

Chest imaging findings in children with influenza A (H1N1)

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ABSTRACT

الأهداف: دراسة نتائج التصوير الإشعاعي للأطفال المصابين بأنفلونزا أ (H1N1).

الطريقة: أُجريت هذه الدراسة الاسترجاعية في مستشفى سوكو الجامعي للأطفال، جامعة سوكو، سوجو، الصين وذلك خلال الفترة من سبتمبر 2009م إلى مارس 2010م. شملت هذه الدراسة 81 طفلاً مصاباً بالتهابات تنفسية حادة حيث تم جمع العينات البلعومية الأنفية وكذلك العينات الارتشافية من القصبة الهوائية، وبعد ذلك تم تحليلها وإثبات إصابتها بأنفلونزا أ (H1N1) باستخدام تقنية التفاعل التسلسلي المبلمر الكمي ذو الوقت الحقيقي. لقد تم الرجوع إلى الصور الصدرية التي أُجريت لهؤلاء المرضى ومن ثم تم معاينتها من قبل طبيبي أشعة مستقلين عن بعضهما البعض وذلك من أجل تحديد المناطق الشاذة ونمط توزيعها في الرئتين.

النتائج: لقد أظهر التصوير الإشعاعي للصدر النتائج التالية: تكثف رئوي لطخي في كلتي الرئتين (48 حالة)، تكثف رئوي منتشر في التجويف الهوائي (18 حالة)، تكثف رئوي فصوي (7 حالات)، وكانت ثمانية صور سليمة وخالية من الشذوذ. لوحظ انتشار ظهور المناطق الشاذة في الجزء الأسفل من فصوي الرئة (في كلتي الرئتين [66 حالة])، في أحد الرئتين [7 حالات] ولقد أشار التصوير المقطعي الذي أُجري على 18 حالة إلى وجود تكثف رئوي في التجويف الهوائي وعتامة خلالية، وبعد ثلاثة أشهر تم عمل أشعة مقطعية عالية الوضوح للحالات المصابة بالتكثف الرئوي المنتشر في التجويف الهوائي وقد أظهرت سماكة خلالية.

خاتمة: أشارت نتائج التصوير للأطفال المصابين بأنفلونزا أ (H1N1) بأن أكثر الحالات كانت تشكو من التكثف الرئوي اللطخي في كلتي الرئتين، وتلى ذلك كلاً من: حالات التكثف الرئوي المنتشر في التجويف الهوائي، والحالات السليمة من الشواذ، وحالات التكثف الرئوي الفصوي.

Objectives: To assess imaging findings at presentation in children diagnosed with influenza A (H1N1) infection.

Methods: This is a retrospective observational cohort study conducted at The Children's Hospital affiliated to Soochow University, Suzhou, China between September 2009 and March 2010. Nasopharyngeal swabs and bronchial aspirate samples from 81 children with acute respiratory infections were tested positive for influenza A (H1N1) using quantitative real-time polymerase chain reaction. Chest imaging for these patients was analyzed retrospectively by 2 independent radiologists for the presence and distribution of abnormalities.

Results: Chest radiograph findings consisted of bilateral patchy areas of consolidation (n=48), diffuse areas of air-space consolidation (n=18), and lobar consolidation (n=7). Eight chest x-rays were normal. Abnormalities were observed more frequently in the lower lobes (bilateral [n=66], unilateral [n=7]). Computed tomography (CT) scans were performed in 18 cases with air-space consolidation and interstitial opacities. Cases with diffuse areas of air-space consolidation were followed-up after 3 months by high resolution CT imaging, which showed interstitial thickening.

Conclusion: The predominant imaging findings in childhood influenza A (H1N1) were bilateral patchy areas of consolidation, followed by diffuse areas of air-space consolidation, normal radiographs, and lobar consolidation.

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In March 2009, a new strain of human influenza A (H1N1) virus was identified in Mexico that caused an acute respiratory epidemic disease.¹ The influenza A (H1N1) virus was characterized by a unique combination of gene segments not previously identified among human or swine influenza viruses. This virus can cause human, swine, and poultry infections, among others.² Most patients with influenza virus infections have relatively mild symptoms of fever, myalgia, and cough, whereas some can develop tachypnea, diarrhea, and sore throat. In addition, some cases have led to acute respiratory distress syndrome (ARDS) and even death, even in previously healthy individuals.³ Imaging investigations have significant differences in their ability to diagnose and assess the severity of influenza illnesses. Perez-Padilla et al⁴ reported the chest radiograph findings from 18 cases with confirmed influenza A (H1N1). The aim of the present study was to report the chest radiograph and computed tomography (CT) findings in children who presented with influenza A (H1N1).

