Differentiation between Mycoplasma and viral community-acquired pneumonia in children with lobe or multi foci infiltration

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Differentiation between Mycoplasma and viral community-acquired pneumonia in children with lobe or multi foci infiltration

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Objectives: The aim of this paper seeks to analyze the clinical features, inflammatory markers, and radiographs of community-acquired pneumonia (CAP) cases with lobe or multi foci infiltration; with a special focus on factors which allow the differential diagnosis of viral and mycoplasma pneumonia.

Setting: This is a retrospective chart review of CAP cases in a large University teaching hospital.

Participants: 126 pediatric CAP cases, with lobe or multi foci infiltration, presenting between May 2012 and April 2013. Demographic data, clinical presentation upon admission or referral, laboratory tests, prior history, and radiography were collected for each case if available.

Primary and secondary outcome measures: We used univariate and multivariate
logistic regression to determine the significant factors which allow the differential diagnosis of viral and mycoplasma CAP with lobe or multi foci infiltration.

**Results:** Overall, there were 71 (56%) male and 55 (44%) female CAP cases with lobar or multi foci infiltration. Seventy pneumonia cases were caused by mycoplasma pneumoniae and eighteen by viruses. Univariate analysis of the mycoplasma and viral causes of the CAP revealed that increased respiratory rate, wheeze, male gender, and lymphocyte percentage were the factors associated with the differentiation of mycoplasma and viral etiologies of pneumonia (P<0.05). A stepwise logistic regression analysis was performed to assess independent factors which allow the differential diagnosis of viral and mycoplasma pneumonia. Increased respiratory rate, wheeze, and lymphocyte percentage were reliable independent factors which allow the differential diagnosis of viral and mycoplasma CAP with lobar or multi foci infiltration.

**Conclusions:** Whether the CAP with lobar or multi foci infiltration was caused by Mycoplasma species or viruses could not be inferred from the radiological patterns. Wheeze, lymphocyte percentage, and respiratory rate were independent factors which allowed the differential diagnosis of viral and mycoplasma CAP with lobar or multi foci infiltration.

**Keywords:** Community-acquired pneumonia; Children; lobar; multi foci; etiology

**Strengths and limitations of this study**
Over a period of 1 year, a retrospective study was carried out in our hospital. A stepwise logistic regression analysis of 88 cases was performed to assess independent predictors which allowed the differential diagnosis of viral and mycoplasma caused CAP. Increased respiratory rate, wheeze and lymphocyte percentage were significantly predictive regarding the differentiation between viral and mycoplasma caused CAP with lobar or multi foci infiltration, as was viral aetiology of CAP with lobar or multi foci infiltration, increase respiratory rate, wheeze and increase lymphocyte percentage.

This study has several limitations. Firstly, it was a retrospective study, and therefore there may have been some selection bias. Secondly, there may be some cases in which the patient had a viral as well as bacterial or a combined bacterial and mycoplasma infection which cannot be detected. Therefore, prospective further, preferably prospective studies on CAP with lobar or multi foci infiltration are needed.

Introduction

For the pediatric population, community-acquired pneumonia (CAP) is among the most frequent causes of hospital admission. CAP remains a major cause of morbidity and mortality worldwide, especially regarding children less than 5 years of age. Most children with CAP live in the developing countries [1]. Viruses and Mycoplasma species are to main of the many pathogenic agents which can cause CAP [2, 3, 4].

The symptoms of Community-acquired pneumonia are varying considerably, depending on their aetiology, its infection pattern, and the underlying medical
conditions. In clinical practice, most of the CAP diagnoses are based on radiography and clinical symptoms. There are some report cases in which the etiologies of CAPs were established on the bases clinical signs, radiological findings, or non-specific inflammatory serum markers [5, 6, 7]. In radiography, Most of CAP cases are diagnosed as bronchopneumonia. However, lobe or multi foci infiltration is the other two important kinds of CAP in clinical.

Both viruses as well as Mycoplasma species can lead to lobe or multi foci infiltration in CAP. The therapy strategy for CAP cases is as controversial as it is crucial. The use of antibiotics before the etiology is found out is debated. On the other hand, to establish the cause of CAP cases needs time. Hence, tests must be devised which allow an early differentiation between viral and mycoplasma pneumonia. Unfortunately, studies focusing on CAP with lobe or multi foci infiltration are yet to be carried out.

Therefore, from May, 2012 to May, 2013, over a period of 1 year, a retrospective study was carried out in our hospital to examine the clinical features, inflammatory markers (C-Reactive Protein, white blood cell counting, and lymphocyte percentage), and radiographs of CAP cases with lobe or multi foci infiltration; with a special focus on factors which would allow the differential diagnosis of viral and mycoplasma pneumonia.

Materials and Methods

Study Subjects

This study was approved by the Institutional Review Board of our Hospital.
Informed consent was enrolled and written by the parents of all children. During a surveillance period of 12 months (from May, 2012 to April, 2013), 126 consecutive, previously healthy children with radiologically confirmed lobar or multi foci infiltration of the lung were treated at our Hospital.

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

The respiratory rates of the 126 patients were measured: they were age-related; The respiratory rate was less than 45 per minute in children younger than 28 days old, less than 40 per minute in children between 29 days and 1 year old, less than 30 per minute in children between 1 and 3 years old, less than 25 per minute in children between 4 and 7 years old, and less than 20 per minute in children older than 8 years.

Nasopharyngeal swab specimens were routinely collected within 24 hours of admission, and bronchial-aspirate samples were obtained after tracheal intubation. Respiratory specimens were tested for influenza A and B, adenovirus, respiratory syncytial virus (RSV), bokavirus, human metapneumovirus (hMPV), and parainfluenza virus (PIFV) 1, 2, and 3; using direct immunofluorescence assays. Viral pneumonia was defined as acute respiratory disease with abnormal chest radiograph findings and positive laboratory tests for one of the aforementioned viruses. In addition, blood specimens were obtained within 24 hours of admission for bacterial cultures. Other blood tests, including for C-reactive protein (CRP), white blood cells,
and lymphocyte percentages and neutrophil percentages, were also performed.

The diagnosis of Mycoplasma pneumonia was based on the results from real-time PCR targeting the P1 cytoadhesion type 1 and 2 genes of the Mycoplasma pneumoniae genome, using DNA extracted from nasopharyngeal-swab specimens. Mycoplasma pneumonia was defined as acute respiratory disease with abnormal chest radiograph findings and positive laboratory tests combined by real-time PCR. Patients with simultaneous viral and mycoplasma infections were excluded from this study.

**Radiography**

The symptoms typically occurred at 4-7 days before the chest radiographs, via an anteroposterior projection with the child lying. Images was independently reviewed by two radiologist, when there has different opinion, they reached a diagnostic conclusion by consensus. Chest radiograph findings were classified as lobar(unilateral or bilateral) or multi foci infiltration. The distribution of abnormalities was categorized as focal, multi foci. A lobar distribution was defined as a single lobar of abnormality. If there were two or more foci, the distribution of abnormality was considered multi foci[3].

**Statistical Analysis**

Data are presented as number (n) and percentage. Univariate comparisons were made using nonparametric one-way Wilcoxon rank sum, chi-squared (χ2), or Fisher’s exact tests; depending on the statistical distribution. To evaluate the ability to differentiate between mycoplasma and viral CAP cases with lobar or multi foci infiltration, a stepwise logistic regression analysis was performed with the statistical
analysis software (SAS) 8. Probability values of $P$ less than 0.05 were considered statistically significant.

**Results**

Overall, there were 71 (56%) male and 55 (44%) female CAP cases with lobar or multi foci infiltration. The median age of the 126 patients was 4 years (range, 1 day to 14 years). The presenting signs and symptoms were cough (97.6%), fever (47.6%), increase of respiratory rate (55.6%), and wheeze (14.3%). Fever and increase of respiratory rate are more common in the “over 5-year” group; however, wheeze is more common in “under 23-month” group (see Table 1).

Findings in chest radiograph included lobar consolidation (see Figure 1) in 54 patients (multiple), unilateral consolidation (see Figure 2) in 26 patients, and bilateral consolidation (see Figure 3) in 46 patients. Seven patients had pleural effusions. An analysis of the correlation between aetiology and radiography findings showed that there were no significant differences between them ($P>0.05$) (Table 2).

