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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 ($\chi 2$), 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, 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 (multipe), 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

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, 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.

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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 lefe 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

Symptoms	0–23 months	2–4 years	≥5 years	p-value	total
sex(M)	24	16	31	0.0364	71
Fever ⁄37,5◦C	7	22	31	0.0011	60
wheeze	13	2	3	<0.0001	18
Increase respiratory rate	12	17	41	0.0001	70
cough	32	38	53	0.2131	123
CRP(>8)	10	27	39	<0.0001	76
Unilateral consolidation(single)	11	18	25	0.9524	54
Unilateral consolidation(multipe)	5	8	13	0.9524	26
Bilateral consolidation	18	13	15	0.0587	46
Pleural fluid	1	2	4	0.8847	7
total	34	39	53	-	126

Table 2. Radiological findings in children with large consideration of CAP

Radiological findings	M	V	unknow	P-value	Total patients
Bilateral consolidation	27	8	11	0.5192	46
Unilateral consolidation(single)	28	7	19	0.8864	54
Unilateral consolidation(multipe)	15	3	8	0.8864	26
Pleural effusion	5	1	1	1.0000	7

M= mycoplasma V= viral

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

findings	M（70）	V（18）	P value
Fever >37.5◦C	42	7	0.1078
Increase respiratory rate	29	14	0.0053
CRP(>8)	44	9	0.2231
WBC(increase)	17	6	0.4359
Increase lymphocyte percentage	10		0.0184
Increase polymorphonuclears percentage	19	4	0.6717
cough	69	16	0.1050
wheeze	3	8	<0.0001
radiograph			
Unilateral consolidation(multipe)	15	3	0.7690
Bilateral consolidation	27	8	0.6498
sex(M)	29	13	0.0197
age（>5 years）	32	6	0.3442

M= mycoplasma V= viral

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

variable	Chi-Square	OR	95%Wald Conficence Limits	P value
Wheeze	23.0077	0.063	0.010-0.271	<0.0001
Increase lymphocyte percentage	8.9954	0.053	0`012-0.337	0.0027
Increase respiratory rate	6.7243	0.093	0.013-0.653	0.0095

Hosmer and Lemeshow Goodness-of-Fit Test (p=0.8979)

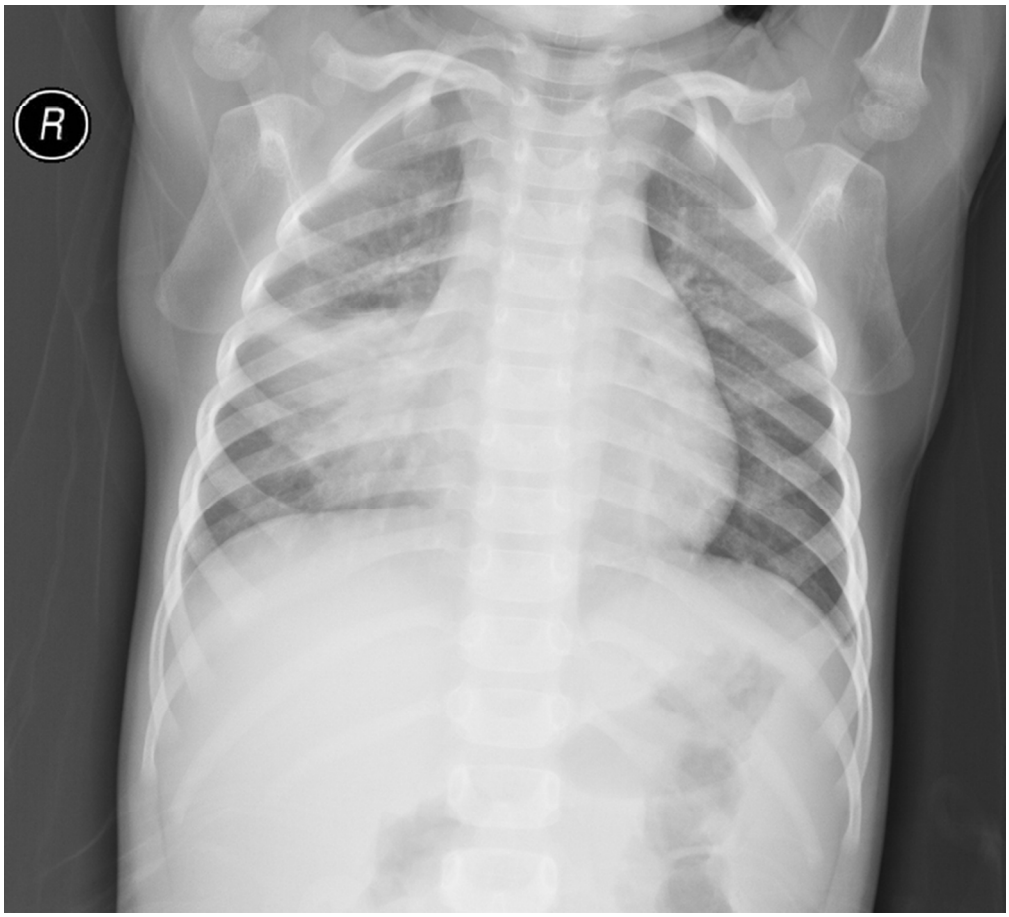


Figure 1. An example of right middle lobe infiltration from a chest radiograph obtained 6 days after the onset of symptoms in a 5-month-old girl with influenza B。
76x69mm (300 x 300 DPI)

