Radiological findings in 210 paediatric patients with viral pneumonia: a retrospective case study

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Objective: The objective of this study was to assess the radiological presentations of different types of viral pneumonia in children.

Methods: Nasopharyngeal swab specimens and bronchial aspirate samples from children with acute respiratory infections were obtained and tested for influenza B, adenovirus, respiratory syncytial virus and parainfluenza (Types 1, 2 and 3) by direct immunofluorescence assay, or for influenza A (Subtype H1N1) by quantitative real-time polymerase chain reaction. The chest radiographs of the 210 confirmed cases of viral pneumonia were analysed retrospectively by two independent radiologists for the identification, characterisation and description of the distribution of imaging abnormalities. The cases were divided into six groups on the basis of confirmed causative viral agent, and radiographic findings were compared, analysed and presented.

Results: The abnormal chest radiograph findings consisted of bilateral patchy areas of consolidation ($n=133$), interstitial lung disease ($n=33$), diffuse areas of air space consolidation ($n=29$) and lobar consolidation ($n=15$). The abnormalities were distributed bilaterally in 195 cases and observed more frequently in the lower zones than in other regions. The radiological findings varied significantly among the six groups ($p=0.0050$). Pairwise comparison showed significant difference between influenza A (H1N1) and adenovirus ($p=0.0031$) only.

Conclusion: The predominant radiological finding in paediatric viral pneumonia was bilateral patchy areas of consolidation. The radiological findings differed significantly only between adenovirus and influenza A pneumonia. The diagnosis of the specific causative organism requires laboratory confirmation.

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Influenza viruses A and B, adenovirus, respiratory syncytial virus (RSV) and parainfluenza viruses Types 1, 2 and 3 (PIFV-1, PIFV-2, PIFV-3) [1–5] are among the most common viruses that cause pneumonia in children. Imaging examination plays a crucial role in the detection and management of patients with pneumonia [6]. Chest radiograph is usually the first imaging modality prescribed in the assessment of acute respiratory symptoms.

When used in conjunction with clinical presentations and laboratory tests, radiological findings could provide useful information for differential diagnosis, management and response prediction in patients with viral pneumonia. To our knowledge, reports on chest radiological findings in paediatric viral pneumonia are scarce. The aim of the current study was to compare the chest radiographic representations among various types of viral pneumonia, to identify radiographic diagnostic indicators that may predispose to viral pneumonia and to assess whether any particular

abnormal radiographic findings are associated with certain specific viral pathogens.

Methods and materials

Study subjects

This study was approved by the institutional review board of our hospital. The medical charts, radiographs and laboratory findings were retrospectively reviewed for patients under 15 years old hospitalised with acute respiratory illness between December 2009 and June 2010 (2715 cases).

Nasopharyngeal swab specimens were routinely collected within 24 h of admission, and bronchial aspirate samples were obtained after tracheal intubation [7]. Respiratory specimens were tested using direct immunofluorescence assays for influenza B, adenovirus, RSV, PIFV-1, -2 and -3, or using quantitative real-time polymerase chain reaction (Q-PCR) for influenza A (Subtype H1N1) [8–10]. Chest radiographs were performed in all patients. In addition, blood specimens were obtained within 24 h of admission for bacterial cultures; the results were negative within the study population. Other blood tests indicative of pneumonia of bacterial origin, including

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Table 1. Patient characteristics

Parameter	Influenza A (H1N1)	RSV	Influenza B	Adenoviruses	PIFV-1	PIFV-3	Total
Male	56	20	9	18	11	18	132
Female	25	18	9	9	7	10	78
Median age (years)	4	0.17	1	3	2	0.75	2.1
MV	18	3		0	3	4	29
No. of deaths	3	0		0	0	0	3
Total	81	38	18	27	18	28	210

MV, mechanical ventilation; PIFV, parainfluenza virus; RSV, respiratory syncytial virus.

erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) [3, 11], were also performed.