Methods. This is a retrospective observational cohort study conducted at The Children's Hospital affiliated to Soochow University, Suzhou, China between September 2009 and March 2010. This study was approved by the Institutional Review Board of our institution. We retrospectively reviewed the archives of patients under 13 years of age who were hospitalized due to an acute respiratory disease. In such patients, nasopharyngeal swab specimens were collected on admission. Respiratory specimens from 2716 patients were tested using quantitative real-time polymerase chain reaction (qPCR) for the detection of influenza A (H1N1). Eighty-one patients fulfilled the criteria for a confirmed case of infection with novel influenza A (H1N1) virus that were established by the Chinese Ministry of Health.⁵ A confirmed case of infection is defined as a person with an influenza-like illness and a novel influenza A (H1N1) viral infection, as confirmed by qPCR or viral culture.⁶ Blood counts erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were also performed in order to exclude pneumonia of bacterial origin.^{7,8} The chest radiograph or CT images were obtained 3-8 days after the onset of symptoms, and further scans were also used to follow up patients. Patients with influenza like illness but with a negative result on qPCR testing for influenza A (H1N1) were excluded in the study. Chest radiographs were obtained using either digital or computed radiography using the anteroposterior projection with the child lying supine. The CT protocols used for our study and the technical parameters included 5 mm collimation at 10 mm intervals. Images were obtained with both mediastinal and parenchymal window settings. Two

chest radiologists independently reviewed the images and diagnostic conclusions were reached by consensus.

Chest radiography and CT findings were classified as normal, bilateral patchy areas of consolidation, lobar consolidation or diffuse areas of air-space consolidation. The distribution of abnormalities was categorized as focal, multifocal, or diffuse. A focal distribution was defined as a single focus of abnormality. A multifocal distribution was given for more than one focus and sub-classified into unilateral or bilateral. A diffuse distribution was given if the abnormality was bilateral and involved an equivalent volume of one or both lungs.

Results. A total of 81 pediatric patients with acute respiratory disease met the criteria for influenza A (H1N1) with diagnoses confirmed by qPCR. Their ages ranged from 50 days to 13 years (median: 4 years), and the cohort included 56 male and 25 female children. These children had a body temperature peak between 38.5 and 40.5°C (mean: 39.6°C) with tachypnea and cough. Few had diarrhea or sore throat. Pre-existing medical conditions existed in 10 patients including sinusitis (n=5), congenital heart disease (n=3), nephropathy syndrome (n=1), and esophageal hiatus hernia (n=1). Chest imaging findings consisted of bilateral patchy areas of consolidation in 48 (Figure 1), lobar consolidation in 7 (Figure 2), normal in 8, and diffuse areas of air-space consolidation in 18 patients (Figures 3 & 4). All 18 cases in the latter group had elevated levels of lactate dehydrogenase, oxygen saturation levels in room air $\leq 90\%$, low partial pressure of oxygen in arterial blood (PaO_2), ARDS, and required mechanical ventilation. Ten of these patients had pre-existing medical conditions, and 3 had congenital heart disease and subsequently died. Bilateral patchy areas of consolidation became gradually confluent after 48 hours in 10 patients. The abnormalities were observed more frequently in the lower lobes, which were distributed bilaterally in 66, and unilaterally in 7 patients. Eleven patients with mild clinical presentations of influenza-like illness were treated as outpatients, and 70 patients (86.4%) were in need of hospitalization. Patients whose imaging revealed bilateral patchy areas of consolidation were hospitalized for a mean average duration of 10.24 days, those with lobar consolidation for 10.67 days, and those with diffuse areas of air-space consolidation for 19.43 days. The cases with diffuse areas of air-space consolidation were followed-up after 3 months, and interstitial thickening was found on high resolution CT imaging (Figure 5).

Discussion. Influenza virus is an enveloped virus with a ribonucleic acid (RNA) genome, which belongs



Figure 1 - A chest radiograph of a 4-year-old female patient with influenza A obtained 5 days after the onset of symptoms reveals bilateral patchy areas of consolidation in the lower lung zones (arrows).

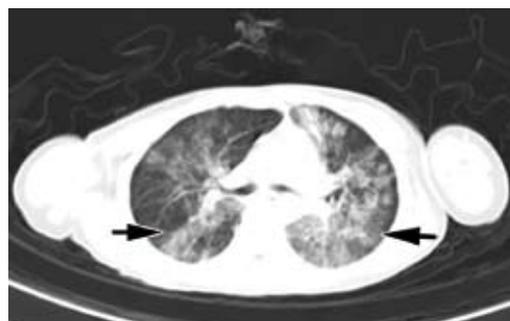


Figure 4 - A 5-year-old female patient with influenza A presented with severe symptoms. A CT scan obtained 5 days after the onset of symptoms shows diffuse consolidation and interstitial thickening throughout both lungs (arrows).



Figure 2 - An 8-year-old male patient with influenza A. This chest radiograph obtained 8 days after the onset of symptoms shows upper lobe consolidation (arrow).

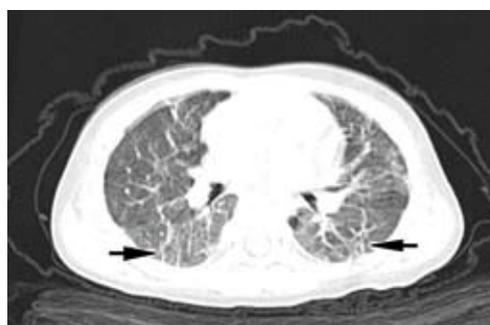


Figure 5 - A 3-year-old male patient with influenza A with interstitial thickening (arrows) shown by high resolution CT imaging.