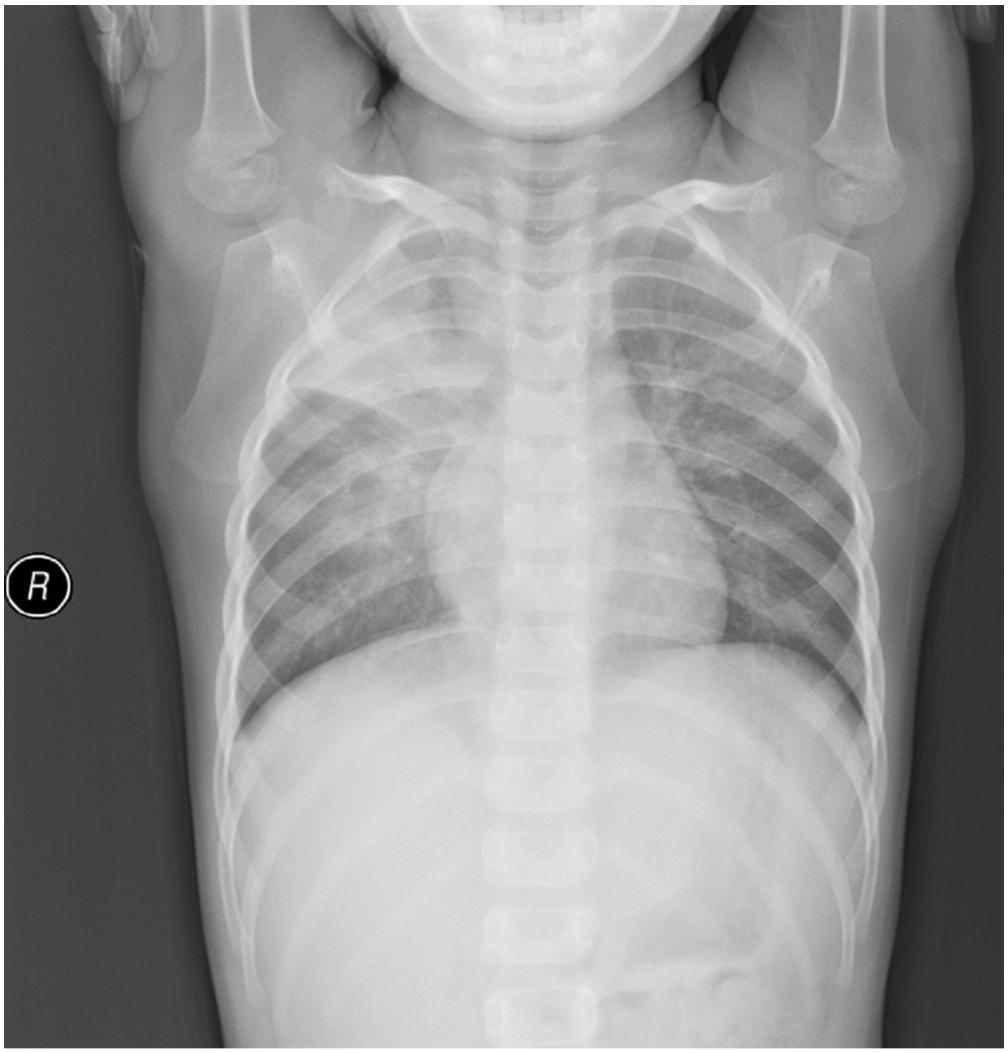


Figure 2. An example of right upper and middle lobe infiltration from a chest radiograph obtained 5 days after the onset of symptoms in a 2-year-old girl with mycoplasma pneumonia.
87x91mm (300 x 300 DPI)

