Etiological profile and clinical characteristics of segmental/lobar pattern pneumonia in hospitalized children

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Abstract

The occurrence of segmental/lobar pattern pneumonia in children increases with years recently. The pathogens of the disease may change for the abuse of antibiotics and the application of pneumococal vaccines. The pathogens of segmental/lobar pattern pneumonia in hospitalized children and their association with clinical characteristics are poorly understood nowadays. The current study retrospectively analyzed the pathogens and clinical characteristics of segmental/lobar pattern pneumonia in children at a single hospital between 1 st Jan 2014 and 31 st Dec 2018. The pathogens and their associations with clinical characteristics were statistically analyzed. A total of 593 children with segmental/lobar pattern pneumonia received treatment at a single hospital during the study period. 451 patients were positive for one pathogen and 83 patients were positive for two pathogens or more. Mycoplasma pneumoniae (M.pneumoniae) (72.34%) was the most commonly detected pathogen, followed by streptococcus pneumoniae (S.pneumoniae) (8.77%). The infection of M.pneumoniae in children with segmental/lobar pattern pneumonia increased with years ($p<0.05$). The positive rate of M.pneumoniae increased with ages of patients ($p<0.05$). M.pneumoniae was statistically associated to the extrapulmonary manifestations while S.pneumoniae was statistically associated with abnormal WBCs and CRPs ($p<0.05$). In a summary, M.pneumoniae was the most positive pathogen of segmental/lobar pattern pneumonia in hospitalized children. The positive rate of M.pneumoniae in children with segmental/lobar pattern pneumonia increased with years and the ages of children. M.pneumoniae was associated with extrapulmonary manifestations while S.pneumoniae was associated with abnormal WBCs and CRPs.

Introduction

Community-acquired pneumonia (CAP) is one of the most common respiratory disorders in children, which often needs hospitalization[1]. Segmental/lobar pattern pneumonia is one of the common CAPs based on chest radiological findings of consolidation. Patients with segmental/lobar pattern pneumonia often suffer from cough, fever, and even serious complications such as pulmonary necrosis, pulmonary atelectasis, pulmonary consolidation and respiratory failure, increasing the rate of morbidity, mortality as well as the cost of health care in our society. However, the epidemiology of pathogens of segmental/lobar pattern pneumonia in hospitalized children has not been ever reported and it may vary with regions, times, antibiotics use, vaccines and so on. The detection of pathogens often needs several hours or even days. Then doctors have to treat patients with antibiotics on experiences usually, which may cause improper use of antibiotics, prolong the suffering of patients and cause more sequelae. Therefore it was important to find the pathogens profile of segmental/lobar pattern pneumonia in hospitalized children and their associations with clinical characteristics.

The occurrence of segmental/lobar pattern pneumonia in hospitalized children has increased recently, which has drawn the great attention of patients and doctors. In this research, the pathogens of segmental/lobar pattern pneumonia and their clinical characteristics were retrospectively analyzed in

children who were hospitalized in Zibo Central Hospital during 1st Jan 2014 and 31st Dec 2018 as follows.

Patients And Methods

Including and excluding criteria

Zibo city is located in the central of Shandong Province in China. Zibo Central hospital serves as a primary source of healthcare for about six million people in the area, which has moderate economic development and stable infrastructure. In the study, a retrospective review of the medical records from children with pneumonia (as defined by the specifications in the International Classification of Diseases, 10th edition, ICD-10 code) who were admitted to Zibo Central Hospital between 1st Jan 2014 and 31st Dec 2018 was conducted.

Patients who presented with clinical signs and symptoms of pneumonia underwent a chest radiograph during hospitalization. The pneumonia pattern was characterized based on the World Health Organization Standardization of Interpretation of Chest Radiographs for the diagnosis of CAP in children[2]. Two experienced pediatric radiologists evaluated chest Radiographs independently and agreed on the conclusion. Patients diagnosed with pneumonia were included in this study if the serological test of pathogens were detected ≥7 days following the onset of the disease and the chest radiographs showed segmental/lobar pattern pneumonia. Patients with pulmonary perihilar linear opacities or infiltrates or reticulonodular infiltrates by chest radiography were excluded. Patients >14 years old or suffering from known coexisting chronic, progressive or oncological illnesses were also excluded from the analysis.

