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Late Abnormal Findings on High-Resolution Computed Tomography After Mycoplasma Pneumonia

Chang Keun Kim, MD*; Churl Young Chung, MD*; Joung Sook Kim, MD‡; Woo Sun Kim, MD§; Yang Park, MD∥; and Young Yull Koh, MD∥

ABSTRACT. Background. The clinical course of Mycoplasma pneumonia is typically mild and self-limited. There are, however, several case reports of severe complication following this illness with considerable morbidity and mortality.

Objectives. This study was conducted to investigate, using high-resolution computed tomography (HRCT), the long-term pulmonary structural abnormalities after Mycoplasma pneumonia and to identify risk factors (chest radiograph findings, antibody titers, and host factors) that might increase the likelihood of developing the sequelae.

Methods. Thirty-eight children requiring hospitalization attributable to Mycoplasma pneumonia were recruited by the retrospective examination of hospital records. They underwent HRCT after an interval of 1.0 to 2.2 years. A control group of 17 children with the history of Mycoplasma upper respiratory infection was also studied after a similar interval.

Results. Abnormal HRCT findings were present in 37% (14/38) of the pneumonia group, compared with 12% (2/17) of the control group. The abnormalities in the pneumonia group, which appeared alone or in combination, included mosaic perfusion (n = 12), bronchiectasis (n = 8), bronchial wall thickening (n = 4), decreased vascularity (n = 1), and air trapping on expiratory scan (9 of 29 tested). The area affected by these abnormalities, usually involving 2 or more lobes, corresponded in all cases to the location of the infiltrate on chest radiograph at the time of pneumonia. Between subjects with abnormal HRCT (n = 14) and normal HRCT (n = 24) in the pneumonia group, significant differences were observed in age at the time of pneumonia (mean ± standard deviation: 5.3 ± 2.0 years vs 7.7 ± 3.4 years) and peak mycoplasma antibody titer (geometric mean [range of 1 standard deviation]; 1:7943 [3126–19 953] vs 1:3093 [832–11 482]).

Conclusions. We conclude that a considerable proportion of children with history of Mycoplasma pneumonia have abnormal findings on HRCT, suggestive of small airway obstruction and that younger age and higher antibody titer at the time of pneumonia may be risk factors for these sequelae. Pediatrics 2000;105:372–378; Mycoplasma pneumonia, HRCT, mosaic perfusion, bronchiectasis, age, mycoplasma antibody titer.

ABBREVIATIONS. HRCT, high-resolution computed tomography; SD, standard deviation; HU, Hounsfield unit.

Lobar pneumonia is typically mild and self-limited. Unresolved lobar pneumonia with pleural effusion or pneumatocele, adult respiratory distress syndrome, coagulopathies, and severe necrotizing pneumonitis have all been described. Mycoplasma pneumonia also may lead to longstanding pulmonary sequelae such as chronic interstitial fibrosis, bronchiolitis obliterans, and the Swyer-James syndrome, a variant of postinfectious bronchiolitis obliterans.

The pathologic sequelae, such as these lesions, after Mycoplasma pneumonia have been infrequently reported, probably because of a relative scarcity of histologic materials. Biopsy is an invasive procedure; therefore, it is rarely performed except in severely ill patients or in special circumstances. Although a few follow-up studies describe pulmonary function after Mycoplasma pneumonia, these studies do not address the pathologic sequelae of this disease. High-resolution computed tomography (HRCT) is currently the best imaging technique to evaluate bronchial and bronchiolar abnormalities noninvasively. It allows assessment of the anatomic abnormalities, as well as of some of the physiologic responses related to these abnormalities. To date, there has been no description of the range of findings on HRCT after Mycoplasma pneumonia.

This study was conducted to investigate, using HRCT, the long-term pulmonary structural abnormalities after Mycoplasma pneumonia and to identify risk factor(s) that may increase the likelihood of developing the sequelae. A control group who had Mycoplasma upper respiratory tract infections was also studied to confirm that long-term abnormalities were in fact caused by the pneumonia.
This study was conducted on the children who underwent HRCT after *Mycoplasma* pneumonia (pneumonia group: \( n = 38 \)), or after upper respiratory tract infection due to *Mycoplasma* (control group: \( n = 17 \)).