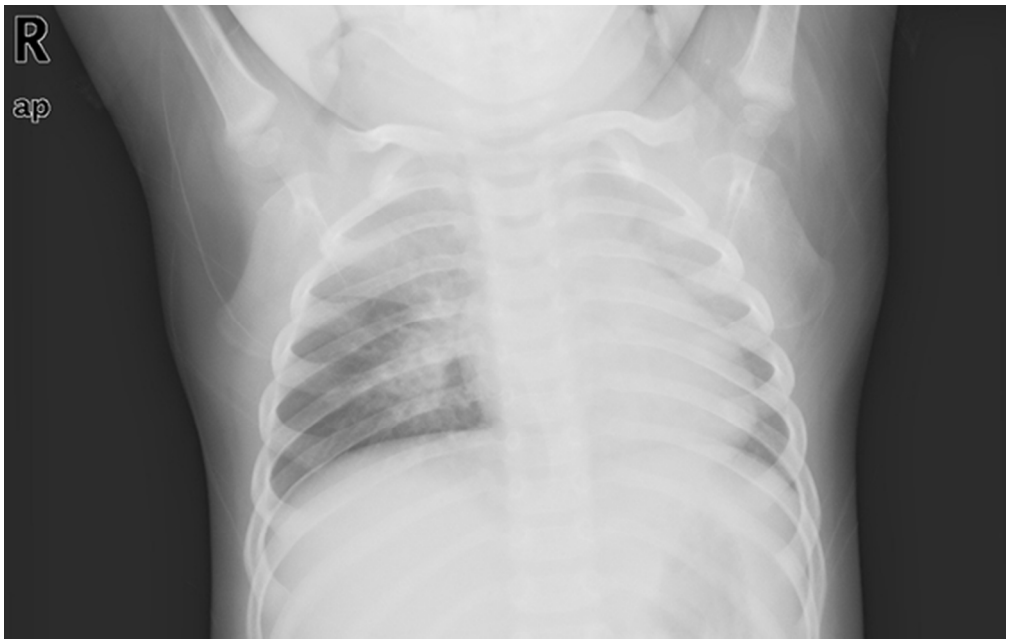
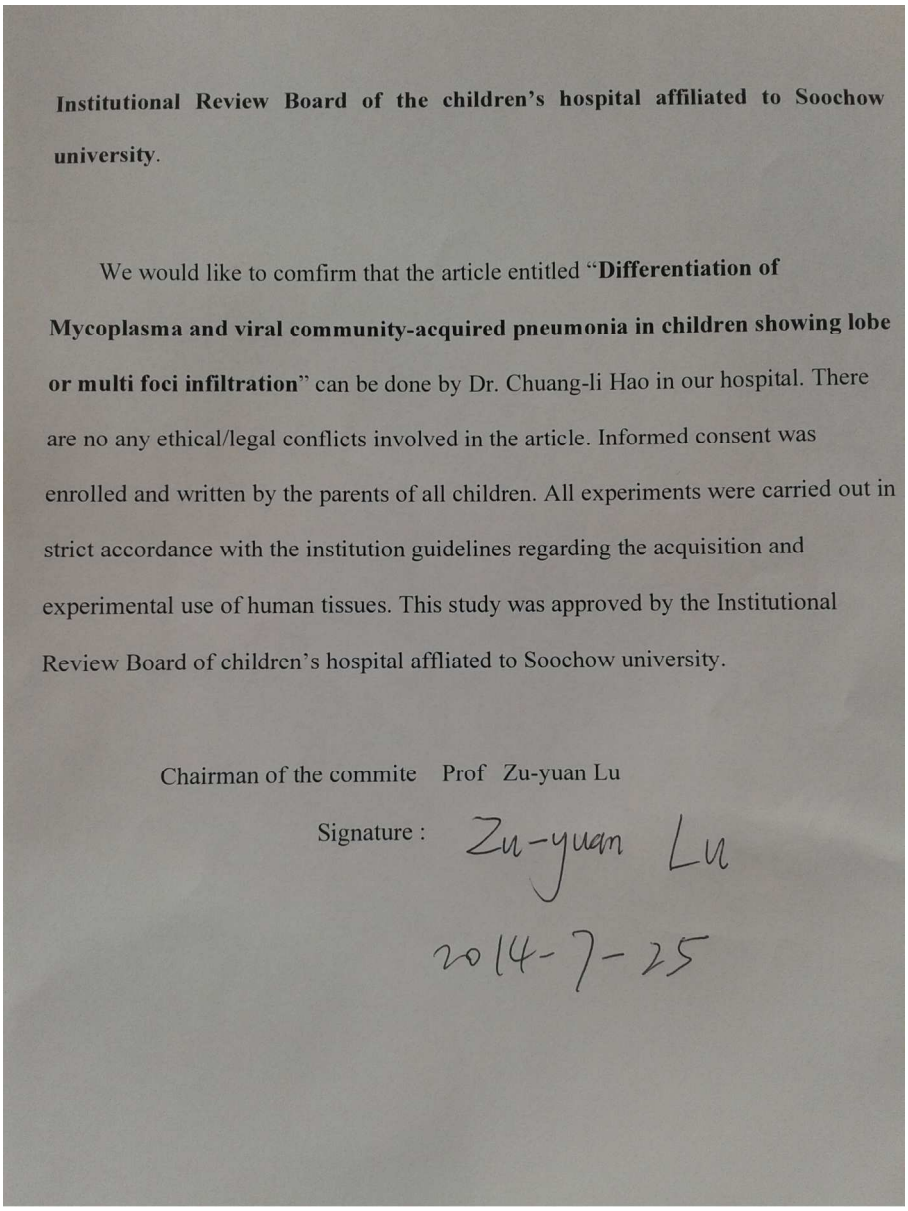