Seventy of the CAP cases were caused by Mycoplasma species and 18 by viruses, including influenza A ($n=2$), influenza B ($n=1$), adenovirus ($n=2$), RSV ($n=9$), bokavirus ($n=2$), and PIFV 3 ($n=2$). Univariate analysis revealed that the factors which allowed the differential diagnosis of viral and mycoplasma CAP were increased respiratory rate, wheeze, male, and lymphocyte percentage ($P<0.05$). There were no significant differences in age, radiological findings, fever, cough, CRP, and WBC ($P>0.05$) (see Table 3).

A stepwise logistic regression analysis of 88 cases was performed to assess
independent predictors which allowed the differential diagnosis of viral and mycoplasma caused CAP. Increased respiratory rate, wheeze and lymphocyte percentage were significantly predictive regarding the differentiation between viral and mycoplasma caused CAP with lobar or multi foci infiltration (see Table 4), as was viral aetiology of CAP with lobar or multi foci infiltration, increase respiratory rate, wheeze and increase lymphocyte percentage. The logistic regression model was consistent with the findings reported by Hosmer and Lemeshow who used the goodness-of-fit test (P=0.8979).

Discussion

In this study, 126 CAP cases with lobar or multi foci infiltration were observed over a period of 1 year. About 19.8% of the CAP cases were caused by mycoplasma species or virus. The etiology of 38 cases could not be detected, partly because the positive of bacterial pathogens in blood culture is very low. Our results are very similar to those of Zhang et al. who reported 707 severe CAP cases; blood cultures were positive in only 5, i.e., 0.7% [2]. This means that new methods with higher sensitivities for bacterial pathogens in blood must be devised which can be routinely used in all laboratories (which is currently not the case) [8]. On the other hand, 55.6% of our patients had tachypnoea and 47.6% had fever, and these symptoms were more common in the “over 5-year” group. The CRP is higher in the “over 5-year” group than in the other two groups; maybe more infiltration foci can be found in the over 5-year” group. Our results are similar to two other studies [9,10]. However wheeze is
more common in the “below 23-month” group; this finding is different from that of a recent study [11], partly because the sample we focus on pneumoniae with lobar or multi foci infiltration.

In clinical practice, the radiographic detection of infiltrations is currently the gold standard for the diagnosis of CAP. Most CAP cases are defined as bronchial pneumonia in radiograph. However, lobe or multi foci infiltrations are the other two radiological manifestations of CAP [3,11]. Some authors reported that in clinical practice lobar infiltrations are often caused by bacteria [6]. However, in this study, 69.8% of the CAP case was caused by viruses and Mycoplasma species: especially, mycoplasma associated with etiological findings, it account 55.6% in this group. This finding is consistent with some previous studies [3,12]. In our study, there were 41 CAP cases with bilateral infiltrations and 61 CAP cases with multi foci. When analysis on distribution and the number of focus. There is no significant difference associating with etiological findings. Even some of cases with pleural effusion, there is no significant difference associating with etiological findings. This means that whether the CAP with lobar or multi foci infiltration was caused by Mycoplasma species or viruses could not be inferred from the radiological patterns In a recent study about pediatric CAP, Korppi et al. analyzed the clinical or radiological characteristics of 101 CAP cases, and they concluded that radiographs are not helpful when it comes to differentiating between viral, pneumococcal, and atypical bacterial aetiology of CAP in children [11]. This conclusion coincides with our results: Radiological pattern did not allow a reliable differentiation between mycoplasma and
To investigate potential factors that may allow differentiating between viral and mycoplasma CAP is very important for clinical practice. In this study, our aim was to describe the utility of some laboratory markers and clinical features regarding the differentiation between mycoplasma and viral CAP with lobar or multi foci infiltrations. Univariate analysis showed that findings such wheeze, lymphocyte percentage, respiratory rate, and sex can help to differentiate between mycoplasma and viral CAP with lobar or multi foci infiltration. Furthermore, multiple logistic regression showed that wheeze, increase of lymphocyte percentage, and increase of respiratory rate are independent factors which allow to differentiate between mycoplasma and viral CAP with lobar or multi focus infiltration. This means that among mycoplasma and viral CAP with lobar or multi foci infiltration, wheeze, increase of lymphocyte percentage, and increase of respiratory rate can help to diagnose viral pneumonia.

Hatipoğlu et al. [13] reported 147 viral CAP cases, and they found that the prominent symptoms of the patients were cough (88.9%) and wheeze (72.2%). This is similar to our results. In another report [11], 101 CAP cases were analyzed. Although the report lacked data on respiratory rate in 20 cases, it included supplementary sensitivity analyses by adding the cases with missing data as non-tachypnoea cases in the analyses. Moreover, the report concluded that tachypnoea is not associated with the aetiology of CAP. The above study is different from our findings. The reason may be that we used multiple factor analysis and selected mycoplasma and viral CAP with
lobar or multi foci infiltration as our object of study. We believe that our will have a significant impact on the efforts to find new treatment strategies for this type of CAP.

Youn et al. [9] reported 95 Mycoplasma pneumoniae cases with segmental or lobar infiltrations. They found that the lymphocyte percentage was at a normal level. Defilippi et al. [10] reported 102 CAP cases with a positive PCR for Mycoplasma pneumoniae: they found that the lymphocyte percentage (median) is at normal level, a result similar to ours. Hatipoğlu et al. [13] reported 147 cases with pneumonia, the percentage of polymorphonuclear leukocytes the viral pneumonia cases was lower than patients Virus not isolated, it suggests that Lymphocyte percentage may be higher in pneumonian in acute phase of pneumonia. The above-mentioned literature suggests that viral pneumonia often presents a higher percentage of lymphocyte. This conclusion is similar to our results.

This study has several limitations. Firstly, it was a retrospective study, and therefore there may have been some selection bias. Secondly, there may be some cases in which the patient had a viral as well as bacterial or a combined bacterial and mycoplasma infection which cannot be detected. Therefore, prospective further, preferably prospective studies on CAP with lobar or multi foci infiltration are needed.

In conclusion, more than half of the CAP cases with lobar or multi foci infiltration are caused by Mycoplasma species or viruses. Whether the CAP with lobar or multi foci infiltration was caused by Mycoplasma species or viruses could not be inferred from the radiological patterns. We found that wheeze, lymphocyte percentage, and respiratory rates were independent factors which allow the differential diagnosis of
viral and mycoplasma caused CAP with lobar or multi foci infiltration.

Reference:


Figure Legends

Figure 1. An example of right middle lobe consolidation from a chest radiograph obtained 6 days after the onset of symptoms in a 5-month-old girl with influenza B.

Figure 2. An example of right upper and middle lobe consolidation from a chest radiograph obtained 5 days after the onset of symptoms in a 2-year-old girl with MB.

Figure 3. An example of bilateral consolidation in the left upper zone, the right upper zone and middle zone from a chest radiograph taken 4 days after the onset of symptoms in a 16-month-old girl with influenza A.
Table 1. Clinical signs and symptoms in 126 children with community-acquired pneumonia, in relation to the age

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>0–23 months</th>
<th>2–4 years</th>
<th>≥5 years</th>
<th>p-value</th>
<th>total</th>
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<tr>
<td>sex(M)</td>
<td>24</td>
<td>16</td>
<td>31</td>
<td>0.0364</td>
<td>71</td>
</tr>
<tr>
<td>Fever &gt;37.5°C</td>
<td>7</td>
<td>22</td>
<td>31</td>
<td>0.0011</td>
<td>60</td>
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<tr>
<td>wheeze</td>
<td>13</td>
<td>2</td>
<td>3</td>
<td>&lt;0.0001</td>
<td>18</td>
</tr>
<tr>
<td>Increase respiratory rate</td>
<td>12</td>
<td>17</td>
<td>41</td>
<td>0.0001</td>
<td>70</td>
</tr>
<tr>
<td>cough</td>
<td>32</td>
<td>38</td>
<td>53</td>
<td>0.2131</td>
<td>123</td>
</tr>
<tr>
<td>CRP(&gt;8)</td>
<td>10</td>
<td>27</td>
<td>39</td>
<td>&lt;0.0001</td>
<td>76</td>
</tr>
<tr>
<td>Unilateral consolidation(s)</td>
<td>11</td>
<td>18</td>
<td>25</td>
<td>0.9524</td>
<td>54</td>
</tr>
<tr>
<td>Unilateral consolidation(m)</td>
<td>5</td>
<td>8</td>
<td>13</td>
<td>0.9524</td>
<td>26</td>
</tr>
<tr>
<td>Bilateral consolidation</td>
<td>18</td>
<td>13</td>
<td>15</td>
<td>0.0587</td>
<td>46</td>
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<tr>
<td>Pleural fluid</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>0.8847</td>
<td>7</td>
</tr>
<tr>
<td>total</td>
<td>34</td>
<td>39</td>
<td>53</td>
<td>-</td>
<td>126</td>
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Table 2. Radiological findings in children with large consolidation of CAP