The pneumonia group consisted of 21 boys and 17 girls, who had been admitted to Seoul National University Children’s Hospital and Inje University Sanggye Paik Hospital with *Mycoplasma* pneumonia from October 1995 through March 1996. The mean (±standard deviation [SD]) age at the time of pneumonia was 6.8 (±3.2) years. The diagnosis of pneumonia was based on clinical (fever, cough, rales, etc.) and radiologic (lobar, patchy, and linear infiltrates) criteria, and on the demonstration of a fourfold or greater increase in the titer of anticytomegalovirus antibodies in acute and convalescent sera. Details regarding the admission were collected by retrospective examination of the hospital records. The titration of anticytomegalovirus antibodies in serum specimen was performed with use of the indirect particle agglutination test (Serodia-Myc II, Fujirebio, Japan). The titer was checked weekly until it showed a tendency to sustain or fall, thus the peak level was ascertained. A total of 55 cases of *Mycoplasma* pneumonia during the above period were enrolled by retrospective screen of hospital records. Fourteen of these cases were excluded because of: incomplete hospitalization data (\( n = 4 \)), failure to ascertain the peak anticytomegalovirus titer (\( n = 2 \)), loss to follow-up (\( n = 4 \)), evidence of an additional lower respiratory tract infection (\( n = 6 \)) and the time of respiratory infection in the interval between the hospitalization for the pneumonia and the time of HRCT (\( n = 2 \)), and no compliance with HRCT (\( n = 2 \)). In addition, 3 cases were excluded because they had had chronic respiratory symptoms before hospitalization.

A control group of 17 patients (9 boys and 8 girls) with the history of *Mycoplasma* upper respiratory tract infection were studied for comparison. The mean age at the time of this illness was 6.4 (±2.27) years. From the record of control cases, the hospital records of children who attended the outpatient clinic during the same period with upper respiratory tract symptoms, fourfold or higher rise in anticytomegalovirus antibody titer between the 2 consecutive serum samples, and normal chest radiographs were reviewed. Letters were sent to their parents requesting cooperation. Of the 24 replies received, 5 declined and 2 failed to attend the study.

HRCT was performed after an interval of 1.0 to 2.2 years (mean: 1.5) following pneumonia (pneumonia group) and after an interval of 1.0 to 2.1 years (mean: 1.4) following upper respiratory tract infection (control group). The HRCT scans were obtained at 10-mm intervals with the subjects in the supine position from the aortic arch to the diaphragm using 120 kVp and 320 mAs. In children older than 5 years of age, the scans were obtained while they held their breath with full inspiration. Subjects younger than 5 years of age needed sedation before HRCT screening because they were too active to lie quietly on the scanning table. In these children, the scans were performed during quiet respiration without breath holding. In 40 cases (29 cases in the pneumonia group and 11 cases in the control group), additional scans were obtained during maximal expiration. The images were photographed at window levels from −600 to −700 Hounsfield unit (HU) and a window width of 1000–1500 HU. A high-resolution (1.0-mm collimation) reconstruction was made using a high-spatial-frequency algorithm.

The HRCT scans were assessed independently by 2 chest radiologists for the presence and distribution of parenchymal, pleural, hilar, or mediastinal abnormalities. In addition, each individual lung lobe was identified and assessed specifically for the presence or absence of bronchial dilation, bronchiolar wall thickening, decreased pulmonary vascularity, and increased or reduced parenchymal attenuation. Air trapping on expiratory HRCT was also assessed. The radiologists were blinded as to which group each patient belonged. Bronchiectasis was considered present when the bronchi appeared larger than the accompanying pulmonary arteries. Bronchial wall thickening was described when the bronchial walls were seen as discrete structures in the distal third of lung parenchyma. Decreased vascularity was defined as a reduction in vessel caliber and/or number. Scattered irregular areas of high- and low-attenuation areas were interpreted as mosaic perfusion. After each observer had assessed the scans independently, they examined them together and reached a final decision by consensus.