Figure 3. An example of bilateral infiltration in the left upper zone, the right upper zone and middle zone from a chest radiograph taken 4 days after the onset of symptoms in a 16-month-old girl with influenza A.
53x33mm (300 x 300 DPI)



Institutional Review Board of the children's hospital affiliated to Soochow university.

We would like to comfirm 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 affliated to Soochow university.

Chairman of the commite Prof Zu-yuan Lu

Signature : Zu-yuan Lu

2014-7-25

ethical statement
677x903mm (72 x 72 DPI)

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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.

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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 pneumoni*a. 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 ($\chi 2$), 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 "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 m*ycoplasma* 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 pneumoni*a.

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 m*ycoplasma 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 analysit: 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:

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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

symptoms	0–23 months(n=34)	2–4 years(n=39)	⩾5 years (n=53)	P value	Total(n=126)
fever >37,5◦C	7	22	31	0.0011	60
wheeze	13	2	3	<0.0001	18
increase respiratory rate	12	17	41	0.0001	70
cough	32	38	53	0.2131	123
CRP(>8)	10	27	39	<0.0001	76
lobar infiltration	11	18	25	0.9524	54
unilateral infiltration (multipe)	5	8	13	0.9524	26
bilateral infiltration	18	13	15	0.0587	46
pleural effusion	1	2	4	0.8847	7
sex(M)	24	16	31	0.0364	71

Table 2. Radiological findings in children with large consolidation of CAP

radiological findings	M	V	unknown	P-value	Total patients
lobar infiltration	28	7	19	0.8864	54
unilateral infiltration (multipe)	15	3	8	0.8864	26
bilateral infiltration	27	8	11	0.5192	46
pleural effusion	5	1	1	1.0000	7

M= mycoplasma V= viral

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

findings	M（n=70）	V（n=18）	P value
fever >37.5◦C	42	7	0.1078
wheeze	3	8	<0.0001
increase respiratory rate	29	14	0.0053
cough	69	16	0.1050
CRP(>8)	44	9	0.2231
WBC(increase)	17	6	0.4359
increase lymphocyte percentage	10	7	0.0184
increase polymorphonuclears percentage	19	4	0.6717
radiograph			
multi foci infiltration (unilateral)	15	3	0.7690
multi foci infiltration (bilateral)	27	8	0.6498
sex(M)	29	13	0.0197
age（>5 years）	32	6	0.3442

M= mycoplasma V= viral

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

variable	Chi-Square	OR	95%Wald Confidence Limits	P value
wheeze	23.0077	0.063	0.010-0.271	<0.0001
increase respiratory rate	6.7243	0.093	0.013-0.653	0.0095
increase lymphocyte percentage	8.9954	0.053	0`012-0.337	0.0027

Hosmer and Lemeshow Goodness-of-Fit Test (p=0.8979)