Case identification and data collection

Viral pneumonia was defined as acute respiratory disease with abnormality on a chest radiograph and positive laboratory tests with one of the aforementioned viruses [12]. This resulted in a study population of 210 paediatric patients (132 male, 78 female; median age 2.1 years, range 10 days to 13 years). The cases identified were divided into six groups based on the causative agent: influenza A, influenza B, adenovirus, RSV, PIFV-1 and PIFV-3. PIFV-2 was not identified in any subject.

Demographic data, clinical presentation upon admission or referral, laboratory tests, prior history and radiography were collected for each case when available. Decisions on prescription of tests, radiograph and confirmatory cultures, were made at the discretion of the attending physicians.

Radiography

The chest radiographs were taken using either digital or computed radiography, via an anteroposterior projection with the child lying. The symptoms typically occurred at 3–8 days before the chest radiographs.

Two radiologists unaware of the laboratory findings reviewed the images independently and reached a diagnostic conclusion by consensus. Chest radiograph findings were classified as interstitial lung disease (reticulation, linear or peribronchial interstitial shadowing), bilateral patchy areas of consolidation, lobar consolidation, or diffuse areas of air space consolidation. The distribution of abnormalities was categorised as focal, multifocal or diffuse. A focal distribution was defined as a single focus of abnormality. If there were two or more foci, the distribution of abnormality was considered multifocal and subclassified as either unilateral or bilateral. A diffuse distribution was defined as bilateral abnormality that involves an equivalent volume of the two lungs. The location of the lesions was recorded as upper (above the anterior end of the second rib), middle (between the second and fourth anterior ribs) or lower (below the anterior end of the fourth rib) zone [13].

Statistical analysis

Data are presented as number (*n*) and percentage. Univariate comparisons were made using the χ^2 test or

Fisher's exact test, depending on statistical distributions, with Statistical Analysis Software (SAS)[®] v. 8.1 (SAS Institute Inc., Cary, NC). Probability values of $p < 0.05$ were considered statistically significant.

Results

The most common cause of viral pneumonia was influenza A infection (81 out of a total of 210 patients). The infecting viruses in the remaining 129 patients (Table 1) were RSV ($n=38$), PIFV-3 ($n=28$), adenovirus ($n=27$), influenza B ($n=18$) and PIFV-1 ($n=18$).

Findings on the chest radiographs included bilateral patchy areas of consolidation (Figure 1) in 133 patients, interstitial lung disease (Figure 2) in 33 patients, diffuse areas of air space consolidation (Figure 3) in 29 patients and lobar consolidation (Figure 4) in 15 patients. Repeat radiographs after 48 h showed that bilateral patchy areas of consolidation became confluent in 33 patients. Mechanical ventilation was required in 29 patients with diffuse areas of consolidation. Three patients infected with influenza A (H1N1) eventually died; all three had pre-existing congenital heart disease.

Lower lobes were the most common site for abnormal radiographic abnormalities. Lesions were bilateral in 195 patients and unilateral in the remaining 15 cases. The χ^2 test revealed an overall difference in the radiographic findings among the six groups based on the causative agents

Figure 1. An example of bilateral patchy areas of consolidation in the lower lung zones and the right upper zone (arrows) a chest radiograph taken 5 days after the onset of symptoms in a 4-year-old male with influenza A. ap, anteroposterior; R, right.

Figure 2. An example of peribronchial interstitial shadowing in the lower lung zones (arrows) on a chest radiograph obtained 6 days after the onset of symptoms in an 8-year-old male with adenovirus. R, right.

($p=0.0050$; Table 2). Pairwise comparison showed a significant difference only between the groups of influenza A (H1N1) and adenovirus pneumonia ($p=0.0031$).