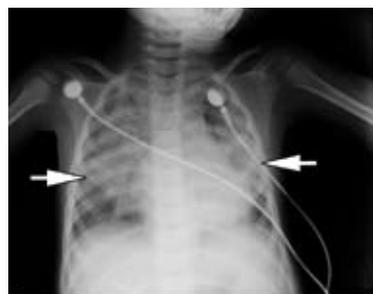


Figure 3 - A 3-year-old male patient with influenza A. The chest radiograph obtained 6 days after the symptom onset shows diffuse consolidation (arrows).

common presenting features. Children under the age of 2 years are at the highest risk for severe complications of novel influenza A (H1N1) infection,⁵ and in the present study, 5 children under the age of 3 years had severe complications, including ARDS and respiratory failure, and 3 patients died. Hematuria and acute necrotizing encephalopathy have also been reported in children with influenza A (H1N1) infection.^{9,10}

In the present study, all 81 patients had cough and fever, and the fever ranged from 38.5-40.5°C (average: 39.6°C), which was higher than in previously reported levels.¹¹ The hospitalization rate of 86.4% in this study was also higher than what was reported,¹¹ which may be correlated with the more serious symptoms of pediatric patients compared with adults. Eighteen patients (22.2%) developed severe respiratory failure that required mechanical ventilation.¹² In our study, the most common radiography findings of bilateral patchy areas of consolidation in the lower lobe were mostly found in the basal area (Figure 1) with a diameter of approximately 2-3 cm. The initial foci may become confluent over 48 hours with patchy areas of peribronchial ground-glass opacities, as was seen in

to the *Orthomyxoviridae* family.² The RNA genome is segmented into 8 different RNA molecules, each with a nucleocapsid protein coat. More often, influenza A (H1N1) is contagious via the respiratory tract. People at any age might be affected, however, children under the age of 5 years, pregnant women, and adults aged 65 years or older are most at risk of severe disease sequelae. The symptoms of influenza A in children may be highly variable. Fever, cough, and tachypnea are the most

10 patients.¹³ When the foci became confluent, the oxygen saturations declined ($\leq 90\%$), and the symptoms worsened with longer hospitalization times compared with those that did not become confluent. The lobar pattern of pneumonia is the least common type seen in influenza A (H1N1), however, in our study, there was no specific pattern and the location of the pneumonia was randomly distributed over the lower, middle, and upper lobes (Figure 2). The average duration of hospitalization was 10.67 days, which was longer than those that had bilateral patchy areas of consolidation, and this result is unlike the findings that have been reported previously.¹⁴ Zhao et al¹³ reported 29 severe H1N1 in a 2009 cases' imaging findings. The foci progression was rapid in the first 3 days, and the radiographic findings was similar to ARDS. In the present study, diffuse areas of air-space consolidation were found in 18 patients (Figure 3). The duration of hospitalization was 19.43 days in children with diffuse air space opacities. The follow-up radiographs of these patients indicated that such abnormalities also took a longer period to disappear. Five of the patients in this type had sinusitis, one had a pre-existing nephropathy syndrome, and one had an esophageal hiatus hernia. It may be the case that pediatric patients with influenza A (H1N1) who have pre-existing medical conditions may develop more severe clinical signs, but this remains to be confirmed by studies with larger sample sizes.

The patterns of anomalies detected by chest radiography in this present study were bilateral and multifocal in 90% of patients with positive findings. The CT also easily identified this feature (Figure 4). Li et al¹⁵ has also a similar report. These abnormalities were observed more frequently in the lower lobes, and were bilaterally distributed in 66, and unilaterally in only 7 patients. On follow-up, interstitial thickening could be seen on high resolution (HR) CT (Figure 5). Interstitial thickening may be caused by interstitial fibrosis, which is similar to reports by Marchiori et al.¹⁶ This bilateral distribution rate was also higher than the previous studies that have identified the patterns of imaging abnormalities in pneumonia caused by bacterium *Legionella* or mycoplasma.^{14,17,18} Thus, bilateral and multifocal distributions were more common in pediatric patients with influenza A (H1N1) infection. The 4 types of imaging findings in this present study (bilateral patchy areas of consolidation, lobar consolidation, diffuse areas of air-space consolidation and normal scans) were similar to the data from the study by Marchiori et al¹⁹ on patients with influenza A (H1N1). Normal radiographic findings in influenza A (H1N1) in children maybe co-exist with mild clinical symptoms, but these cases should still be followed-up, as some will have abnormalities in HRCT.^{19,20}

Our study had more clinically serious influenza A (H1N1) cases. A selection bias might have occurred and this could be one of the limitations of our study.

In conclusion, we analyzed the chest imaging findings in pediatric patients with influenza A (H1N1). The most common imaging finding was bilateral patchy areas of consolidation, followed by diffuse areas of air-space consolidation, normal images and lobar consolidation. Patients who presented with diffuse areas of air-space consolidation developed interstitial thickening on HRCT 3 months after discharge.

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