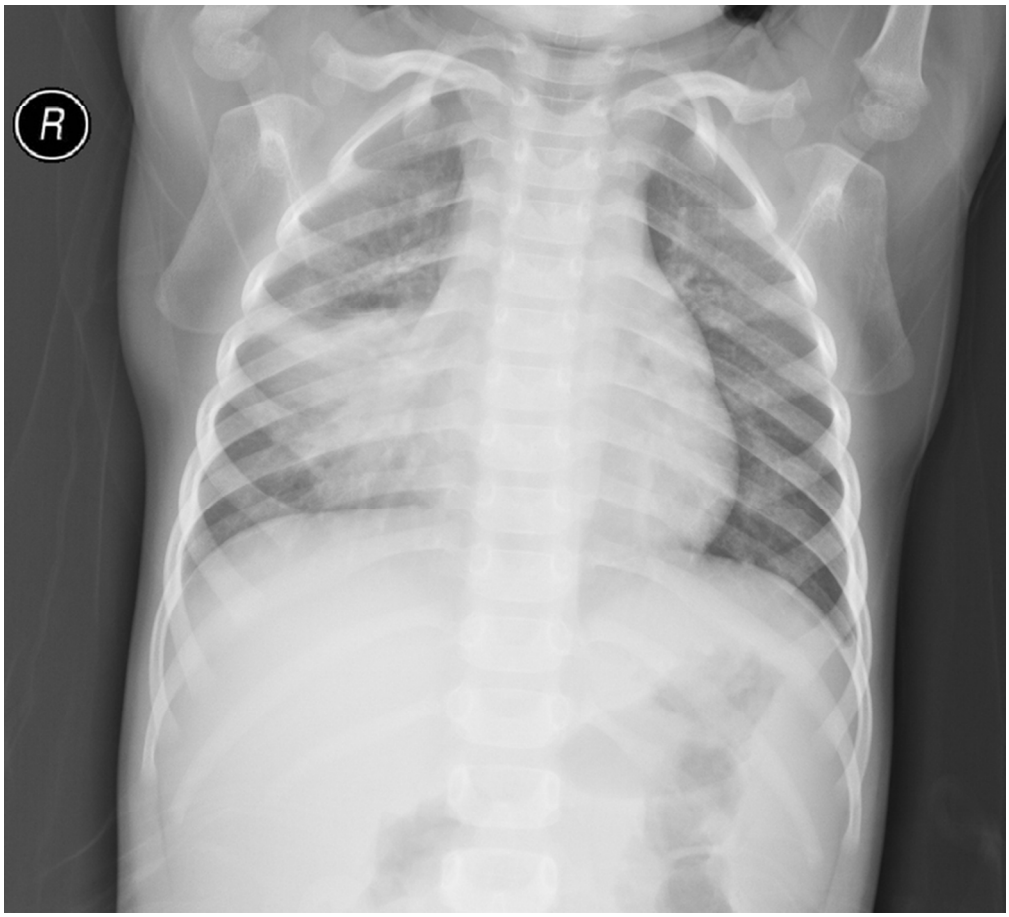

Figure 1. An example of right middle lobe infiltration from a chest radiograph obtained 6 days after the onset of symptoms in a 5-month-old girl with influenza B。
76x69mm (300 x 300 DPI)

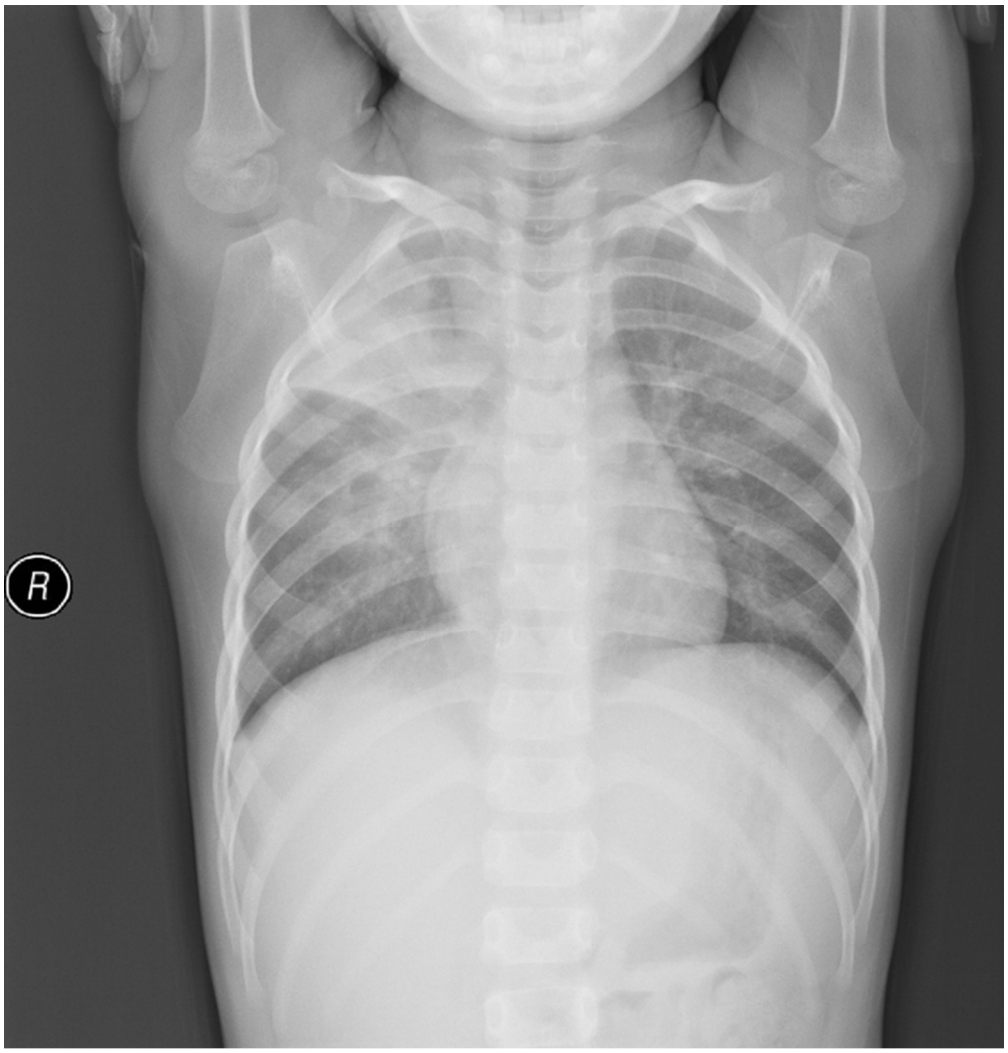

Figure 2. An example of right upper and middle lobe infiltration from a chest radiograph obtained 5 days after the onset of symptoms in a 2-year-old girl with mycoplasma pneumonia.
87x91mm (300 x 300 DPI)

