Mycoplasma pneumoniae Pneumonia: Differential Diagnosis by Computerized Tomography

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Abstract

Objective and background  This study was designed to clarify chest computerized tomography (CT) findings of Mycoplasma pneumoniae pneumonia facilitating differential diagnosis from CAP (community acquired pneumonia) caused by other organisms.

Methods  We retrospectively reviewed the CT findings of 36 patients (median age 33 years, 15 males, 21 females) with serologically proven M. pneumoniae pneumonia and 52 patients (median age 61 years, 37 males, 15 females) suffering from CAP with no serological evidence of M. pneumoniae infection. The CT images were analyzed by experienced pulmonologists.

Results  The most common finding in the M. pneumoniae pneumonia group was bronchial wall thickening, when we compared it with the CAP group (p<0.0001, Fisher’s exact probability test). In the CAP group infected with other organisms, dense consolidations with air bronchograms were more frequent than any other findings (p=0.0279, chi-square test).

Conclusions  The diagnosis of M. pneumoniae pneumonia would appear to be reliable when we found bronchial wall thickening in the chest CT images.

Key words: computerized tomography (CT), Mycoplasma pneumoniae pneumonia, community-acquired pneumonia

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Introduction

Mycoplasma pneumoniae pneumonia (MpP) is among the common infectious diseases involving the respiratory tract (1-3). Mycoplasma pneumoniae (Mp) can cause both upper and lower respiratory tract infections and typically occurs in young adults (4); however, it is considered to be a causative agent in more than 15% of community-acquired pneumonias (CAP) in patients above age 40 years (4).

While most MpP patients have a relatively favorable clinical course (1, 3, 5), some have poor outcomes, such as Guillain-Barré syndrome (6, 7), encephalitis (8), bronchial asthma (9) and bronchiolitis obliterans (1). In general, MpP is unresponsive to beta-lactam antibiotics because theMp bacterium has no cell wall. Tetracyclines, macrolides and quinolones are known to be effective as these antibiotics interfere with protein or DNA synthesis (10, 11). It is important to correctly diagnose MpP at the initial evaluation in order to assure the most favorable clinical course.

Usually, chest radiography is the first imaging technique employed when radiologically examining patients. However, CT can more accurately provide detailed information about the lung parenchyma than routine chest radiography.

To our knowledge, there have been relatively few reports focusing on the differences between Mp infection and other CAP organisms such as Streptococcus pneumoniae, while there are numerous publications describing the CT manifestations of MpP. The aim of our present study was to identify chest CT findings of serologically proven MpP which distinguish it from CAP.

Materials and Methods

We retrospectively reviewed conventional chest CT scans obtained in 36 patients with MpP (Mp group) and 52 with

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CAP other than MpP (CAP group). All patients had been diagnosed as having MpP or CAP other than MpP between 1996 and 2005 in one of four medical centers (Nippon Medical School, Tokyo, Ebina General Hospital, Kanagawa, Katsuta Hospital, Ibaraki, National Hospital Organization Ibaraki-higashi National Hospital Ibaraki, Japan). In all patients, chest X-ray films and CT images were obtained before treatment with effective antibiotics.

CAP group immunoglobulins A and G of Chlamydophila pneumoniae and Mp (complement fixation; CF) were measured in all 88 patients. Those with high antibody titers (C. pneumoniae index > 1.6 and Mp titer of 64 by the CF method) were excluded. However, Coxiella burnetti infection was not adequately excluded. Only one case, in the CAP group, had pneumonia caused by Legionella pneumophila serogroup 1.

In the MpP group, cases suspected to have mixed infections were not assessed. We considered a mixed infection to be present under the following conditions; bacteria other than Mp were identified or purulent sputum was observed. Although Haemophilus parahemolyticus was detected in sputum from one case, we assumed this finding to represent colonization and decided to include this patient in the MpP group, because there was no evidence of leukocytic phagocytosis and the sputum was not purulent.

The MpP patients were 11-70 years old (median age, 33 years), with a male to female ratio of 15 : 21. MpP was diagnosed based on serologic tests (CF method) with elevated single titers exceeding 64 or a four-fold titer increase (12) for at least 2 weeks after presentation. The CAP patients were 23-85 years old (median age, 61 years), with a male to female ratio of 37 : 15. CAP was diagnosed based on multiple isolations of the pathogenic bacteria from sputum and/or positive urinary antigen tests for S. pneumoniae (NOW® Streptococcus pneumoniae Antigen Test; Binax, Inc. Scarborough, Maine, US). In all CAP group patients, serological tests were negative according to the aforementioned criteria.