<table>
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<tr>
<th>Radiological findings</th>
<th>M</th>
<th>V</th>
<th>unknown</th>
<th>P-value</th>
<th>Total patients</th>
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<tr>
<td>Bilateral consolidation</td>
<td>27</td>
<td>8</td>
<td>11</td>
<td>0.5192</td>
<td>46</td>
</tr>
<tr>
<td>Unilateral consolidation(s)</td>
<td>28</td>
<td>7</td>
<td>19</td>
<td>0.8864</td>
<td>54</td>
</tr>
<tr>
<td>Unilateral consolidation(m)</td>
<td>15</td>
<td>3</td>
<td>8</td>
<td>0.8864</td>
<td>26</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1.0000</td>
<td>7</td>
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M= mycoplasma               V= viral
Table 3. Clinical signs in relation to the aetiology of pneumonia, viral aetiology Vs mycoplasma

<table>
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<th>findings</th>
<th>M (70)</th>
<th>V (18)</th>
<th>P value</th>
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<tr>
<td>Fever &gt;37.5°C</td>
<td>42</td>
<td>7</td>
<td>0.1078</td>
</tr>
<tr>
<td>Increase respiratory rate</td>
<td>29</td>
<td>14</td>
<td>0.0053</td>
</tr>
<tr>
<td>CRP(&gt;8)</td>
<td>44</td>
<td>9</td>
<td>0.2231</td>
</tr>
<tr>
<td>WBC(increase)</td>
<td>17</td>
<td>6</td>
<td>0.4359</td>
</tr>
<tr>
<td>Increase lymphocyte percentage</td>
<td>10</td>
<td></td>
<td>0.0184</td>
</tr>
<tr>
<td>Increase polymorphonuclears</td>
<td>19</td>
<td>4</td>
<td>0.6717</td>
</tr>
<tr>
<td>Cough</td>
<td>69</td>
<td>16</td>
<td>0.1050</td>
</tr>
<tr>
<td>Wheeze</td>
<td>3</td>
<td>8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Radiograph</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral consolidation(multipe)</td>
<td>15</td>
<td>3</td>
<td>0.7690</td>
</tr>
<tr>
<td>Bilateral consolidation</td>
<td>27</td>
<td>8</td>
<td>0.6498</td>
</tr>
<tr>
<td>Sex(M)</td>
<td>29</td>
<td>13</td>
<td>0.0197</td>
</tr>
<tr>
<td>Age (&gt;5 years)</td>
<td>32</td>
<td>6</td>
<td>0.3442</td>
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</table>

M= mycoplasma V= viral

Table 4. Stepwise logistic regression model for significant predictors of viral aetiology of CAP showing lobar or multi foci infiltration

<table>
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<tr>
<th>variable</th>
<th>Chi-Square</th>
<th>OR</th>
<th>95% Wald Confidence Limits</th>
<th>P value</th>
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<td>Wheeze</td>
<td>23.0077</td>
<td>0.063</td>
<td>0.010-0.271</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Increase lymphocyte percentage</td>
<td>8.9954</td>
<td>0.053</td>
<td>0.012-0.337</td>
<td>0.0027</td>
</tr>
<tr>
<td>Increase respiratory rate</td>
<td>6.7243</td>
<td>0.093</td>
<td>0.013-0.653</td>
<td>0.0095</td>
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Hosmer and Lemeshow Goodness-of-Fit Test (p=0.8979)
Figure 1. An example of right middle lobe infiltration from a chest radiograph obtained 6 days after the onset of symptoms in a 5-month-old girl with influenza B.
Figure 2. An example of right upper and middle lobe infiltration from a chest radiograph obtained 5 days after the onset of symptoms in a 2-year-old girl with mycoplasma pneumonia.

87x91mm (300 x 300 DPI)
Figure 3. An example of bilateral infiltration in the left upper zone, the right upper zone and middle zone from a chest radiograph taken 4 days after the onset of symptoms in a 16-month-old girl with influenza A. 53x33mm (300 x 300 DPI)
Institutional Review Board of the children’s hospital affiliated to Soochow university.

We would like to confirm that the article entitled “Differentiation of Mycoplasma and viral community-acquired pneumonia in children showing lobe or multi foci infiltration” can be done by Dr. Chuang-li Hao in our hospital. There are no any ethical/legal conflicts involved in the article. Informed consent was enrolled and written by the parents of all children. All experiments were carried out in strict accordance with the institution guidelines regarding the acquisition and experimental use of human tissues. This study was approved by the Institutional Review Board of children’s hospital affiliated to Soochow university.

Chairman of the committee Prof. Zu-yuan Lu

Signature: Zu-yuan Lu

2014-7-25

ethical statement

677x903mm (72 x 72 DPI)
Differentiation between Mycoplasm and viral community-acquired pneumonia in children with lobe or multi foci infiltration: a retrospective case study

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                          | Zhu, Li-yuan; the Children's Hospital Affiliated to Soochow University, Respiratory department  
                          | Hao, Chuang-li; the Children's Hospital Affiliated to Soochow University, Respiratory department |
| Primary Subject Heading: | Paediatrics               |
| Secondary Subject Heading: | Infectious diseases, Paediatrics, Radiology and imaging |
| Keywords:       | Paediatric radiology < PAEDIATRICS, Paediatric thoracic medicine < PAEDIATRICS, Paediatric infectious disease & immunisation < PAEDIATRICS |
Differentiation between Mycoplasma and viral community-acquired pneumonia in children with lobe or multi foci infiltration: a retrospective case study

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Objectives: The aim of this paper seeks to analyze the clinical features, inflammatory markers, and radiographs of community-acquired pneumonia (CAP) cases with lobe or multi foci infiltration; with a special focus on factors which allow the differential diagnosis of viral and mycoplasma pneumonia.

Setting: This is a retrospective chart review of CAP cases in a large University teaching hospital.

Participants: 126 pediatric CAP cases, with lobe or multi foci infiltration, presenting between May 2012 and April 2013. Demographic data, clinical presentation upon admission or referral, laboratory tests, prior history, and radiography were collected for each case if available.

Primary and secondary outcome measures: We used univariate and multivariate
logistic regression to determine the significant factors which allow the differential
diagnosis of *viral* and *mycoplasma* CAP with lobe or multi foci infiltration.

**Results:** Overall, there were 71 (56%) male and 55 (44%) female CAP cases with
lobar or multi foci infiltration. Seventy pneumonia cases were caused by *mycoplasma
pneumoniae* and eighteen by viruses. Univariate analysis of the *mycoplasma* and *viral*
causes of the CAP revealed that increased respiratory rate, wheeze, male gender, and
lymphocyte percentage were the factors associated with the differentiation of
*mycoplasma* and *viral* etiologies of pneumonia (P<0.05). A stepwise logistic
regression analysis was performed to assess independent factors which allow the
differential diagnosis of *viral* and *mycoplasma pneumonia*. Increased respiratory rate,
wheeze, and lymphocyte percentage were reliable independent factors which allow
the differential diagnosis of *viral* and *mycoplasma* CAP with lobar or multi foci
infiltration.

**Conclusions:** Whether the CAP with lobar or multi foci infiltration was caused by
*mycoplasma* species or *viruses* could not be inferred from the radiological patterns.
Wheeze, lymphocyte percentage, and respiratory rate were independent factors which
allowed the differential diagnosis of *viral* and *mycoplasma* CAP with lobar or multi
foci infiltration.

**Keywords:** Community-acquired pneumonia; Children; lobar; multi foci; etiology

**Strengths and limitations of this study**
Over a period of 1 year, a retrospective study was carried out in our hospital. A stepwise logistic regression analysis of 88 cases was performed to assess independent predictors which allowed the differential diagnosis of viral and mycoplasma caused CAP. Increased respiratory rate, wheeze and lymphocyte percentage were significantly predictive regarding the differentiation between viral and mycoplasma caused CAP with lobar or multi foci infiltration, as was viral aetiology of CAP with lobar or multi foci infiltration, increase respiratory rate, wheeze and increase lymphocyte percentage.