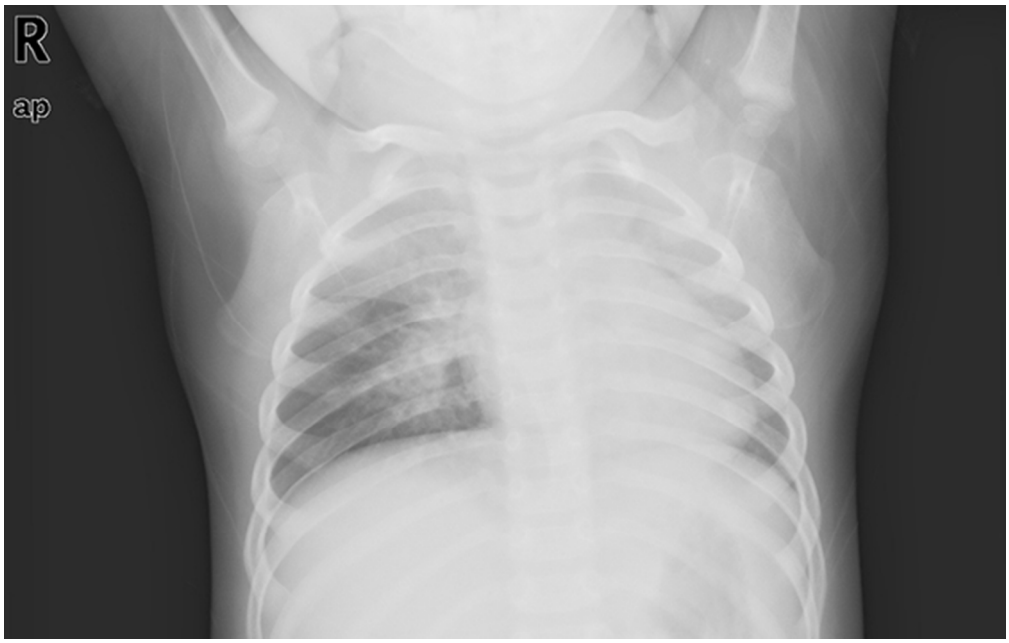

Figure 3. An example of bilateral infiltration in the left upper zone, the right upper zone and middle zone from a chest radiograph taken 4 days after the onset of symptoms in a 16-month-old girl with influenza A.
53x33mm (300 x 300 DPI)

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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 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 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.

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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).

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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 M*ycoplasma 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 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.

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:

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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

symptoms	0–23 months(n=34)	2–4 years(n=39)	⩾5 years (n=53)	P value	Total(n=126)
fever >37.5℃	7	22	31	0.0011	60
wheeze	13	2	3	<0.0001	18
increase respiratory rate	12	17	41	0.0001	70
cough	32	38	53	0.2131	123
CRP(>8)	10	27	39	<0.0001	76
lobar infiltration	11	18	25	0.9524	54
unilateral infiltration (multipe)	5	8	13	0.9524	26
bilateral infiltration	18	13	15	0.0587	46
pleural effusion	1	2	4	0.8847	7
sex(M)	24	16	31	0.0364	71

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

radiological findings	aetiology of pneumonia			P value	Total patients
	M（n=70）	V（n=18）	unknown（n=38）		
lobar infiltration	28	7	19	0.8864	54
unilateral infiltration (multipe)	15	3	8	0.8864	26
bilateral infiltration	27	8	11	0.5192	46
pleural effusion	5	1	1	1.0000	7

M= mycoplasma V= viral

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

findings	M（n=70）	V（n=18）	P value
fever >37.5℃	42	7	0.1078
wheeze	3	8	<0.0001
increase respiratory rate	29	14	0.0053
cough	69	16	0.1050
CRP(>8)	44	9	0.2231
WBC(increase)	17	6	0.4359
increase lymphocyte percentage	10	7	0.0184
increase polymorphonuclears percentage	19	4	0.6717
radiograph			
multi foci infiltration (unilateral)	15	3	0.7690
multi foci infiltration (bilateral)	27	8	0.6498
sex(M)	29	13	0.0197
age（>5 years）	32	6	0.3442