Causative organisms in the CAP group included S. pneumoniae in 20 patients, H. influenzae in 12, Klebsiella pneumoniae in 2, L. pneumophila in one and others in 7. The causative organisms could not be identified in 17 cases.

The median time from symptom onset until CT examination was 1 day (range, 0-4 days). CT scans, performed with commercially available scanners (X-vision/GX, Toshiba, Tokyo, Japan; Asteion Multi 4, Toshiba, Tokyo, Japan; and SOMATOM Sensation 4, Siemens, Tokyo, Japan), were obtained at 10-mm intervals throughout the chest using 5-7.5 mm collimation. High resolution CT (HRCT) images, with 1-2 mm collimation, were obtained in 2 patients.

The images were reconstructed at window level settings appropriate for assessment of the lung parenchyma (level, -700 HU; width, 1000-1500 HU) and soft tissue in the mediastinum and chest wall (level, 40 HU; width, 300-400 HU).

The images were evaluated by experienced pulmonologists (T.N and Y.M. only for MpP). Chest CT findings were divided into 4 patterns according to the features and distribution of abnormal opacities; generalized bronchial wall thickening, over the entire length of the bronchus at the segmental/subsegmental level (Fig. 1), peribronchovascular centrilobular small nodules (Fig. 2), multiple acinar or lobular opacities along the bronchovascular bundles (Fig. 3) and dense coalescent shadows with air bronchograms (Fig. 4). In some cases without HRCT images, differentiation of ground glass opacity from consolidation was difficult (Fig. 3). Clinical features and CT findings of the MpP and CAP groups were compared to detect statistically significant differences.

The clinical characteristics of both groups of patients and their CT findings were statistically analyzed using Fisher’s exact probability test, the chi-square test, Mann-Whitney U test and the Student’s t test, as appropriate.
Figure 3. 30-year-old female with MpP. Multiple patchy opacities with acinar or lobular involvement around the bronchial wall. At top right, findings are presented schematically.

Figure 4. 56-year-old male with CAP (due to *S. pneumoniae*). Dense coalescent consolidation with air bronchograms. At top right, findings are presented schematically.

### Results

The CAP group patients were, on average, older than the MpP group patients (p<0.0001, Student’s t test; Table 1). There were no immunocompromised patients, e.g., with HIV infection or neutropenia secondary to chemotherapy. Among systemic symptoms, cough and fever were most common in both groups and there were no significant differences in the time between symptom onset and diagnosis (data not shown). Table 1 presents the major laboratory findings. The mean white blood cell and neutrophil counts were significantly higher in the CAP group than in the MpP group. There were no significant differences in lymphocyte count or serum AST and ALT levels (data not shown).

Chest CT findings were divided into 4 patterns listed in Table 2 and shown in Fig. 1 to 4. Generalized bronchial wall thickening was identified in 35 (97%) of 36 MpP group patients. On the other hand, in the CAP group, generalized bronchial wall thickening was seen in only 8 (15.2%) of 52 patients (p<0.0001, Fisher’s exact probability test). Small centrilobular nodules around the bronchial wall were less common in CAP (5 of 52 patients, 10%) than in MpP (9 of 27 patients, 33%), though the difference did not reach statistical significance (p=0.08, Fisher’s exact probability test). Patchy acinar or lobular opacities around bronchi were seen in both the MpP and the CAP group (37 of 52 patients, 71%) than in MpP (9 of 27 patients, 33%), though the difference did not reach statistical significance (p=0.08, Fisher’s exact probability test). The combination of generalized bronchial wall thickening and peribronchial abnormal opacities was more often identified in the MpP group (p<0.0001, Fisher’s exact probability test). Dens coalescent consolidations with air bronchograms were seen significantly more frequently in the CAP group (37 of 52 patients, 71%) than in the MpP group (17 of 37 patients, 42%; p=0.0234, chi-square test). Combined findings of acinar or lobular opacities along the bronchial wall and dense coalescent consolidations with air bronchograms were common in both groups (44% of MpP and 40% of CAP patients). The combination of generalized bronchial wall thickening and peribronchial abnormal opacities was more often identified in the MpP group (p<0.0001, Fisher’s exact probability test).