This study has several limitations. Firstly, it was a retrospective study, and therefore there may have been some selection bias. Secondly, viral pneumonia could be missed due to the sensitivity of immunofluorescence and the limit number of virus we detected. Thirdly, there may be some cases in which the patient had a viral as well as bacterial or a combined bacterial and mycoplasma infection which cannot be detected. Therefore, prospective further, preferably prospective studies on CAP with lobar or multi foci infiltration are needed.

Introduction

For the pediatric population, community-acquired pneumonia (CAP) is among the most frequent causes of hospital admission. CAP remains a major cause of morbidity and mortality worldwide, especially regarding children less than 5 years of age. Most children with CAP live in the developing countries [1]. Viruses and mycoplasma species are two main of the many pathogenic agents which can cause CAP [2, 3, 4].
The symptoms of Community-acquired pneumonia are varying considerably depending on their aetiology, its infection pattern, and the underlying medical conditions. In clinical practice, most of the CAP diagnoses are based on radiography and clinical symptoms. There are some report cases in which the etiologies of CAPs were established on the bases clinical signs, radiological findings, or non-specific inflammatory serum markers [5, 6, 7]. In radiography, most of CAP cases are indicated by patchy areas of lung consolidation distributed along the lung markings, and diagnosed as bronchopneumonia. However, lobe or multi foci infiltration is the other two important kinds of CAP in clinical.

Both *viruses* as well as *mycoplasma* species can lead to lobe or multi foci infiltration in CAP. The therapy strategy for CAP cases is as controversial as it is crucial. The use of antibiotics before the etiology is found out is debated. On the other hand, to establish the cause of CAP cases needs time. Hence, tests must be devised which allow an early differentiation between *viral* and *mycoplasma pneumonia*. Unfortunately, studies focusing on CAP with lobe or multi foci infiltration are yet to be carried out.

Therefore, from May, 2012 to May, 2013, over a period of 1 year, a retrospective study was carried out in our hospital to examine the clinical features, inflammatory markers (C-Reactive Protein, white blood cell counting, and lymphocyte percentage), and radiographs of CAP cases with lobe or multi foci infiltration; with a special focus on factors which would allow the differential diagnosis of *viral* and *mycoplasma pneumonia*. 
Materials and Methods

Study Subjects

This study was approved by the Institutional Review Board of the Children’s Hospital Affiliated to Soochow University. Informed consent was enrolled and written by the parents of all children. During a surveillance period of 12 months (from May, 2012 to April, 2013), 126 consecutive, previously healthy children with radiologically confirmed lobar or multi foci infiltration of the lung were treated at our Hospital.

One hundred twenty six CAP patients were analyzed for gender, fever, wheeze, increase of respiratory rate, cough, CRP, and radiological findings among three different age groups namely 0-23 months, 2-4 years, and older than 5 years. Then, incidence of proven viral and mycoplasma CAP was investigated. Of these 88 proven CAP patients, fever, increase of respiratory rate, CRP, WBC, cough, wheeze, and radiological findings were statistically analyzed.

The respiratory rates of the 126 patients were measured; they were age-related; The respiratory rate was less than 45 per minute in children younger than 28 days old, less than 40 per minute in children between 29 days and 1 year old, less than 30 per minute in children between 1 and 3 years old, less than 25 per minute in children between 4 and 7 years old, and less than 20 per minute in children older than 8 years.

Nasopharyngeal swab specimens were routinely collected within 24 hours of admission, and bronchial-aspirate samples were obtained after tracheal intubation. Respiratory specimens were tested for influenza A and B, adenovirus, respiratory syncytial virus (RSV), bokavirus, human metapneumovirus (hMPV),
and parainfluenza virus (PIFV) 1, 2, and 3; using direct immunofluorescence assays.

Viral pneumonia was defined as acute respiratory disease with abnormal chest radiograph findings and positive laboratory tests for one of the aforementioned viruses.

In addition, blood specimens were obtained within 24 hours of admission for bacterial cultures. Other blood tests, including for C-reactive protein (CRP), white blood cells, and lymphocyte percentages and neutrophil percentages, were also performed.

The diagnosis of mycoplasma pneumonia was based on the results from real-time PCR targeting the P1 cytoadhesion type 1 and 2 genes of the mycoplasma pneumoniae genome, using DNA extracted from nasopharyngeal-swab specimens. Mycoplasma pneumonia was defined as acute respiratory disease with abnormal chest radiograph findings and positive laboratory tests combined by real-time PCR. Patients with simultaneous viral and mycoplasma infections were excluded from this study.

Radiography

The symptoms typically occurred at 4-7 days before the chest radiographs, via an anteroposterior projection with the child lying. Images was independently reviewed by two radiologist, when there has different opinion, they reached a diagnostic conclusion by consensus. Chest radiograph findings were classified as lobar or multi foci infiltration (unilateral or bilateral). The distribution of abnormalities was categorized as lobar, multi foci. A lobar distribution was defined as a single lobar of abnormality. If there were two or more foci(unilateral or bilateral), the distribution of abnormality was considered multi foci[3].

Statistical Analysis
Data are presented as number (n) and percentage. Univariate comparisons were made using nonparametric one-way Wilcoxon rank sum, chi-squared (χ²), or Fisher’s exact tests; depending on the statistical distribution. To evaluate the ability to differentiate between mycoplasma and viral CAP cases with lobar or multi foci infiltration, a stepwise logistic regression analysis was performed with the statistical analysis software (SAS) 8. Probability values of P less than 0.05 were considered statistically significant.

Results

Overall, there were 71 (56%) male and 55 (44%) female CAP cases with lobar or multi foci infiltration. The median age of the 126 patients was 4 years (range, 11 days to 14 years). The presenting signs and symptoms were fever (47.6%), wheeze (14.3%)(without history of asthma ), increase of respiratory rate (55.6%) and cough (97.6%). Fever and increase of respiratory rate are more common in the “over 5-year” group; however, wheeze is more common in “under 23-month” group (see Table 1).

Findings in chest radiograph included lobar infiltration (see Figure 1) in 54 patients, multi foci infiltration including unilateral infiltration(see Figure 2) in 26 patients, and bilateral infiltration(see Figure 3) in 46 patients. Seven patients had pleural effusions. An analysis of the correlation between aetiology and radiography findings showed that there were no significant differences between them (P>0.05) (Table 2).

Seventy of the CAP cases were caused by mycoplasma species and 18 by viruses, including influenza A (n=2), influenza B (n=1), adenovirus (n=2), RSV (n=9), bokavirus (n=2), and PIFV 3 (n=2). Univariate analysis revealed that the factors
which allowed the differential diagnosis of viral and mycoplasma CAP were increased respiratory rate, wheeze, male, and lymphocyte percentage ($P<0.05$). There were no significant differences in age, radiological findings, fever, cough, CRP, and WBC ($P>0.05$) (see Table 3).

A stepwise logistic regression analysis of 88 cases was performed to assess independent predictors which allowed the differential diagnosis of viral and mycoplasma caused CAP. Increased respiratory rate, wheeze and lymphocyte percentage were significantly predictive regarding the differentiation between viral and mycoplasma caused CAP with lobar or multi foci infiltration (see Table 4), as was viral aetiology of CAP with lobar or multi foci infiltration, increase respiratory rate, wheeze and increase lymphocyte percentage. The logistic regression model was consistent with the findings reported by Hosmer and Lemeshow who used the goodness-of-fit test ($P=0.8979$).

**Discussion**

In this study, 126 CAP cases with lobar or multi foci infiltration were observed over a period of 1 year. About 69.8% of the CAP cases were caused by mycoplasma species or virus. The etiology of 38 cases could not be detected, partly because the positive of bacterial pathogens in blood culture is very low. Our results are very similar to those of Zhang et al. who reported 707 severe CAP cases; blood cultures were positive in only 5, i.e., 0.7% [2]. This means that new methods with higher sensitivities for bacterial pathogens in blood must be devised which can be routinely
used in all laboratories (which is currently not the case) [8]. On the other hand, 55.6% of our patients had tachypnoea and 47.6% had fever, and these symptoms were more common in the “over 5-year” group. The CRP is higher in the “over 5-year” group than in the other two groups; maybe more infiltration foci can be found in the over 5-year” group. Our results are similar to two other studies [9,10]. However wheeze is more common in the “below 23-month” group; this finding is different from that of a recent study [11], partly because the sample we focus on pneumoniae with lobar or multi foci infiltration.