M= mycoplasma V= viral

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

variable	Chi-Square	OR	95%Wald Confidence Limits	P value
wheeze	23.0077	0.063	0.010-0.271	<0.0001
increase respiratory rate	6.7243	0.093	0.013-0.653	0.0095
increase lymphocyte percentage	8.9954	0.053	0.012-0.337	0.0027

Hosmer and Lemeshow Goodness-of-Fit Test (p=0.8979)

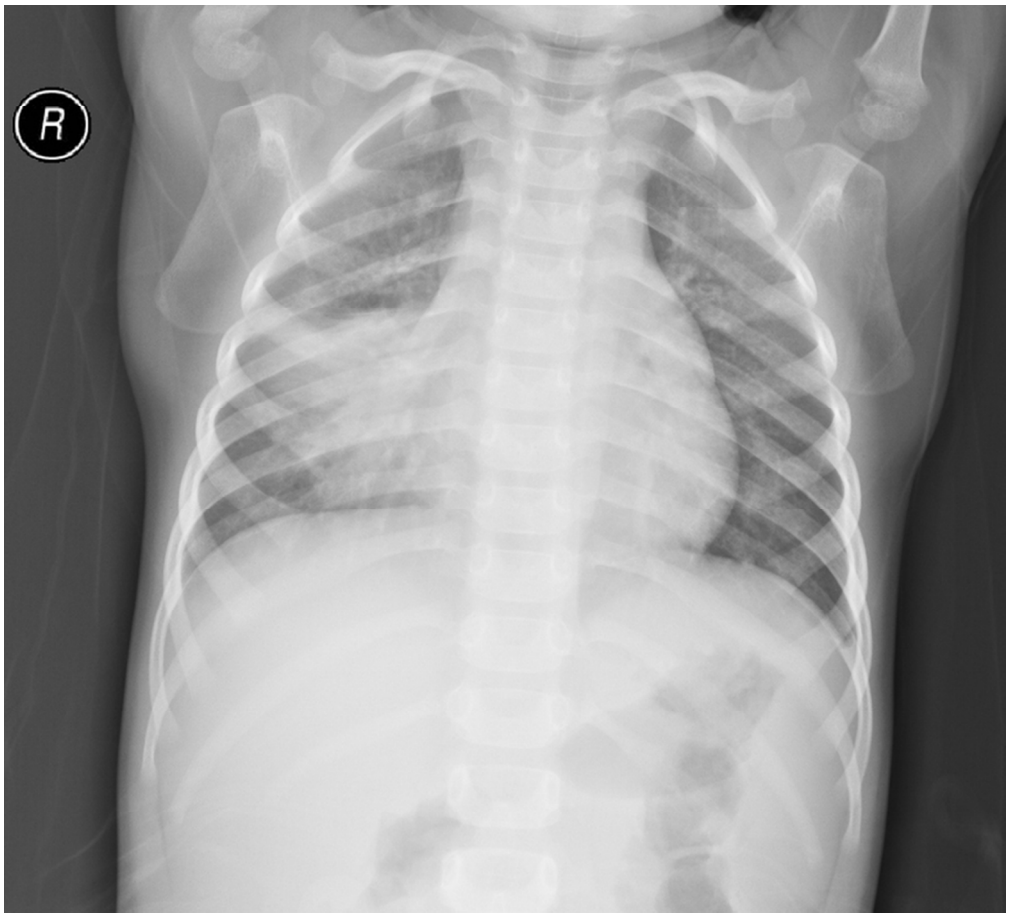

Figure 1. An example of right middle lobe infiltration from a chest radiograph obtained 6 days after the onset of symptoms in a patient with influenza B.
76x69mm (300 x 300 DPI)