Parents of the subjects enrolled in this study gave informed consent and the study was approved by the hospital’s ethics committee.

### Statistical Analysis

Results were expressed as mean ± SD unless otherwise indicated. A comparison of values or incidences between the groups and among the subgroups was made using unpaired Student’s t tests or χ² tests. In each case, a P value < .05 was considered statistically significant.

### RESULTS

In the pneumonia group (\( n = 38 \)), the mean (±SD) duration of hospital stay was 10.0 (±5.1) days, and that of fever and cough was 9.9 (±4.8) days and 3.0 (±9) weeks, respectively. Wheezing was recorded in 7 children. The chest radiographs were divided into 3 patterns:10 lobar (13 patients), patchy (11 patients), and linear (14 patients). On diagnosis, treatment with oral erythromycin or roxithromycin was started immediately and continued for 14 days. Three children received oxygen therapy, but no one was treated with mechanical ventilation. The geometric mean (range of 1 SD) of peak anticytomegalovirus antibody titer, usually obtained 2 or 3 weeks after admission, was 1:3890 (1148–13183). During the follow-up period from pneumonia to HRCT, recurrent cough and intermittent wheeze or dyspnea were noted occasionally in 10 patients. These episodes occurred usually in association with upper respiratory infection and were not affected by bronchodilator therapy.

Pulmonary abnormalities were detected on HRCT in 14 (36.8%) of the pneumonia group (Table 1). Abnormal HRCT findings were mosaic perfusion (\( n = 12, 31.6\% \)), bronchiectasis (\( n = 10, 26.3\% \)), bronchial wall thickening (\( n = 4, 10.5\% \)), and decreased pulmonary vascularity (\( n = 1, 2.6\% \)). Nine (31.0%) of the 29 patients who underwent expiratory HRCT had air trapping. Eleven had at least 2 of the 5 findings on HRCT and all 9 patients with air trapping also had other abnormal findings. The most frequent finding was mosaic perfusion, and 8 of 12 patients with this finding also had bronchiectasis. Bronchiectasis was observed at segmental or subsegmental level, usually in combination with mosaic perfusion or bronchial wall thickening. One subject (subject 3) had unilateral hyperlucent lung on a chest radiograph. This subject showed decreased pulmonary vascularity in addition to mosaic perfusion and bronchiectasis on HRCT.

Pulmonary abnormalities were detected on HRCT in 2 (11.8%) of the control group, bronchiectasis in 1 and bronchial wall thickening in 1, respectively. Mosaic perfusion, decreased pulmonary vascularity, or air trapping on expiratory HRCT was not seen in the control subjects (data not shown).

Table 2 shows extent of abnormal findings on HRCT in the pneumonia group. The number of lobes most commonly involved were 2 lobes for mosaic perfusion and bronchiectasis and 3 or more lobes for air trapping. Bronchial wall thickening was confined to 1 or 2 lobes, and decreased vascularity, to 2 lobes. The involved area on HRCT corresponded to that of infiltrate on a chest radiograph at the time of pneumonia in all 14 patients. Figure 1 is an illustrative example for this. Bronchiectasis or bronchial wall...
thickening found in control subjects was confined to 1 lobe (data not shown).

Based on the presence or absence of abnormal HRCT findings, the pneumonia group was classified into 2 groups (Table 3). There were no differences with respect to sex, duration of hospital stay, fever or cough, occurrence of wheeze, pattern of chest radiograph, white blood cell count, and erythrocyte sedimentation rate at the time of pneumonia. However, significant intergroup differences were observed in age at the time of pneumonia (abnormal HRCT group: 5.3 ± 2.0 years vs normal HRCT group: 7.7 ± 3.4 years; $P < .05$) and peak antibody titer (geometric mean [range of 1 SD]: abnormal HRCT group, 1:7943 [3126–19 953] vs normal HRCT group, 1:3093 [832–11 482]; $P < .05$). The interval from pneumonia to HRCT was not different between the 2 groups.