In clinical practice, the radiographic detection of infiltrations is currently the gold standard for the diagnosis of CAP. Most CAP cases are diagnosed as bronchial pneumonia in radiograph. However, lobe or multi foci infiltrations are the other two radiological manifestations of CAP [3,11]. Some authors reported that in clinical practice lobar infiltrations are often caused by bacteria [6]. However, in this study, 69.8% of the CAP case was caused by viruses and mycoplasma species: especially, mycoplasma associated with etiological findings, it account 55.6% in this group. This finding is consistent with some previous studies [3,12]. In our study, there were 41 CAP cases with bilateral infiltrations and 61 CAP cases with multi foci. When analysis on distribution and the number of focus. There is no significant difference associating with etiological findings. Even some of cases with pleural effusion, there is no significant difference associating with etiological findings. This means that whether the CAP with lobar or multi foci infiltration was caused by mycoplasma species or viruses could not be inferred from the radiological patterns. In a recent
study about pediatric CAP, Korppi et al. analyzed the clinical or radiological characteristics of 101 CAP cases, and they concluded that radiographs are not helpful when it comes to differentiating between viral, pneumococcal, and atypical bacterial aetiology of CAP in children [11]. This conclusion coincides with our results: Radiological pattern did not allow a reliable differentiation between mycoplasma and viral CAP.

To investigate potential factors that may allow differentiating between viral and mycoplasma CAP is very important for clinical practice. In this study, our aim was to describe the utility of some laboratory markers and clinical features regarding the differentiation between mycoplasma and viral CAP with lobar or multi foci infiltrations. Univariate analysis showed that findings such wheeze, lymphocyte percentage, respiratory rate, and sex can help to differentiate between mycoplasma and viral CAP with lobar or multi foci infiltration. Furthermore, multiple logistic regression showed that wheeze, increase of lymphocyte percentage, and increase of respiratory rate are independent factors which allow to differentiate between mycoplasma and viral CAP with lobar or multi focus infiltration. This means that among mycoplasma and viral CAP with lobar or multi foci infiltration, wheeze, increase of lymphocyte percentage, and increase of respiratory rate can help to diagnose viral pneumonia.

Hatipoğlu et al. [13] reported 147 viral CAP cases, and they found that the prominent symptoms of the patients were cough (88.9%) and wheeze (72.2%). This is similar to our results. In another report [11], 101 CAP cases were analyzed. Although
the report lacked data on respiratory rate in 20 cases, it included supplementary sensitivity analyses by adding the cases with missing data as non-tachypnoea cases in the analyses. Moreover, the report concluded that tachypnoea is not associated with the aetiology of CAP. The above study is different from our findings. The reason may be that we used multiple factor analysis and selected mycoplasma and viral CAP with lobar or multi foci infiltration as our object of study. We believe that our will have a significant impact on the efforts to find new treatment strategies for this type of CAP.

Youn et al. [9] reported 95 *mycoplasma pneumoniae* cases with segmental or lobar infiltrations. They found that the lymphocyte percentage was at a normal level.

Defilippi et al. [10] reported 102 CAP cases with a positive PCR for *mycoplasma pneumoniae*: they found that the lymphocyte percentage (median) is at normal level, a result similar to ours. Hatipoğlu et al. [13] reported 147 cases with pneumonia, the percentage of polymorphonuclear leukocytes the *viral pneumonia* cases was lower than patients *virus* not isolated, it suggests that Lymphocyte percentage may be higher in pneumonian in acute phase of pneumonia. The above-mentioned literature suggests that *viral pneumonia* often presents a higher percentage of lymphocyte. This conclusion is similar to our results.

This study has several limitations. Firstly, it was a retrospective study, and therefore there may have been some selection bias. Secondly, *viral pneumonia* could be missed due to the sensitivity of immunofluorescence and the limit number of *virus* we detected. Thirdly, there may be some cases in which the patient had a viral as well as *bacterial* or a combined *bacterial* and *mycoplasma* infection which cannot be
detected. Therefore, prospective further, preferably prospective studies on CAP with lobar or multi foci infiltration are needed.

In conclusion, more than half of the CAP cases with lobar or multi foci infiltration are caused by *mycoplasma* species or *viruses*. Whether the CAP with lobar or multi foci infiltration was caused by *mycoplasma* species or *viruses* could not be inferred from the radiological patterns. We found that wheeze, lymphocyte percentage, and respiratory rates were independent factors which allow the differential diagnosis of *viral* and *mycoplasma* caused CAP with lobar or multi foci infiltration, as was *viral* aetiology of CAP with lobar or multi foci infiltration, increase respiratory rate, wheeze and increase lymphocyte percentage.

**Contributorship**

study design and paper writing: Chuang-li Hao

data collection and paper writing: Wan-liang Guo, Jian Wang

data collection and data analysis: li-yuan Zhu

All authors have read and approved the content, and agree to submit for consideration for publication in this journal. There is no any legal conflicts involved in the article.

**Data sharing**

No additional data available

**Competing Interests**

None
Reference:


**Figure Legends**

Figure 1. An example of right middle lobe infiltration from a chest radiograph obtained 6 days after the onset of symptoms in a 5-month-old girl with influenza B.

Figure 2. An example of right upper and middle lobe infiltration from a chest radiograph obtained 5 days after the onset of symptoms in a 2-year-old girl with mycoplasma pneumonia.

Figure 3. An example of bilateral infiltration in the left upper zone, the right upper zone and middle zone from a chest radiograph taken 4 days after the onset of symptoms in a 16-month-old girl with influenza A.
Table 1. Clinical signs and symptoms in 126 children with CAP, in relation to the age

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>0–23 months (n=34)</th>
<th>2–4 years (n=39)</th>
<th>≥ 5 years (n=53)</th>
<th>P value</th>
<th>Total (n=126)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever &gt;37.5°C</td>
<td>7</td>
<td>22</td>
<td>31</td>
<td>0.0011</td>
<td>60</td>
</tr>
<tr>
<td>Wheeze</td>
<td>13</td>
<td>2</td>
<td>3</td>
<td>&lt;0.0001</td>
<td>18</td>
</tr>
<tr>
<td>Increase respiratory rate</td>
<td>12</td>
<td>17</td>
<td>41</td>
<td>0.0001</td>
<td>70</td>
</tr>
<tr>
<td>Cough</td>
<td>32</td>
<td>38</td>
<td>53</td>
<td>0.2131</td>
<td>123</td>
</tr>
<tr>
<td>CRP(&gt;8)</td>
<td>10</td>
<td>27</td>
<td>39</td>
<td>&lt;0.0001</td>
<td>76</td>
</tr>
<tr>
<td>Lobar infiltration</td>
<td>11</td>
<td>18</td>
<td>25</td>
<td>0.9524</td>
<td>54</td>
</tr>
<tr>
<td>Unilateral infiltration (multi)</td>
<td>5</td>
<td>8</td>
<td>13</td>
<td>0.9524</td>
<td>26</td>
</tr>
<tr>
<td>Bilateral infiltration</td>
<td>18</td>
<td>13</td>
<td>15</td>
<td>0.0587</td>
<td>46</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>0.8847</td>
<td>7</td>
</tr>
<tr>
<td>Sex (M)</td>
<td>24</td>
<td>16</td>
<td>31</td>
<td>0.0364</td>
<td>71</td>
</tr>
</tbody>
</table>
Table 2. Radiological findings in children with large consolidation of CAP

<table>
<thead>
<tr>
<th>radiological findings</th>
<th>M</th>
<th>V</th>
<th>unknown</th>
<th>P-value</th>
<th>Total patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>lobar infiltration</td>
<td>28</td>
<td>7</td>
<td>19</td>
<td>0.8864</td>
<td>54</td>
</tr>
<tr>
<td>unilateral infiltration</td>
<td>15</td>
<td>3</td>
<td>8</td>
<td>0.8864</td>
<td>26</td>
</tr>
<tr>
<td>bilateral infiltration</td>
<td>27</td>
<td>8</td>
<td>11</td>
<td>0.5192</td>
<td>46</td>
</tr>
<tr>
<td>pleural effusion</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1.0000</td>
<td>7</td>
</tr>
</tbody>
</table>

M= mycoplasma   V= viral

Table 3. Clinical signs in relation to the aetiology of pneumonia, viral aetiology Vs mycoplasma