Bilateral patchy areas of consolidation were detected in 59% (48/81) of the patients with influenza A and 66% (18/27) of the patients infected with adenovirus (Table 3). There were no significant differences in either the prevalence or distribution of bilateral patchy areas of consolidation between adenovirus and influenza A pneumonia (χ^2 test, $p=0.5846$). Diffuse areas of air space consolidation were seen most commonly in patients with influenza A (22%), and were not identified in any patients with adenovirus pneumonia (Fisher's exact test, $p=0.0056$). Interstitial lung disease was seen more commonly in adenovirus than in influenza A pneumonia (30% vs 10%; χ^2 test, $p=0.0244$). Lobar consolidation was detected in seven patients with influenza A (9%) and one

Figure 3. Example of diffuse consolidation (arrows) on a chest radiograph obtained 4 days after the onset of symptoms in a 42-day-old male with influenza A. R, right.

Figure 4. An example of right middle lobe consolidation (arrow) on a chest radiograph obtained 4 days after the onset of symptoms in a 5-year-old female with influenza B. ap, anteroposterior; R, right.

patient with adenovirus (4%), but the difference was not statistically different (Fisher's exact test, $p=0.6764$).

Discussion

Viruses are common pathogens associated with respiratory symptoms in children [7, 8]. Morbidity associated with viral pneumonia is particularly high in children [8]. Distinguishing viral from bacterial pneumonia is helpful in initiating appropriate care (using antiviral vs antibacterial agents) in a timely fashion. In this regard, imaging examination can provide useful information to supplement laboratory findings [6].

The current study included seven major respiratory viruses: influenza A, influenza B, adenovirus, RSV, PIFV-1, PIFV-2 and PIFV-3. Pneumonia accounts for 14–47% of the lower respiratory tract infections caused by these agents [7, 14]. Radiographic findings of pneumonia have traditionally been classified into lobar pneumonia, bronchopneumonia and interstitial pneumonia [9]. Lobar pneumonia is most commonly caused by *Streptococcus pneumoniae* and *Klebsiella pneumoniae*. Common causes of bronchopneumonia include *Staphylococcus aureus*, Gram-negative bacteria, *Mycoplasma pneumoniae* and fungi. Interstitial pneumonia is mostly caused by viruses [9]. In addition to pneumonia, lower respiratory tract viral infection may occur in the forms of tracheobronchitis and bronchiolitis; radiographic features of these conditions include increased/blurbed bilateral lung markings and double contour [7, 9].

Kim et al [15] reported that the radiological findings of viral pneumonia are highly variable in adults, and could include poorly defined nodules, patchy areas of peribronchial ground-glass opacity and air space consolidation. CT findings, which were also overlapping, consisted of poorly defined centrilobular nodules, ground-glass attenuation with a lobular distribution, segmental consolidation and diffuse ground-glass attenuation with

Table 2. Radiological findings in viral pneumonia

Radiological findings	Influenza A (H1N1)	RSV	Influenza B	Adenoviruses	PIFV-1	PIFV-3	Total
Interstitial lung disease	8	3	7	8	1	6	33
Bilateral patchy consolidation	48	31	7	18	13	16	133
Lobar consolidation	7	1	3	1	1	2	15
Diffuse air space consolidation	18	3	1	—	3	4	29
Total	81	38	18	27	18	28	210

PIFV, parainfluenza viruses; RSV, respiratory syncytial virus.

χ^2 test revealed an overall difference in the radiographic findings among the six groups ($p=0.0050$). Pairwise comparison showed a significant difference only between the groups of influenza A (H1N1) and adenovirus pneumonia ($p=0.0031$).

thickened interlobular septa. The varying radiological findings reflect different underlying histopathological features: diffuse alveolar damage (intra-alveolar oedema, fibrin, and variable cellular infiltrates with a hyaline membrane), intra-alveolar haemorrhage, and interstitial (intrapulmonary or airway) inflammatory cell infiltration. Clinical features (*e.g.* patient age, immune status, time of year, illness in other family members, community outbreaks, symptom onset/severity/duration and the presence of a rash) remain important aids in diagnosing viral causes of both atypical pneumonia and pneumonia in immunocompromised patients. In our study, the predominant radiographic finding was bilateral patchy areas of lung consolidation (typically 2–3 cm in diameter), mainly affecting the basal area of the lower zones (Figure 1). Some of these areas appear as patchy areas of peribronchial ground-glass opacity. Similar to a report by Perez-Padilla et al [16], such areas became confluent after 48 h in some patients in our study. When the foci become confluent, oxygen saturation of the patient usually declines ($\leq 90\%$) and symptoms worsen compared with those patients with no confluent imaging manifestations.