A total of 9342 patients with pneumonia were admitted during the study period, of which 593 patients with segmental/lobar pattern pneumonia were included in this study. Data were collected regarding age, gender, clinical signs and symptoms, laboratory and radiological findings, complications and duration of hospitalization. Microflora was also detected using blood or sputum specimens by culturing and processing in accordance with standard microbiological procedures.

Statistical analysis.

Statistical analyses were performed using the Statistical package for the Social Science for Windows version 11.5 (SPSS, Inc., Chicago, IL, USA). Continuous variables were reported as the mean ±standard deviation. The levels of certain laboratory indices including white blood cell counts (WBCs), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) may have an association with ages of patients, so these quantitative data were transformed into categorical data (normal or abnormal). Statistical significance was assessed using the Chi-square test for categorical variables and the t-test for continuous variables. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Overview of patients

Of 9342 children hospitalized with pneumonia from 1st Jan 2014 to 31st Dec 2018, 593 patients with S/L-PP consisting of 398 boys and 195 girls were included in this study. The male to female ratio was about 2:1. The age of the patients with S/L-PP ranged from 1 year to 13 years (7.4±3.1years). The number of patients with S/L-PP each year was 86, 98,115,137 and 157 respectively during the study period. The annual incidence of children with S/L-PP increased with years over the study period ($P<0.05$). The duration of fever and cough were 4.6±2.1 days and 10.6±8.7 days respectively. 169 patients had a gasping and 208 patients had pulmonary crackles at onset. There were 149 patients with extrapulmonary manifestations including erythematous maculopapular rash, liver and kidney function lesions, and neurological complications. Only a few patients had pleural effusion. There were 383 patients with abnormal WBCs, 69 patients with abnormal ESR and 148 patients with abnormal CRP. The duration of hospital stay was 15.5±3.1 days.

Pathogen distribution with years

Table.1 summarized the distribution of pathogens with years including *M. pneumoniae*, *respiratory syncytial virus (RSV), chlamydia pneumonia (CP), influenza A virus (IFA), parainfluenza virus (PIVS), adenovirus (ADV), Q fever Coxiella (COX), Legionella pneumophila (LP), influenza B virus (IFB), S.pneumoniae, Staphylococcus aureus (S. aureus), Pseudomonas aeruginosa (P.aeruginosa), Escherichia coli (E.coli), Klebsiella pneumoniae (K.pneumoniae)*. The positive rate of *M.pneumoniae* increased over time. The number of patients infected by *M.pneumoniae* was 43, 67, 96 106, and 117 each year respectively. There were significant differences in the positive rate of *M.pneumoniae* between the groups divided by years of patients ($p<0.05$). But no significant differences were found in the positive rate for other pathogens between the groups.

Age distribution of pathogens

Table.2 summarized the distribution of pathogens with age group and showed that the positive rate of *M.pneumoniae* increased with ages. Significant differences were observed in the positive rate of *M.pneumoniae* between the age groups ($p<0.05$). However, no significant differences were found in the positive rate of other pathogens between the age groups.

Sex distribution of pathogens

Significant differences were not observed for *M. pneumoniae* and *S.pneumoniae* between male patients and female patients. 18 patients were positive for *IFB* including 6 male patients and 12 female patients. Female patients displayed significantly higher positive rate for *IFB* than male ones. No significant difference was observed for the other pathogens between sex groups.

Seasonal distribution of pathogens

In general, the seasonality profile of each individual pathogen was diverse. However, we did not observe distinct patterns for the pathogens.

Mixed infection types of pathogens

Co-infections with multiple pathogens were common. There were 91 patients in whom 2 or more pathogens were positive, representing 15.34% of the patients, and the types of co-infection were complex. These data indicated that 27.40% of the children with *M.pneumoniae* infections were co-infected with other pathogens. A total of 15 patients showed infection with 3 pathogens or more. (Table.3)

Association between pathogens and patients' demographic and clinical characteristics

Table.4 summarized the patients' demographic and clinical information found in association with pathogen infections. The patients groups were divided according to pathogens. Patients with co-infections of pathogens were excluded. Since the sample size was too small to obtain significance in some statistical analyses, only *M. pneumoniae* and *S.pneumoniae* were included in the statistical analyses. *M.pneumoniae* was statistically related to the extrapulmonary manifestations. *S.pneumoniae* was statistically associated with abnormal WBCs and CRPs. (Table.5)

