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【 ORIGINAL ARTICLE 】

The Correlation between Chest X-ray Scores and the Clinical Findings in Children and Adults with *Mycoplasma pneumoniae* Pneumonia

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Abstract:

Objective To compare the radiological and laboratory data of children and adults with *Mycoplasma pneumoniae* pneumonia (MPP) and to evaluate the correlation between the total affected lung area and the clinical findings.

Methods We retrospectively examined the data from MPP patients who visited our hospital during the period from April 2006 to July 2014. All data were retrieved at the time of the diagnosis of MPP and were analyzed to investigate the correlation between the clinical findings and the total affected lung area using a chest X-ray scoring system.

Results We identified 71 children and 54 adults with MPP. The incidence of consolidation, which was the most common chest X-ray finding in both groups, was similar (children: n = 62, 87.3%; adults: n = 45, 83.3%). In contrast, air bronchogram, bronchial thickening, and atelectasis were observed significantly more frequently among children than among adults. In both groups, a chest X-ray scoring system revealed a zonal predominance of the affected area (middle-to-lower lung fields). The body temperature and serum data such as the C-reactive protein level, white blood cell count, and lactate dehydrogenase level were significantly higher in the child group than in the adult group. The total score did not significantly correlate with the above-mentioned inflammatory markers or the presence of hypoxemia in either group.

Conclusion This study showed the first evidence of a correlation between the extent of lung abnormalities on chest X-ray (calculated as a total score) and the clinical findings, including the presence of hypoxemia, in children and adults with MPP.

Key words: *Mycoplasma pneumoniae* pneumonia, chest X-ray, scoring system, hypoxemia, child and adult

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Introduction

Mycoplasma pneumoniae (MP) pneumonia (MPP) is well known for its diverse radiological findings. In a previous report, we developed a system for scoring the affected area on thoracic computed tomography (CT) in adult patents with MPP, and reported that the affected area was associated with the presence of hypoxemia (1). However, to the best of our knowledge, no one has elucidated the correlation between the areas of lung involvement on chest X-ray and the clinical findings in both children and adults with MPP. In the present study, we retrospectively analyzed the data of MPP, to investigate the association between the values obtained by a chest X-ray scoring system and the clinical findings.

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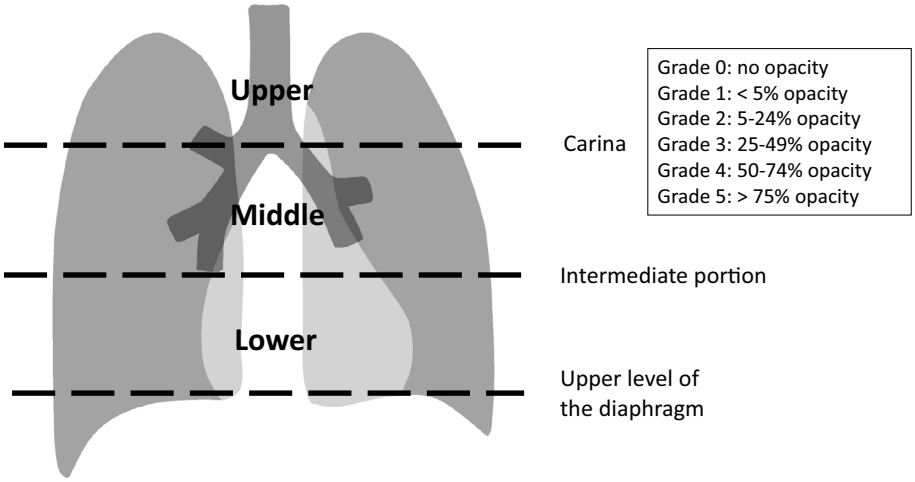

Figure 1. **The chest X-ray was divided into three levels: 1) the bronchial bifurcation, 2) the upper level of the diaphragm, and 3) halfway between levels 1) and 2). Each area was calculated as follows: Grade 0, no opacity; Grade 1, <5% opacity; Grade 2, 5-24% opacity; Grade 3, 25-49% opacity; Grade 4, 50-74% opacity; and Grade 5, >75% opacity. The total score was calculated as the sum of the scores for the six areas.**

Materials and Methods

We retrospectively examined the data of MPP patients who visited our hospital during from April 2006 to July 2014. This study was approved by the ethics committee of Kyorin University on July 2014 (approval number: H26-032).

For the purpose of the present study, "child" was defined as <15 years of age, while "adult" was defined as ≥15 years of age. The diagnostic criteria for MPP were as follows: 1) the presence of new abnormal lung shadows on a chest X-ray, and one of the following: 2) a ≥4-fold titer rise [complement fixation (CF) or particle agglutination (PA) tests] during the convalescent phase in comparison to the acute phase; or a single PA titer of >1:160; or 3) the isolation of MP in sputum culture.