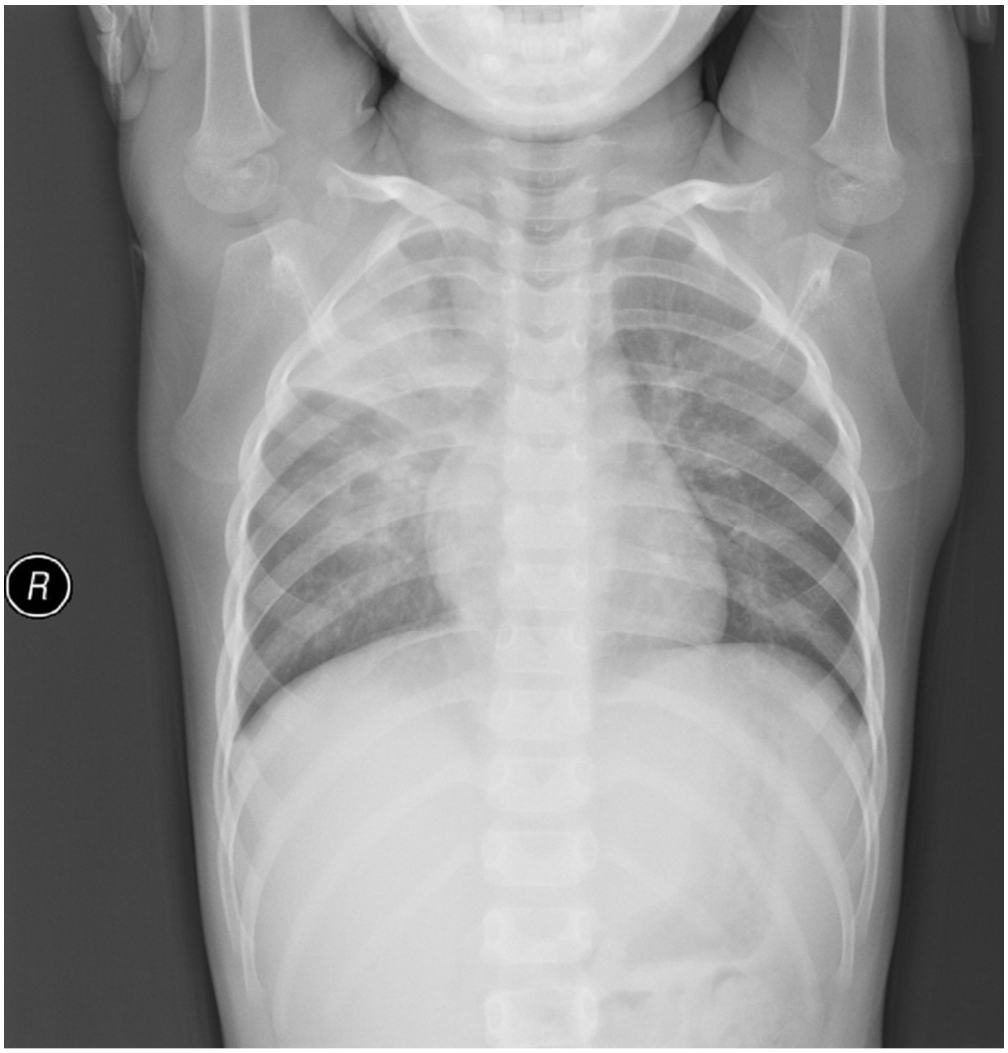

Figure 2. An example of right upper and middle lobe infiltration from a chest radiograph obtained 5 days after the onset of symptoms in a patient with mycoplasma pneumonia.
87x91mm (300 x 300 DPI)

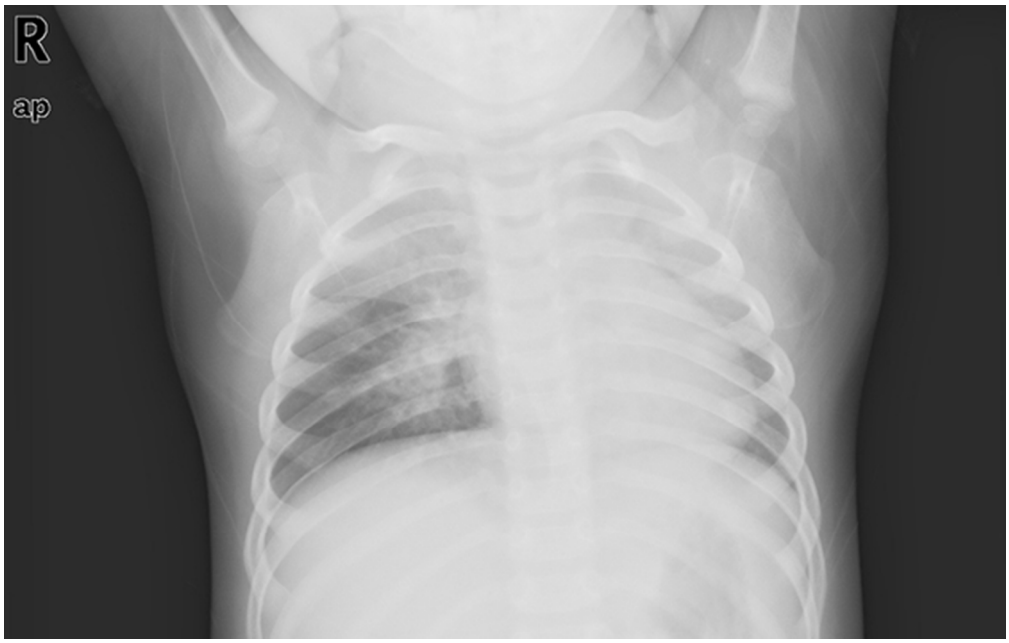

Figure 3. An example of bilateral infiltration in the left upper zone, the right upper zone and middle zone from a chest radiograph taken 4 days after the onset of symptoms in a patient with influenza A.
53x33mm (300 x 300 DPI)