<table>
<thead>
<tr>
<th>findings</th>
<th>M (n=70)</th>
<th>V (n=18)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>fever &gt;37.5°C</td>
<td>42</td>
<td>7</td>
<td>0.1078</td>
</tr>
<tr>
<td>wheeze</td>
<td>3</td>
<td>8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>increase respiratory rate</td>
<td>29</td>
<td>14</td>
<td>0.0053</td>
</tr>
<tr>
<td>cough</td>
<td>69</td>
<td>16</td>
<td>0.1050</td>
</tr>
<tr>
<td>CRP(&gt;8)</td>
<td>44</td>
<td>9</td>
<td>0.2231</td>
</tr>
<tr>
<td>WBC(increase)</td>
<td>17</td>
<td>6</td>
<td>0.4359</td>
</tr>
<tr>
<td>increase lymphocyte percentage</td>
<td>10</td>
<td>7</td>
<td>0.0184</td>
</tr>
<tr>
<td>increase polymorphonuclears</td>
<td>19</td>
<td>4</td>
<td>0.6717</td>
</tr>
<tr>
<td>radiograph</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>multi foci infiltration (unilateral)</td>
<td>15</td>
<td>3</td>
<td>0.7690</td>
</tr>
<tr>
<td>multi foci infiltration (bilateral)</td>
<td>27</td>
<td>8</td>
<td>0.6498</td>
</tr>
<tr>
<td>sex(M)</td>
<td>29</td>
<td>13</td>
<td>0.0197</td>
</tr>
<tr>
<td>age (&gt;5 years)</td>
<td>32</td>
<td>6</td>
<td>0.3442</td>
</tr>
</tbody>
</table>
Table 4. Stepwise logistic regression model for significant predictors of viral aetiology of CAP showing lobar or multi foci infiltration

<table>
<thead>
<tr>
<th>variable</th>
<th>Chi-Square</th>
<th>OR</th>
<th>95% Wald Confidence Limits</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>wheeze</td>
<td>23.0077</td>
<td>0.063</td>
<td>0.010-0.271</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>increase respiratory rate</td>
<td>6.7243</td>
<td>0.093</td>
<td>0.013-0.653</td>
<td>0.0095</td>
</tr>
<tr>
<td>increase lymphocyte percentage</td>
<td>8.9954</td>
<td>0.053</td>
<td>0.012-0.337</td>
<td>0.0027</td>
</tr>
</tbody>
</table>

Hosmer and Lemeshow Goodness-of-Fit Test (p=0.8979)
Figure 1. An example of right middle lobe infiltration from a chest radiograph obtained 6 days after the onset of symptoms in a 5-month-old girl with influenza B.

76x69mm (300 x 300 DPI)
Figure 2. An example of right upper and middle lobe infiltration from a chest radiograph obtained 5 days after the onset of symptoms in a 2-year-old girl with mycoplasma pneumonia. 87x91mm (300 x 300 DPI)
Figure 3. An example of bilateral infiltration in the left upper zone, the right upper zone and middle zone from a chest radiograph taken 4 days after the onset of symptoms in a 16-month-old girl with influenza A. 53x33mm (300 x 300 DPI)
Differentiation between mycoplasma and viral community-acquired pneumonia in children with lobe or multi foci infiltration: a retrospective case study

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| **Keywords**: | Paediatric radiology < PAEDIATRICS, Paediatric thoracic medicine < PAEDIATRICS, Paediatric infectious disease & immunisation < PAEDIATRICS |
Differentiation between mycoplasma and viral community-acquired pneumonia in children with lobe or multi foci infiltration: a retrospective case study

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ABSTRACT

Objectives: The aim of this paper seeks to analyze the clinical features, inflammatory markers, and radiographs of community-acquired pneumonia (CAP) cases with lobe or multi foci infiltration; with a special focus on factors which allow the differential diagnosis of viral and mycoplasma pneumonia.

Setting: This is a retrospective chart review of CAP cases in a large University teaching hospital.

Participants: 126 pediatric CAP cases, with lobe or multi foci infiltration, presenting between May 2012 and April 2013. Demographic data, clinical presentation upon admission or referral, laboratory tests, prior history, and radiography were collected for each case if available.

Primary and secondary outcome measures: We used univariate and multivariate logistic regression to determine the significant factors which allow the differential diagnosis of viral and mycoplasma CAP with lobe or multi foci infiltration.

Results: Overall, there were 71 (56%) male and 55 (44%) female CAP cases with lobar or multi foci infiltration. Seventy pneumonia cases were caused by Mycoplasma pneumoniae and eighteen by viruses. Univariate analysis of the mycoplasma and viral causes of the CAP revealed that increased respiratory rate, wheeze, male gender, and lymphocyte percentage were the factors associated with the differentiation of mycoplasma and viral etiologies of pneumonia (P<0.05). A stepwise logistic regression analysis was performed to assess independent factors which allow the differential diagnosis of viral and mycoplasma pneumonia. Increased respiratory rate,
wheeze, and lymphocyte percentage were reliable independent factors which allow
the differential diagnosis of viral and mycoplasma CAP with lobar or multi foci
infiltration.

Conclusions: Whether the CAP with lobar or multi foci infiltration was caused by
mycoplasma species or viruses could not be inferred from the radiological patterns.
Wheeze, lymphocyte percentage, and respiratory rate were independent factors which
allowed the differential diagnosis of viral and mycoplasma CAP with lobar or multi
foci infiltration.

Keywords: Community-acquired pneumonia; Children; Lobar; Multi foci; Etiology

Strengths and limitations of this study

Over a period of 1 year, a retrospective study was carried out in our hospital. A
stepwise logistic regression analysis of 88 cases was performed to assess independent
predictors which allowed the differential diagnosis of viral and mycoplasma caused
CAP. Increased respiratory rate, wheeze and lymphocyte percentage were
significantly predictive regarding the differentiation between viral and mycoplasma
cause CAP with lobar or multi foci infiltration, as was viral aetiology of CAP with
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This study has several limitations. Firstly, it was a retrospective study, and
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be missed due to the sensitivity of immunofluorescence and the limited number of
virus we detected. Thirdly, there may be some cases in which the patient had a viral as
well as bacterial or a combined bacterial and mycoplasma infection which cannot be
detected.

**Introduction**

For the pediatric population, community-acquired pneumonia (CAP) is among the
most frequent causes of hospital admission. CAP remains a major cause of morbidity
and mortality worldwide, especially regarding children less than 5 years of age. Most
children with CAP live in the developing countries [1]. Viruses and mycoplasma
species are two main of the many pathogenic agents which can cause CAP [2, 3, 4].

The symptoms of community-acquired pneumonia are varying considerably
depending on their aetiology, its infection pattern, and the underlying medical
conditions. In clinical practice, most of the CAP diagnoses are based on radiography
and clinical symptoms. There are some reported cases in which the etiologies of CAP
were established on the bases clinical signs, radiological findings, or non-specific
inflammatory serum markers [5, 6, 7]. In radiography, most of CAP cases are
indicated by patchy areas of lung consolidation distributed along the lung markings,
and diagnosed as bronchopneumonia. However, lobe or multi foci infiltration is the
other two important kinds of CAP in clinical.

Both viruses as well as mycoplasma species can lead to lobe or multi foci
infiltration in CAP. The therapeutic strategy for CAP cases is as controversial as it is
crucial. The use of antibiotics before the etiology is found out is debated. On the other
hand, to establish the cause of CAP cases needs time. Hence, tests must be devised which allow an early differentiation between viral and mycoplasma pneumonia. Unfortunately, studies focusing on CAP with lobe or multi foci infiltration are yet to be carried out.

Therefore, from May, 2012 to May, 2013, over a period of 1 year, a retrospective study was carried out in our hospital to examine the clinical features, inflammatory markers (C-Reactive Protein, white blood cell counting, and lymphocyte percentage), and radiographs of CAP cases with lobe or multi foci infiltration; with a special focus on factors which would allow the differential diagnosis of viral and mycoplasma pneumonia.

Materials and Methods

Study Subjects

This study was approved by the Institutional Review Board of the Children’s Hospital Affiliated to Soochow University. Informed consent was enrolled and written by the parents of all children. During a surveillance period of 12 months (from May, 2012 to April, 2013), 126 consecutive, previously healthy children with radiologically confirmed lobar or multi foci infiltration of the lung were treated at our Hospital. The medical charts, radiographs and laboratory findings were retrospectively reviewed by both respiratory physician and radiologist. Patients with history of asthma were excluded from this study.