Discussion

Segmental/lobar pattern pneumonia, one kind of the community-acquired pneumonias (CAP), is a common pediatric lower respiratory tract infection[3]**.** The increasing incidence of segmental/lobar pattern pneumonia with extensive alveolar infiltrates has been noted over the years. Currently therapeutic strategies on pediatric segmental/lobar pattern pneumonia are not standardized[3]. Although new antibiotics are increasingly developed, the morbidity and mortality of segmental/lobar pattern pneumonia have not met a marked fall. Generally, the patients with segmental/lobar pattern pneumonia often have more severe symptoms than those with no segmental/lobar pattern pneumonia. Segmental/lobar pattern pneumonia was more closely associated with severe manifestations, including higher rates of fever, pleural effusion, extrapulmonary manifestations, abnormal WBCs, abnormal CRP and bacterial co-infection, as well as longer durations of fever and hospitalization[4]. In our research, the duration of fever and hospitalization of the patients with segmental/lobar pattern pneumonia were 4.6±2.1 days and 15.5±3.1 days, which were similar to the previous report[4]. However, the epidemeology of pathogens of the disease and their association with clinical characteristics in children has not ever been found to be reported. Isolation of microbes is slightly difficult in children with segmental/lobar pattern pneumonia due to the difficulties in sputum expectoration and low positive rate of blood culture[5]. Some detection may be positive about a week after the onset of the disease. Therefore, the treatment of the disease based on knowledge and experience is very important. This research described the pathogens and their association with clinical characteristics in the patients with segmental/lobar pattern pneumonia, which can add knowledge and experience of the disease for doctors.

The positive rate of the pathogens in patients with segmental/lobar pattern pneumonia was highly diverse in this research. *M. pneumoniae* was the most commonly detected pathogen. The total positive rate of *M. pneumoniae* was 72.34 %(429/593). *M. pneumoniae* infection increased with time. That suggested *M. pneumoniae* has become the main pathogen of the disease. It was different from the previous report[6-7]. In fact, *M. pneumoniae* is an important cause of respiratory tract infections, and are estimated to be accountable for up to 30-40% of CAP[8-11]. The classical radiological presentations of *M. pneumoniae* pneumonia includes segmental/lobar air-space consolidation and diffuse tiny centrilobular nodules and bronchovascular thickening[12-15]. The segmental/lobar pattern pneumonia is considered to account for 17-76.5% of pediatric *M. pneumoniae* pneumonia cases and have shown an increasing trend in incidence[16-19]. Therefore, *M. pneumoniae* has drawn the great attention of clinical doctors and patients. The positive rate of *M. pneumoniae* in patients with segmental/lobar pattern pneumonia increased with ages of children. However, there have been no well explanations found for this. Then it was postulated with 3 explanations. First, there has been no any type of vaccines approved for use against *M. pneumoniae* now[20]. Second, old patients prefer social life and chances for them to be infected were higher. Third, the progression of the immune system in the patients was different between old children and young ones. A report suggested that *M. pneumoniae* pneumonia was closely correlated with the immune system of the patients[20]. The different progression state of the immune system between old patients and young ones may be related with the different positive rate of *M. pneumoniae* in the patients. The positive rate of *M.pneumoniae* in male patients was not statistically different from female ones, which suggested that *M.pneumoniae* infection was not affected by sex ratio. The patients with segmental/lobar pattern pneumonia infected by *M.pneumoniae* occurred all the year round and didn't vary with the change of seasons. The extrapulmonary complications in patients with segmental/lobar pattern pneumonia infected by *M.pneumoniae* were common and the prevalence rate may be up to 26.17 %[4], which was similar to the results in this research. However the extrapulmonary complications occurred few in patients infected by other pathogens and it was not discussed in the research.

The second positive rate of pathogen in patients with segmental/lobar pattern pneumonia was *S.pneumoniae* and it was 8% in the research. The positive rate of *S.pneumoniae* was much lower than that of *M.pneumoniae*, which was different from the previous understanding[6-7]. It may be associated with the wide application of *S.pneumoniae* vaccines in China, which can prohibit the prevalence of *S.pneumoniae* infection[21-24]. The misuse of antibiotics was common in the nationwide, which can also cut down the infection of *S.pneumoniae*. The germ culture was a low positive method. And samples used for germ culture were usually taken after the patients had taken oral or intravenous antibiotics, which was another reason for the low positive rate of *S.pneumoniae* in the study. Compared with other pathogens, *S.pneumoniae* was significantly associated with higher WBCs and CRP, which may be used for the determination of segmental/lobar pattern pneumonia pathogens in clinical practice. But it should be studied further. However, *M.pneumoniae* and *S.pneumoniae* in children with lobar pneumonia counted for 81.1% of the pathogens in total, which was much higher than that reported by Saraya T [25]. Other pathogens had low positive rate in this research, which was not discussed here.