Lobar pneumonia can be caused by viruses represented by RSV [17]. This pattern was the least common imaging observation in the present study. Don et al [11] reported 21 cases of paediatric viral pneumonia and found that the appearance of interstitial lung disease was more common in children aged over 5 years than in those aged under 5 years. As in a report by Fraser et al [9], 33 patients (median age 2.1 years) in the current study showed interstitial pneumonia on their chest radiographs.

Diffuse areas of air space consolidation were found in 29 patients, 18 of whom were infected with influenza A. All the patients with diffuse areas of air space consolidation developed acute respiratory distress syndrome (ARDS; elevated lactate dehydrogenase levels, low PaO_2 , and $\leq 90\%$ oxygen saturation), and required mechanical ventilation [10, 13]. Davis et al [18] reported that pneumonia is the most frequent cause of paediatric ARDS cases. Of the 18 patients with diffuse areas of air space consolidation and positive influenza A, the

duration of hospitalisation was longer in those with diffuse air space opacities than in those with the other types of radiological abnormalities. The follow-up imaging also indicated that this abnormality took longer to dissipate from the radiographs.

Common radiographic features in viral pneumonia include bilateral patchy consolidation [19], lobar consolidation, diffuse areas of air space consolidation or interstitial lung disease [15]. In the current study, we noticed a statistically significant rate of interstitial lung disease and diffuse air space consolidation between pneumonia patients infected with influenza A and those infected with adenovirus. The findings of bilateral patchy areas of consolidation and lobar consolidation were not significantly different between adenovirus and influenza A infection, although interstitial pneumonia was more common in patients infected with adenovirus than in those infected with influenza A. Diffuse areas of air space consolidation were noted in 18 out of 81 cases of influenza A infection, but in none of the 27 patients in the adenovirus group.

Consistent with a previous study by Donnelly [19], 92% of the cases in this study had bilateral or multifocal radiographic abnormality, typically in the lower lobes. The frequency of bilateral distribution (195 out of a total of 210 cases) is higher than that seen with pneumonia caused by bacteria, *Legionella* or *Mycoplasma* [20–22]. Identification of the specific organism causing pneumonia cannot be made on the basis of radiological findings without laboratory testing [15]. However, the features on the chest radiograph, when used in combination with laboratory testing and clinical presentation/history, could provide useful information on distinguishing viral from bacterial pneumonia in children.

The current study was carried out in the months when influenza A (H1N1) was endemic. Accordingly, overrepresentation of influenza A (H1N1) is a limitation. Also, some community-acquired paediatric pneumonias may be indicative of both viral and bacterial infections [23, 24]. Blood bacteria culture was negative in our study, but false negativity should be considered.

Table 3. Radiological findings of viral pneumonia: influenza A (H1N1) vs adenovirus

Radiological finding	Influenza A (H1N1)	Adenoviruses	<i>p</i> -value
Interstitial lung disease	8 (10%)	8 (30%)	0.0244 <0.05 ^a
Bilateral patchy consolidation	48 (59%)	18 (66%)	0.5846 >0.05 ^a
Lobar consolidation	7 (9%)	1 (4%)	0.6764 >0.05 ^b
Diffuse air space consolidation	18 (22%)	— (0%)	0.0056 <0.05 ^b

^a χ^2 test.

^bFisher's exact test.

In conclusion, radiographic findings in childhood viral pneumonia include bilateral patchy areas of consolidation, diffuse areas of air space consolidation, lobar consolidation and interstitial disease. The rate of interstitial lung disease and diffuse air space consolidation differed significantly between patients infected with adenovirus and influenza A.

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