frequent than a previous report which showed more than half of the patients had normal initial chest radiographs.[10,12] The reason for the different results was probably due to our study focusing on hospitalized patients who had tendency for more aggressive symptoms and more underlying diseases than the non-hospitalized patient group. Lee et al reported 95% and 100% abnormal chest radiographs in pediatric patients with brief hospitalization and intensive care with respiratory support, respectively.[4]

In our study, the most common chest radiograph abnormalities were peribronchial opacification, patchy opacification and confluent opacification followed by air trapping that were similar to the pattern of typical pneumonia from respiratory syncytial virus, parainfluenza virus, influenza virus, severe acute respiratory syndrome (SARS) and mycoplasma pneumoniae. In contrast, pneumonia from measles virus, cytomegalovirus, varicella and Epstein-Barr virus may demonstrate hilar adenopathy on chest radiographs which is probably helpful to differentiate from H1N1 2009 influenza pneumonia.[13] However, Lee, et al reported the most frequent abnormal pattern was consolidation (38% and 57% in brief hospitalization and intensive care units with respiration support, respectively) which is quite different to our study.[9]

Not many prior studies have reported about pneumothorax or pneumomediastinum in pediatric patient with H1N1 2009 influenza viral infection. The cause of pneumothorax and pneumomediastinum in one of our cases was possibly a complication of mechanical ventilation. However, in another case, it occurred spontaneously after day 18 of admission. However, we believed pneumonia can be the cause itself. The small airways in patients with pneumonia are more susceptible to obstructions by secretions and inflammatory cells, causing generalized hyperaeration, air trapping or atelectasis which may induce increased intrathoracic pressure and spontaneous pneumothorax.

We found 3 cases (6.98%) had normal initial chest radiographs which implied that negative initial chest radiographs cannot rule out the possibility of the pandemic H1N1 2009 influenza virus infection in the pediatric population, particularly in their early stage or an uncomplicated influenza infection.[14]

The limitation of this study is its retrospective design focusing on hospitalized patients. All cases in our series did not undergo computed tomography (CT) scan which is a sensitive modality to detect some subtle lesions such as ground-glass opacification. Previous studies done in adults reported more frequent ground-glass opacification on CT scan in comparison to chest radiographs.[15,16] Thus, the ground-glass opacity could be underestimated in our study. Finally, there were poor to fair inter-observer variations in many chest radiographic abnormalities, especially in subtle findings or partly overlapping findings which might have caused difficulties in making decisions. In contrast, for the more obvious findings such as ARDS, pleural effusion and pneumothorax we found better interobserver variations.

We concluded that most hospitalized pediatric patients with H1N1 influenza virus infection had abnormal chest radiographs. The most common abnormality was peribronchial opacification followed by patchy opacification, confluent opacification and air trapping. These lesions tended to be bilateral, multifocal and centrally located.

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