Some patients were infected by two or more pathogens in the research. Two pathogens co-infection type was the most common one. The common co-infection type of two pathogens was *M.pneumoniae* and *S.pneumoniae*. The co-infection of 3 pathogens or more was less. The association between co-infection of pathogens and their clinical characteristics were not further discussed here for small cases.

The study is also associated with some limitations. First, clinical data were retrospectively collected based on medical records, and therefore there may have been some selection bias. Second, the sample size was not sufficiently large to obtain significance in some statistical analyses. Third, some pathogens may not be found due to the limitation of the detection method.

In a summary, *M.pneumoniae* was the commonest pathogen in the children with segmental/lobar pattern pneumonia. The prevalence of *M.pneumoniae* infection increased with time and ages of children. Old patients are more prone to be infected by *M.pneumoniae*. *M.pneumoniae* was associated with extrapulmonary manifestation while *S.pneumoniae* was associated with higher WBCs and CRPs.

Declarations

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Authors' contributions

Li yuyun and Wang yanxia conceptualized the study. Li yuyun and Wang yanxia were responsible for data curation, formal analysis and wrote the original draft. Ma liji, Li ying, Zheng yanfei and Zhang xiaoyue were responsible for resources, supervision, validation and visualization. All authors read and approved the final manuscript.

Ethical statement.and consent to participate

This study was approved by the Institutional Ethical Review Board of Zibo Central Hospital. Written informed consent was obtained from the guardians of the patients.

Patients consent for publication

Written informed consent for the publication was obtained from the guardians of the patients.

Availability of data and materials

The datasets used and/or analyzed during the current study are available fronm the corresponding author on reasonable request.

Conflicts of interest

The authors declare no conflict of interest.

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Tables

Table.1. Pathogen distribution with years in patients with segmental/lobar pattern pneumonia

year	2014	2015	2016	2017	2018	X2	p
n	86	98	115	137	157		
M.pneumoniae	43	67	96	106	117	31.46	<0.01
RSV	5	4	5	3	3	3.68	>0.05
CP	4	4	4	2	2	4.24	>0.05
IFA	4	1	3	3	2	3.76	>0.05
PIVS	6	5	5	6	4	2.76	>0.05
ADV	5	5	4	4	2	4.68	>0.05
COX	4	5	5	4	4	1.71	>0.05
LP	3	3	4	1	1	5.37	>0.05
IFB	4	4	2	4	3	2.54	>0.05
S.pneumoniae	11	10	10	11	10	3.22	>0.05

Table.2. Age distribution of pathogens in patients with segmental/lobar pattern pneumonia

age	age<3year	3≤age□6	6≤age□9	9≤age□14	X2	p
n	81	108	169	235		
M.pneumoniae	45	67	128	189	25.79	<0.01
RSV	5	4	5	6	2.56	>0.05
CP	2	5	2	7	3.10	>0.05
IFA	2	2	2	7	1.57	>0.05
PIVS	2	5	10	9	1.84	>0.05
ADV	6	2	7	4	7.44	>0.05
COX	3	3	6	11	0.81	>0.05
LP	2	3	2	5	1.01	>0.05
IFB	5	3	3	7	3.65	>0.05
S.pneumoniae	7	9	17	19	0.73	>0.05

Table.3. Mixed infection types of pathogens

Co-infection type	number
2 pathogens	76
M.pneumoniae +RSV	5
M.pneumoniae +CP	4
M.pneumoniae +IFA	4
M.pneumoniae +PIVS	7
M.pneumoniae +ADV	4
M.pneumoniae +COX	10
M.pneumoniae +LP	4
M.pneumoniae +IFB	6
M.pneumoniae + S.pneumoniae	20
M.pneumoniae + S. aureus	2
M.pneumoniae + K.pneumoniae	1
M.pneumoniae + E.coli	1
RSV+CP	1
RSV+ E.coli	1
CP+IFA	1
CP+PIVS	1
CP+ADV	1
CP+ S.pneumoniae	1
IFA+LP	1
COX+LP	1
3	14
M.pneumoniae +CP+ADV	1
RSV+LP+IFB	1
PIVS+ADV+COX	1
M.pneumoniae +PIVS+ADV	1
M.pneumoniae +CP+ S.pneumoniae	1
M.pneumoniae +RSV+LP	1
M.pneumoniae +CP+IFA	1