Nasopharyngeal swab specimens were routinely collected within 24 hours of admission, and bronchial-aspirate samples were obtained after tracheal intubation.
Respiratory specimens were tested for influenza A and B, adenovirus, respiratory syncytial virus (RSV), bokavirus, human metapneumovirus (hMPV), and parainfluenza virus (PIFV) 1, 2, and 3; using direct immunofluorescence assays. Viral pneumonia was defined as acute respiratory disease with abnormal chest radiograph findings and positive laboratory tests for one of the aforementioned viruses. In addition, blood specimens were obtained within 24 hours of admission for bacterial cultures. Other blood tests, including for C-reactive protein (CRP), white blood cells, and lymphocyte percentages and neutrophil percentages, were also performed.

The diagnosis of mycoplasma pneumonia was based on the results from real-time PCR targeting the P1 cytoadhesion type 1 and 2 genes of the *Mycoplasma pneumoniae* genome, using DNA extracted from nasopharyngeal-swab specimens. Mycoplasma pneumonia was defined as acute respiratory disease with abnormal chest radiograph findings and positive laboratory tests combined by real-time PCR. Patients with simultaneous viral and mycoplasma infections were excluded from this study.

**Radiography**

The symptoms typically occurred at 4-7 days before the chest radiographs, via an anteroposterior projection with the child lying. Images was independently reviewed by two radiologists, when there has different opinion, they reached a diagnostic conclusion by consensus. Chest radiograph findings were classified as lobar or multi foci infiltration (unilateral or bilateral). The distribution of abnormalities was categorized as lobar, multi foci. A lobar distribution was defined as a single lobar of abnormality. If there were two or more foci (unilateral or bilateral), the distribution of
abnormality was considered multi foci[3]. Pleural effusion was evaluated by both chest radiograph and ultrasound.

Factors Analysis

One hundred twenty six CAP patients were analyzed for gender, fever, wheeze, increase of respiratory rate, cough, CRP, and radiological findings among three different age groups namely 0-23 months, 2-4 years, and older than 5 years. Then, incidence of proven viral and mycoplasma CAP was investigated. Of these 88 proven CAP patients, fever, increase of respiratory rate, CRP, WBC, cough, wheeze, and radiological findings were statistically analyzed.

The respiratory rates of the 126 patients were measured: they were age-related; The respiratory rate was less than 45 per minute in children younger than 28 days old, less than 40 per minute in children between 29 days and 1 year old, less than 30 per minute in children between 1 and 3 years old, less than 25 per minute in children between 4 and 7 years old, and less than 20 per minute in children older than 8 years.

Statistical Analysis

Data are presented as number ($n$) and percentage. Univariate comparisons were made using nonparametric one-way Wilcoxon rank sum, chi-squared ($\chi^2$), or Fisher’s exact tests; depending on the statistical distribution. To evaluate the ability to differentiate between mycoplasma and viral CAP cases with lobar or multi foci infiltration, a stepwise logistic regression analysis was performed with the statistical analysis software (SAS) 8. Probability values of $P$ less than 0.05 were considered statistically significant.
Results

Overall, there were 71 (56%) male and 55 (44%) female CAP cases with lobar or multi foci infiltration. The median age of the 126 patients was 4 years (range, 11 days to 14 years). The presenting signs and symptoms were fever (47.6%), wheeze (14.3%) (without history of asthma), increase of respiratory rate (55.6%) and cough (97.6%). Fever and increase of respiratory rate are more common in the “older than 5 years” group; however, wheeze is more common in “0-23 months” group (see Table 1).

Findings in chest radiograph included lobar infiltration (see Figure 1) in 54 patients, multi foci infiltration including unilateral infiltration (see Figure 2) in 26 patients, and bilateral infiltration (see Figure 3) in 46 patients. Seven patients had pleural effusions. An analysis of the correlation between aetiology and radiography findings showed that there were no significant differences between them (P>0.05) (Table 2).

Seventy of the CAP cases were caused by mycoplasma species and 18 by viruses, including influenza A (n=2), influenza B (n=1), adenovirus (n=2), RSV (n=9), bokavirus (n=2), and PIFV 3 (n=2). Univariate analysis revealed that the factors which allowed the differential diagnosis of viral and mycoplasma CAP were increased respiratory rate, wheeze, male, and lymphocyte percentage (P<0.05). There were no significant differences in age, radiological findings, fever, cough, CRP, and WBC (P>0.05) (see Table 3).

A stepwise logistic regression analysis of 88 cases was performed to assess independent predictors which allowed the differential diagnosis of viral and
mycoplasma caused CAP. Increased respiratory rate, wheeze and lymphocyte percentage were significantly predictive regarding the differentiation between viral and mycoplasma caused CAP with lobar or multi foci infiltration (see Table 4), as was viral aetiology of CAP with lobar or multi foci infiltration, increase respiratory rate, wheeze and increase lymphocyte percentage. The logistic regression model was consistent with the findings reported by Hosmer and Lemeshow who used the goodness-of-fit test (P=0.8979).

Discussion

**General Findings in Three Age Groups**

In this study, about 69.8% of the CAP cases were caused by mycoplasma species or virus. The etiology of 38 cases (31.2%) could not be detected, partly because the positive of bacterial pathogens in blood culture is very low. Our results are very similar to those of Zhang et al. who reported 707 severe CAP cases; blood cultures were positive in only 5, i.e., 0.7% [2]. This means that new methods with higher sensitivities for bacterial pathogens in blood must be devised which can be routinely used in all laboratories[8]. On the other hand, 55.6% of our patients had tachypnoea and 47.6% had fever, and these symptoms were more common in the “older than 5 years” group. The CRP is higher in the “older than 5 years” group than in the other two groups; maybe more infiltration foci can be found in the “older than 5 years” group. Our results are similar to two other studies [9,10]. However wheeze is more common in the “0-23 months” group; this finding is different from that of a recent
study [11], partly because the sample we focus on pneumoniae with lobar or multi foci infiltration.

**Radiological Patterns between Mycoplasma and Viral CAP**

In clinical practice, the radiographic detection of infiltrations is currently the gold standard for the diagnosis of CAP. Most CAP cases are diagnosed as bronchopneumonia in radiograph. However, lobe or multi foci infiltrations are the other two radiological manifestations of CAP [3,11]. Some authors reported that in clinical practice lobar infiltrations are often caused by bacteria [6]. However, in this study, 69.8% of the CAP case was caused by viruses and mycoplasma species: especially, mycoplasma associated with etiological findings, it account 55.6% in this group. This finding is consistent with some previous studies [3,12]. In our study, there were 41 CAP cases with bilateral infiltrations and 61 CAP cases with multi foci. When analysis on distribution and the number of focus. There is no significant difference associating with etiological findings. Even some of cases with pleural effusion, there is no significant difference associating with etiological findings. This means that whether the CAP with lobar or multi foci infiltration was caused by mycoplasma species or viruses could not be inferred from the radiological patterns. In a recent study about pediatric CAP, Korppi et al. analyzed the clinical or radiological characteristics of 101 CAP cases, and they concluded that radiographs are not helpful when it comes to differentiating between viral, pneumococcal, and atypical bacterial aetiology of CAP in children [11]. This conclusion coincides with our results: Radiological pattern did not allow a reliable differentiation between mycoplasma and
viral CAP.

**Related Factors between Mycoplasma and Viral CAP**

To investigate potential factors that may allow differentiating between viral and mycoplasma CAP is very important for clinical practice. In this study, our aim was to describe the utility of some laboratory markers and clinical features regarding the differentiation between mycoplasma and viral CAP with lobar or multi foci infiltrations. Univariate analysis showed that findings such wheeze, lymphocyte percentage, respiratory rate, and sex can help to differentiate between mycoplasma and viral CAP with lobar or multi foci infiltration. Furthermore, multiple logistic regression showed that wheeze, increase of lymphocyte percentage, and increase of respiratory rate are independent factors which allow to differentiate between mycoplasma and viral CAP with lobar or multi focus infiltration. This means that among mycoplasma and viral CAP with lobar or multi foci infiltration, wheeze, increase of lymphocyte percentage, and increase of respiratory rate can help to diagnose viral pneumonia.

Hatipoğlu et al. [13] reported 147 viral CAP cases, and they found that the prominent symptoms of the patients were cough (88.9%) and wheeze (72.2%). This is similar to our results. In another report [11], 101 CAP cases were analyzed. Although the report lacked data on respiratory rate in 20 cases, it included supplementary sensitivity analyses by adding the cases with missing data as non-tachypnoea cases in the analyses. Moreover, the report concluded that tachypnoea is not associated with the aetiology of CAP. The above study is different from our findings. The reason may
be that we used multiple factor analysis and selected mycoplasma and viral CAP with lobar or multi foci infiltration as our object of study.