To further substantiate risk factors that may increase the likelihood of developing abnormal HRCT findings, we stratified the pneumonia group patients according to age at the time of pneumonia and peak antibody titer (Table 4). The abnormal findings were more commonly seen in patients with younger age at the time of pneumonia (<8 years) than in patients with older age (≥8 years; 52.4% [11/21] vs 17.6% [3/17]; $P < .05$). This tendency was noted, although not statistically significant, when the patients were divided into 2 groups based on peak titer level (high titer: 69.2% vs 37.5% and low titer: 25% vs 0%). In the total population, the abnormal findings were more commonly seen in patients with high peak titer (antibody titer: ≥1:5120) than in patients with low peak titer (antibody titer: <1:2560; 57.1% [12/21] vs 11.8% [2/17]; $P < .05$). This tendency was noted, although not statistically significant, when the patients were divided into 2 age groups (younger age: 69.2% vs 25% and older age: 37.5% vs 0%).

An open lung biopsy was performed in subject 3 to see whether the HRCT findings correlated with the histologic findings (Fig 2). Histologic section demonstrated peribronchiolar inflammation, bronchial dilation, reduction of vessel size, and filling of bronchiolar lumens with inflammatory exudate. In this patient, mosaic perfusion, bronchiectasis, and decreased vascularity were seen on HRCT.

### DISCUSSION

Long-term pulmonary sequelae on HRCT were found in 37% (14/38) of those who had had *Mycoplasma* pneumonia—considerably higher than the 12% (2/17) incidence in the control group ($P < .05$). This finding, together with the observation that the involved site of these sequelae on HRCT in all cases corresponded to that of the infiltrate on the chest radiograph at the time of pneumonia, strongly suggests that the complications are attributable to the pneumonic infection and not related to the presence of the microorganisms in the upper respiratory tract. We also attempted to investigate whether there were any possible factors predisposing to pulmonary sequelae on HRCT. The factors identified in the present study were younger age and higher peak antibody titer at the time of pneumonia.

The clinical course of *Mycoplasma* pneumonia is typically mild and self-limited.3 There are, however, several case reports of severe complications following this infection with considerable morbidity and mortality.5–12 Residual lung function abnormalities after *Mycoplasma* pneumonia were also found. Mok et al13 discovered long-term impairment of small airways function, and Sabato et al15 demonstrated persistent spirometric abnormalities, even in symptom-free children, at 3 years’ follow-up. These data, however, did not address pathologic sequelae of this disease. Lung biopsy is an invasive procedure that is rarely performed except in severely ill patients or in special circumstances.13 Although some of our pa-
Patients presented with recurrent cough, breathlessness, or abnormal sounds on chest auscultation, open lung biopsy could not be clinically justified in all but 1 case. HRCT is a noninvasive procedure that has high spatial and contrast resolution. It has significantly improved our ability to detect and evaluate air-space and airway diseases, especially those associated with small airway obstruction.21

The abnormal findings on HRCT in the present study included mosaic perfusion, bronchiectasis, bronchial wall thickening, air trapping, and Swyer-James syndrome. Mosaic perfusion, patchy or geographic areas of increased and decreased lung attenuation, was the most frequent finding. This is presumably caused by decreased perfusion of areas with bronchiolar obstruction and flow redistribution to normal areas.22 Bronchiectasis was mild and peripheral in location. In interpreting this finding, the overall distribution of the pulmonary blood flow was taken into account, because the small diameter of pulmonary arteries with an oligemic parenchymal zone may lead to a false-positive diagnosis.19 Bronchiectasis was seen mostly in the patients with mosaic perfusion. In these patients, the lung parenchyma in the bronchiectatic segments was decreased markedly in density compared with the surrounding lung. The assessment of bronchial wall thickening is subjective, because precise measurement of wall thickness cannot be made accurately. To avoid this bias, 2 radiologists reached consensus of opinion regarding its presence. Air trapping, which is best seen on expiratory scans,23 may be a consequence of collateral air drift into the alveoli beyond the narrowed or obstructed bronchus or bronchiole. Thickening of bronchial walls and air trapping were seen exclusively in patients with mosaic perfusion and/or