M.pneumoniae +ADV+IFB	1
M.pneumoniae +PIVS+COX	1
M.pneumoniae +LP+ S.pneumoniae	1
M.pneumoniae +IFA+ P.aeruginosa	1
M.pneumoniae +ADV+COX	1
M.pneumoniae +RSV+CP	1
M.pneumoniae +IFA+COX	1
4	1
M.pneumoniae +IFA+ADV+COX	1

Table.4. Association between pathogens and patients’ demographic and clinical characteristics

variables	M.pneumoniae	RSV	CP	IFA	PIVS	ADV	COX	LP	IFB	S.pneumoniae
N	353	11	7	3	14	8	6	4	8	28
gender										
male	246	10	3	3	10	4	3	2	4	20
female	107	1	4	0	4	4	3	2	4	8
age	7.8±4.1	8.4±3.1	10.2±2.6	5.4±3.6	6.5±5.2	6.8±4.5	7.6±3.8	8.3±5.2	6.8±3.9	7.9±3.5
fever										
yes	302	8	5	3	10	7	4	3	6	21
no	51	3	2	0	4	1	2	1	2	7
Duration of fever(days)	4.9±2.8	5.7±3.2	3.5±2.6	4.3±3.2	3.8±2.3	4.5±1.9	5.6±2.4	4.1±2.6	4.7±2.6	4.5±2.4
Duration of cough(days)	10.2±6.2	8.6±5.8	13.6±6.5	10.3±6.9	11.8±9.3	8.9±4.3	10.1±6.8	8.2±4.3	9.4±7.6	11.3±6.4
gasping										
Yes	122	3	0	0	1	2	0	0	0	2
No	231	8	7	3	13	6	6	4	8	26
Pulmonary crackles at onset										
yes	120	3	2	0	4	2	2	1	3	9
no	233	8	5	3	10	6	4	3	5	19
Pleural effusion										
Yes	15	2	1	0	1	0	0	0	1	1
no	340	9	6	3	13	8	6	4	7	23
Extrapulmonary manifestations										
Yes	102	0	0	1	2	1	0	0	1	3
no	251	11	7	2	11	7	6	4	7	25
WBC										

abnormal	245	5	4	2	6	5	5	2	4	27
normal	108	6	3	1	6	3	4	2	4	1
ESR										
abnormal	36	1	2	0	1	1	0	1	2	3
normal	317	10	5	3	12	7	6	3	6	25
CRP										
abnormal	81	3	2	1	4	3	2	1	3	24
normal	272	8	5	2	8	5	4	3	5	4
Duration of hospitalization (days)	15.8±4.1	14.2±4.3	13.6±5.8	12.5±3.6	14.9±5.2	15.1±3.7	13.9±6.2	14.7±5.1	14.6±2.4	15.3±4.4

Table.5. Comparison between M.pneumoniae and S.pneumoniae with patients' demographic and clinical characteristics

variables	M.pneumoniae	S.pneumoniae	X2	p
N	353	28		
gender				
male	246	20	2.06	>0.05
female	107	8		
age	7.8±4.1	7.9±3.5	0.13	>0.05
fever				
yes	302	21		
no	51	7	1.5>0.05	
Duration of fever(days)	4.9±2.8	4.5±2.4	0.73	>0.05
Duration of cough(days)	10.2±6.2	11.3±6.4	0.90	>0.05
gasping				
Yes	122	2		
No	231	26	8.88<0.01	
Pulmonary crackles at onset				
yes	120	9		
no	233	19	0.05>0.05	
Pleural effusion				
Yes	15	1		
no	340	23	0.26>0.05	
Extrapulmonary manifestations				
Yes	102	3		
no	251	25	4.3<0.05	
WBC				
abnormal	245	27		
normal	108	1	9.28<0.01	
ESR				
abnormal	36	3		
normal	317	25	0.06>0.05	

CRP				
abnormal	81	24		
normal	272	4	51.2<0.01	
Duration of hospitalization (days)	15.8±4.1	15.3±4.4	0.62	>0.05