Youn et al. [9] reported 95 *Mycoplasma pneumoniae* cases with segmental or lobar infiltrations. They found that the lymphocyte percentage was at a normal level. Defilippi et al. [10] reported 102 CAP cases with a positive PCR for *Mycoplasma pneumoniae*: they found that the lymphocyte percentage (median) is at normal level, a result similar to ours. Hatipoğlu et al. [13] reported 147 cases with pneumonia, the percentage of polymorphonuclear leukocytes the viral pneumonia cases was lower than patients virus not isolated, it suggests that Lymphocyte percentage may be higher in pneumonian in acute phase of pneumonia. The above-mentioned literature suggests that viral pneumonia often presents a higher percentage of lymphocyte. This conclusion is similar to our results.

**Limitations**

This study has several limitations. Firstly, it was a retrospective study, and therefore there may have been some selection bias. Secondly, viral pneumonia could be missed due to the sensitivity of immunofluorescence and the limit number of virus we detected. Thirdly, there may be some cases in which the patient had a viral as well as bacterial or a combined bacterial and mycoplasma infection which cannot be detected. Therefore, prospective further, preferably prospective studies on CAP with lobar or multi foci infiltration are needed.

**Conclusions**

In conclusion, more than half of the CAP cases with lobar or multi foci infiltration
are caused by mycoplasma species or viruses. Whether the CAP with lobar or multi 
ofoci infiltration was caused by mycoplasma species or viruses could not be inferred 
from the radiological patterns. We found that wheeze, lymphocyte percentage, and 
respiratory rates were independent factors which allow the differential diagnosis of 
viral and mycoplasma caused CAP with lobar or multi foci infiltration, as was viral 
aetiology of CAP with lobar or multi foci infiltration, increase respiratory rate, 
wheeze and increase lymphocyte percentage.

Authors’ Contributions:

Chuang-li Hao participated in study design and paper writing. Wan-liang Guo and 
Jian Wang participated in data collection and paper writing. Li-yuan Zhu 
participated in data collection and analysis. All authors read and approved the final 
manuscript.

Competing interests:

The authors declare that they have no competing interests.

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Data Sharing Statement:

No additional data available.

Reference:


Figure Legends

Figure 1. An example of right middle lobe infiltration from a chest radiograph obtained 6 days after the onset of symptoms in a patient with influenza B.

Figure 2. An example of right upper and middle lobe infiltration from a chest radiograph obtained 5 days after the onset of symptoms in a patient with mycoplasma pneumonia.

Figure 3. An example of bilateral infiltration in the left upper zone, the right upper zone and middle zone from a chest radiograph taken 4 days after the onset of symptoms in a patient with influenza A.
Table 1. Clinical signs and symptoms in 126 children with CAP, in relation to the age

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>0–23 months (n=34)</th>
<th>2–4 years (n=39)</th>
<th>≥5 years (n=53)</th>
<th>P value</th>
<th>Total (n=126)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever &gt;37.5°C</td>
<td>7</td>
<td>22</td>
<td>31</td>
<td>0.0011</td>
<td>60</td>
</tr>
<tr>
<td>Wheeze</td>
<td>13</td>
<td>2</td>
<td>3</td>
<td>&lt;0.0001</td>
<td>18</td>
</tr>
<tr>
<td>Increase respiratory rate</td>
<td>12</td>
<td>17</td>
<td>41</td>
<td>0.0001</td>
<td>70</td>
</tr>
<tr>
<td>Cough</td>
<td>32</td>
<td>38</td>
<td>53</td>
<td>0.2131</td>
<td>123</td>
</tr>
<tr>
<td>CRP (&gt;8)</td>
<td>10</td>
<td>27</td>
<td>39</td>
<td>&lt;0.0001</td>
<td>76</td>
</tr>
<tr>
<td>Lobar infiltration</td>
<td>11</td>
<td>18</td>
<td>25</td>
<td>0.9524</td>
<td>54</td>
</tr>
<tr>
<td>Unilateral infiltration</td>
<td>5</td>
<td>8</td>
<td>13</td>
<td>0.9524</td>
<td>26</td>
</tr>
<tr>
<td>(multiple)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral infiltration</td>
<td>18</td>
<td>13</td>
<td>15</td>
<td>0.0587</td>
<td>46</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>0.8847</td>
<td>7</td>
</tr>
<tr>
<td>Sex (M)</td>
<td>24</td>
<td>16</td>
<td>31</td>
<td>0.0364</td>
<td>71</td>
</tr>
</tbody>
</table>

Table 2. Radiological findings of CAP in children with lobe or multi foci infiltration

<table>
<thead>
<tr>
<th>Radiological findings</th>
<th>Aetiology of pneumonia</th>
<th>P value</th>
<th>Total patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobar infiltration</td>
<td>M (n=70)</td>
<td>V (n=18)</td>
<td>unknown (n=38)</td>
</tr>
<tr>
<td>Unilateral infiltration</td>
<td>28</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td>(multiple)</td>
<td>15</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Bilateral infiltration</td>
<td>27</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>5</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

M= mycoplasma     V= viral

Table 3. Clinical signs in relation to the aetiology of pneumonia, viral
aetiology Vs mycoplasma
<table>
<thead>
<tr>
<th>findings</th>
<th>M (n=70)</th>
<th>V (n=18)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>fever &gt;37.5 °C</td>
<td>42</td>
<td>7</td>
<td>0.1078</td>
</tr>
<tr>
<td>wheeze</td>
<td>3</td>
<td>8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>increase respiratory rate</td>
<td>29</td>
<td>14</td>
<td>0.0053</td>
</tr>
<tr>
<td>cough</td>
<td>69</td>
<td>16</td>
<td>0.1050</td>
</tr>
<tr>
<td>CRP(&gt;8)</td>
<td>44</td>
<td>9</td>
<td>0.2231</td>
</tr>
<tr>
<td>WBC(increase)</td>
<td>17</td>
<td>6</td>
<td>0.4359</td>
</tr>
<tr>
<td>increase lymphocyte percentage</td>
<td>10</td>
<td>7</td>
<td>0.0184</td>
</tr>
<tr>
<td>increase polymorphonuclears</td>
<td>19</td>
<td>4</td>
<td>0.6717</td>
</tr>
<tr>
<td>radiograph</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>multi foci infiltration (unilateral)</td>
<td>15</td>
<td>3</td>
<td>0.7690</td>
</tr>
<tr>
<td>multi foci infiltration (bilateral)</td>
<td>27</td>
<td>8</td>
<td>0.6498</td>
</tr>
<tr>
<td>sex(M)</td>
<td>29</td>
<td>13</td>
<td>0.0197</td>
</tr>
<tr>
<td>age (&gt;5 years)</td>
<td>32</td>
<td>6</td>
<td>0.3442</td>
</tr>
</tbody>
</table>

M= mycoplasma  V= viral

Table 4. Stepwise logistic regression model for significant predictors of viral aetiology of CAP showing lobar or multi foci infiltration

<table>
<thead>
<tr>
<th>variable</th>
<th>Chi-Square</th>
<th>OR</th>
<th>95% Wald Confidence Limits</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>wheeze</td>
<td>23.0077</td>
<td>0.063</td>
<td>0.010-0.271</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>increase respiratory rate</td>
<td>6.7243</td>
<td>0.093</td>
<td>0.013-0.653</td>
<td>0.0095</td>
</tr>
<tr>
<td>increase lymphocyte percentage</td>
<td>8.9954</td>
<td>0.053</td>
<td>0.012-0.337</td>
<td>0.0027</td>
</tr>
</tbody>
</table>

Hosmer and Lemeshow Goodness-of-Fit Test (p=0.8979)
Figure 1. An example of right middle lobe infiltration from a chest radiograph obtained 6 days after the onset of symptoms in a patient with influenza B.

76x69mm (300 x 300 DPI)
Figure 2. An example of right upper and middle lobe infiltration from a chest radiograph obtained 5 days after the onset of symptoms in a patient with mycoplasma pneumonia.

87x91mm (300 x 300 DPI)
Figure 3. An example of bilateral infiltration in the left upper zone, the right upper zone and middle zone from a chest radiograph taken 4 days after the onset of symptoms in a patient with influenza A.
53x33mm (300 x 300 DPI)
Differentiation between mycoplasma and viral community-acquired pneumonia in children with lobe or multi foci infiltration: a retrospective case study
Wan-liang Guo, Jian Wang, Li-yuan Zhu and Chuang-li Hao

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