Fig 1. An illustrative example showing that the involved area on HRCT corresponds to that of infiltrate on a chest radiograph at the time of pneumonia in a 8-year-old boy (subject 1). A, chest posteroanterior film at the time of pneumonia shows homogeneous consolidation in right lower lobe. B, HRCT undertaken 14 months later demonstrates mosaic attenuation and bronchiectasis in right lower lobe (arrow).
It is possible that those families who believed their children to be abnormal were more likely to comply with this study.

Because the frequency of pulmonary complication after *Mycoplasma* pneumonia has been presumed to be low, little is known about the factors that influence the progression from pneumonia to the sequelae. In our study, younger age and higher antibody titer at the time of pneumonia were found to increase the likelihood of developing pulmonary sequelae on HRCT.

In young children, airway closure occurs more readily because of low elastic recoil pressure and low lung volume. Another characteristic is that peripheral airway resistance contributes a relatively large proportion of the total pulmonary resistance. Thus, the added stress of inflammatory changes in and around small airways may impair the ability of younger child to compensate for the acute histopathological changes and predispose to the structural changes that may develop. It is not clear whether greater likelihood of young age at the time of pneumonia to develop the sequelae is associated with more harmful effects of the disease on growing lungs or whether it is the consequence of halted lung growth because of injury. Our results are consistent with findings of Todisco et al., who showed that young age at the time of *Mycoplasma* pneumonia increases the chance of developing long-term pulmonary function abnormalities.

Serologic tests are most commonly used for the diagnosis of *Mycoplasma* infection, with a fourfold or greater rise in antmycoplasma antibody titer considered diagnostic. We ascertained the peak antibody titer by measuring weekly until the titer showed a tendency to sustain or fall. The role of the host’s immune response in the pathogenesis of *M pneumoniae* disease has been a subject of increasing interest. It has been shown that the frequency and the height of the antibody response are related directly to the severity of pneumonic involvement. Many features of experimental infection in the hamster model suggest that the pneumonia is an expression of the host immune response to the organism attached to the ciliated mucosal cells. That the reaction is primarily an immune response is supported by the observation that it is completely suppressed by anti-
Because the abnormal findings on HRCT in our study may represent the end-result of lower respiratory tract damage in which the small airways become obstructed, it is conceivable that patients with a higher antibody response manifest a more intense immunopathological response, with a tendency toward pulmonary sequelae. One may be tempted to speculate that heightened antibody response, by itself or by the interaction of antibody with antigen, could cause damage to the respiratory epithelium, but additional studies will be needed to elucidate this possibility.

CONCLUSION

In summary, this study has shown that a considerable proportion of children with history of *Mycoplasma* pneumonia have abnormal findings on HRCT, suggestive of small airway obstruction. Careful follow-up is important for *Mycoplasma* pneumonia in younger children or with higher peak antibody titers in view of the greater chance that these sequelae may develop.

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**Fig 2.** A correlation of the histologic findings with the abnormal HRCT findings in a 4-year-old boy (subject 3). A, histologic section of the left lower lobe biopsy shows peribronchiolar inflammation, bronchial dilatation, decreased vascularity, and filling of bronchiolar lumen with inflammatory exudate that lead to narrowing of the bronchiolar lumen (hematoxylin-eosin stain; original magnification ×25). B, HRCT scan at the level of lower lobe bronchus demonstrates dilatation and wall thickening of superior segmental bronchus indicating bronchiectasis and mosaic attenuation of surrounding lung parenchyma. Also noted are left lung shrinkage and mosaic attenuation of the right lower lobe.
Putting excessive attention to low-probability events accompanied by high drama and overlook events that happen in routine fashion . . . as a result, we forget about regression to the mean, overstay our positions, and end up in trouble.”

Peter Bernstein, quoted in Sennett R. The Corrosion of Character. WW Norton; 1998
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