The chest X-ray films were divided into three levels: 1) the bronchial bifurcation, 2) the upper level of the diaphragm, and 3) halfway between 1) and 2) (Fig. 1), and total visual scores were defined as follows: grade 0, no opacity; grade 1, 5% opacity; grade 2, 5-24% opacity; grade 3, 25-49% opacity; grade 4, 50-74% opacity; and grade 5, ≥ 75%. The scoring system that was applied in the present study consisted of a total of six areas, the scores for each area were summed to determine the total score (range, 0-30). Two pulmonologists and one radiologist with >10 years of experience independently reviewed each chest X-ray film; the final decisions were made after the examiners reached a consensus. The correlations between the total score and the clinical and/or laboratory data were also evaluated.

Statistical analysis

The distribution and variance of numeric data were evaluated using the Kolmogorov-Smirnov test and Levene's median test, respectively. Categorical data are presented as percentages of the total or numerically, as appropriate. Statistical comparisons of nonparametric data were performed using the Mann-Whitney test. Categorical data were compared using the chi-squared test. All tests were two-sided. p values of <0.05 were considered to indicate statistical significance. All statistical analyses were performed using the SPSS software program (version 19.0 for Windows).

Results

The clinical characteristics of the children and adults with MPP

We identified a total of 71 children and 54 adults with MPP. The characteristics of the two groups were comparable with regard to the proportions of sex, underlying respiratory diseases, the incidence of hypoxemia, and incidence of antecedent treatment with macrolide therapy (Table 1). Furthermore, the duration from the onset of symptoms until the referral of the patient to our hospital (with/without treatments at the local hospital) was similar in the two groups (mean± SD: children, 7.1±2.4 days versus adults, 6.9±4.6 days; not significant) (Table 1). However, the child group showed significantly higher body temperatures (children, 38.4 ± 0.8 vs. adults, 37.7 ± 1.1°C, p = 0.03) and higher serum levels of lactate dehydrogenase (LDH; 369 ± 142 vs. 237 ± 68.2 IU/L; p <0.001) and aspartate aminotransferase (36.4 ± 14.8 vs. 28.0 ± 16.8 IU/L, p <0.001) in comparison to the adult group. In contrast, the serum C-reactive protein levels in the adult group were significantly higher in comparison to the child group (adult group, 9.2 ± 9.0 mg/dL vs. child group, 3.0 ± 3.6 mg/dL; p <0.001).

Table 1. Comparisons of Clinical Characteristics between the Child and Adult MPP Groups.

	Child (n=71)	Adult (n=54)	p value
Age (years)	7.9 ± 3.6	37.6 ± 18.1	p<0.001
M:F	34:37	18:36	NS
Underlying diseases (%)	11.1 (7/63)	23.4 (11/47)	NS
Asthma	7	9	NS
Emphysema	0	1	NS
Lung caner	0	1	NS
Initial onset to first visit to our hospital (days)*	7.1±2.4	6.9±4.6	NS
BT (°C)	38.4 ± 0.8	37.7 ± 1.1	p=0.03
Hypoxemia (%)	18.1 (4/22)	12.2 (5/41)	NS
Antecedent macrolide treatment (%)	46 (23/50)	38.2 (18/47)	NS
WBC ($\times 10^3/\mu L$)	8.5 ± 5.5	8.5 ± 4.4	NS
CRP (mg/dL)	3.0 ± 3.6	9.2 ± 9.0	p<0.001
LDH (IU/L)	369 ± 142	237 ± 68.2	p<0.001
AST (IU/L)	36.4 ± 14.8	28.0 ± 16.8	p<0.001
ALT(IU/L)	23.9 ± 22.3	22.4 ± 18.2	NS
Diagnostic method			
Single titer (PA≥1:320 or CF≥1:64)	66 (93.0%)	40 (74.1%)	p=0.005
Pair (×4)	5 (7.0%)	14 (25.9%)	p=0.005
Culture	0 (0)	1 (1.9%)	NS

AST: aspartate aminotransferase, ALT; alanine aminotransferase, BT: body temperature, CRP: C-reactive protein, F: female, LDH: lactase dehydrogenase, M:male, WBC: white blood cell counts

* Data are presented as mean±standard deviation

Table 2. Comparisons of Radiological Findings between the Child and Adult MPP Groups.

	CHILD (%)	ADULT (%)	p value
Total number of patients	71	54	
Consolidation	62 (87.3)	45 (83.3)	NS
Air bronchogram	43 (60.6)	18 (33.3)	p=0.004
Reticular shadowing	20 (28.2)	11 (20.4)	NS
Tiny nodules	17 (24.0)	12 (22.2)	NS
Bronchial wall thickening	24 (33.8)	8 (14.8)	p=0.022
Pleural effusion	1 (1.4)	4 (7.41)	NS
Atelectasis	7 (9.9)	0 (0)	p=0.019

The radiological findings between children and adults with MPP

Regarding the chest X-ray findings, consolidation was a major radiological finding in both groups (Table 2). Air bronchogram, bronchial wall thickening, and atelectasis were observed significantly more frequently in the child group than in the adult group. Other findings, such as reticular shadowing, tiny nodules, and pleural effusion, did not differ to a statistically significant extent.

The clinical significance of the chest X-ray score and the zonal predominance of MPP

The correlation between hypoxemia and the total affected lung areas (calculated according to the total score) was not statistically significant in either of the groups (Fig. 2A, D). Importantly, no correlation was found between the time from the onset of symptoms to referral to our hospital and the total score in either group (data not shown). Regarding zonal predominance, MPP predominantly affected the middle-to-lower lung fields in both groups (Fig. 2B, E). Interestingly, a moderate positive correlation was found between the total score and the maximum PA titer value ($r = 0.409$, $p < 0.001$), but only in the child group (Fig. 2C, F). The total score was not significantly correlated with the serum inflammatory markers [white blood cell count (WBC), LDH, and C-reactive protein (CRP)] in either group (data not shown).

The correlations between the serum LDH levels and the proportion of hypoxemia in children and adults with MPP

No correlation was found between the presence of hypoxemia and the serum LDH levels in either the child group or the adult group; however, a non-significant positive correlation was observed in the latter group ($p = 0.074$) (Fig. 3).

Discussion

This study provides the first evidence of the relevance of the total affected lung area (calculated as a total score) on chest X-ray films and the clinical and laboratory findings in both children and adults with MPP.

Firstly, no correlation was found between the total score and the presence of hypoxemia in either children or adults with MPP. This was contrary to our previous report, in which a scoring method was applied to assess the thoracic

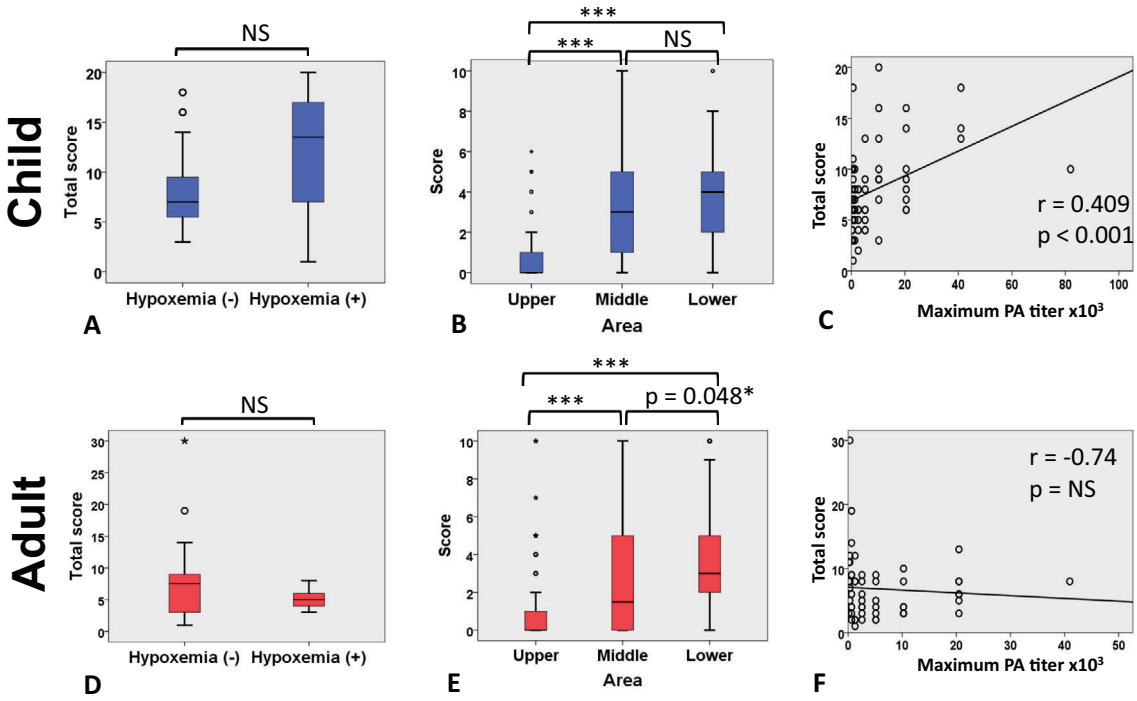

Figure 2. **No significant correlation between hypoxemia and the total score was found in the child group or the adult group (A, C). MPP was predominantly located in the middle-to-lower lung fields in both groups (B, D). A moderate positive correlation was found between the total score and maximum PA titer value (r=0.409, p<0.001) only in the child group (C, F). *p value <0.05. ***p value <0.001**

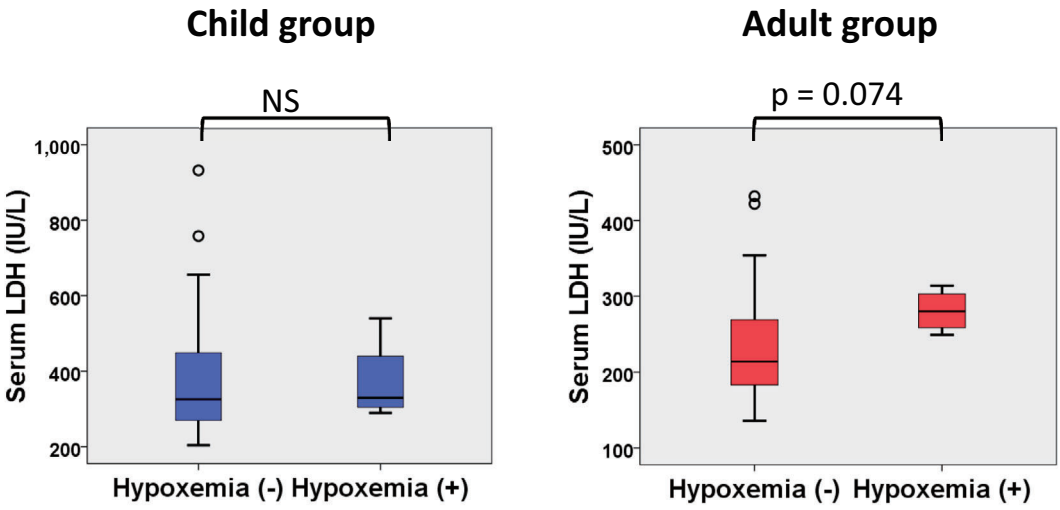

Figure 3. **No correlation was found between the presence of hypoxemia and the serum LDH level in either group.**

CT scans of adults with MPP (1). This may be because chest X-rays show lower sensitivity in the detection of faint shadowing in comparison to thoracic CT or due to absence of severe MPP patients who required admission to an ICU and/or mechanical ventilation.

Secondly, this study clearly demonstrated that the middle-to-lower lung fields were predominantly affected by MPP. Previous studies in which chest X-ray films were analyzed implied that the lower lung field was predominantly affected in both children and adults with MPP (2, 3), while peribronchial and perivascular interstitial infiltration and/or air space consolidation were the common radiological patterns. These trends were quantitatively confirmed in the present study, with the use of the chest X-ray scoring system and by the assessment of the radiological patterns.

Although the precise reason why the incidence of atelectasis in children with MPP was significantly higher in comparison to adults with MPP is unknown, it was possibly

caused by the obstruction of the airway by a mucus plug due to the increased expression of mucins by the bronchial epithelial cells after MP infection (4).

Thirdly, a positive correlation between the maximum PA titer and the total score was only observed in children with MPP . This discrepancy suggested the possibility that an excessive immune reaction to MP antigens (5-7), which was predominantly attributed to the inflammatory process, occurred in children rather than adults. Indeed, the findings of Tanaka et al. (8, 9) and the data from our previous studies (5-7) demonstrated that the enhanced cellular-mediated and/or humoral immune response to MP can exaggerate lung inflammation in mouse models.

Notably, the total lung score was not correlated with the presence of hypoxemia. This finding was anticipated by general physicians who treat MPP pneumonia. The serum LDH level has been considered a marker for refractory MPP (10); however, no one has elucidated the significance of LDH levels in predicting hypoxemia. In this regard, the present study demonstrated a lack of correlation between these factors.

This study is associated with some limitations. Firstly, the extent of lung abnormalities might have been underestimated due to the low sensitivity of chest X-rays in the detection of tiny nodules and reticular shadowing, which might have affected the relationship between the total score and the laboratory/clinical findings. Furthermore, this study was conducted at a regional referral center; thus, the adult MPP patients seemed to have a greater incidence of underlying respiratory disease in comparison to the typical MPP patients described in previous reports (11) who were usually treated in local hospitals. This might have affected the results of our study.

However, physicians who treat MPP patients have usually recognized that no correlation exists between the extent of lung involvement on chest X-ray and the presence of hypoxemia. The results of the present study are compatible with their position.

Conclusion

This study showed the first evidence of a correlation between the quantitatively calculated area of lung abnormalities on chest X-ray films and the clinical findings, including the presence of hypoxemia, in both children and adults with MPP.

The authors state that they have no Conflict of Interest (COI).

Takeshi Saraya and Takayasu Watanabe contributed equally to this work.

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