Unilateral abnormal opacities were detected in 34 MpP

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**Table 1. Characteristics of the Two Patient Groups**

<table>
<thead>
<tr>
<th></th>
<th>MpP</th>
<th>CAP</th>
<th>p-value</th>
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<tbody>
<tr>
<td>number</td>
<td>36</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>age</td>
<td>33 years (11-70)</td>
<td>61 years (23-85)</td>
<td>0.0001</td>
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<tr>
<td>sex</td>
<td>male 15, female 21</td>
<td>male 17, female 25</td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>6780 / µL</td>
<td>11401 / µL</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Neut</td>
<td>4516/µL</td>
<td>9301/µL</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lymph</td>
<td>1316/µL</td>
<td>1142/µL</td>
<td>N.S.</td>
</tr>
<tr>
<td>CRP</td>
<td>9.58mg/dl</td>
<td>18.75mg/dl</td>
<td>&lt;0.0005</td>
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**Table 2. Chest CT Findings**

<table>
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<th></th>
<th>MpP</th>
<th>CAP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>① generalized bronchial wall thickening</td>
<td>35/36</td>
<td>8/52</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>② centrilobular nodules around bronchial walls</td>
<td>9/36</td>
<td>5/52</td>
<td>0.075*</td>
</tr>
<tr>
<td>③ acinar or lobular opacities around bronchial walls</td>
<td>31/36</td>
<td>37/52</td>
<td>0.10*</td>
</tr>
<tr>
<td>④ dense coalescent consolidation with air bronchograms</td>
<td>17/36</td>
<td>37/52</td>
<td>0.0279**</td>
</tr>
</tbody>
</table>

* = Fisher’s exact probability test
** = chi-square test

Note. Numbers in parentheses are ranges (minimum-maximum); *= Mann-Whitney U-test; **= chi-square test; § = These data were obtained from blood tests on admission and biochemical examinations done within 2 days of hospitalization.
patients (94%) and 33 CAP patients (80%). In both groups, abnormal opacities were more common in the right lung (24 in the MpP and 22 in the CAP group). These opacities were significantly more common in the right lung in the MpP group (p=0.0235, chi-square test). A bilateral distribution was seen in 10 CAP patients (19%), but in only 2 MpP patients (6%).

There were no significant differences in the aforementioned 4 patterns of CT findings between S. pneumoniae and H. influenzae. However, generalized bronchial wall thickening was more common in CAP due to H. influenzae than with any other CAP pathogens (Fig. 5, p=0.0041, Fisher’s exact probability test).

Discussion

Mycoplasma pneumoniae (MpP) is one of the smallest bacteria, being approximately 330 nm in diameter (1) with a genome of 816 kbp coding for 687 genes (13). It is a pleomorphic organism lacking a cell wall and is the smallest known free-living organism on earth. Mp infection is acquired by inhalation of the organisms, followed by an incubation period of 2-3 weeks (3).

Mycoplasma pneumoniae pneumonia (MpP) shows a wide spectrum of symptoms including fever, cough and sputum production, and is often complicated by fatigue, malaise and myalgia (3). These prolonged respiratory symptoms, especially the paroxysmal cough often seen in this disease, are thought to be attributable to inhibition of ciliary movement (14), since the organism has a filamentous end allowing it to embed itself between cilia within the respiratory epithelium (15).

Histopathological findings characteristically include acute cellular bronchiolitis with edematous and erosive or ulcerative lesions of the bronchial lumen (16) as well as peribronchial and perivascular interstitial disease extension of lymphocytic inflammation (17, 18). Mononuclear cells infiltrate the parenchyma surrounding the inflamed bronchioles to variable degrees. As MpP becomes increasingly severe, air-space exudation may occur and, on occasion, can lead to acute respiratory distress syndrome (3).

Generally, the most common radiographic findings of MpP are air-space consolidation and ground-glass opacities (2, 9-22). According to Putman et al, who conducted a radiological study of their patients with MpP (20), two distinct chest roentgenographic presentations are recognizable. In their first group (48% of their patients), the radiographic findings included segmental or lobar consolidation associated with air bronchograms. In their second group (28% of their patients), pneumonia progressed to a diffuse, bilateral reticulogranular pattern with neither lobar nor segmental consolidation.

Compared with chest radiography, CT can more accurately demonstrate both centrilobular nodules and the lobular distribution of consolidation. CT can also detect faint ground glass opacities more accurately than chest roentgenograms. Reittner et al examined 28 MpP patients with high-resolution CT (HRCT) (22) and found areas of ground-glass attenuation in 24 (86%) and air-space consolidation in 22 (79%). In 13 patients (59%), the areas of consolidation had a lobular distribution which was evident on CT. They described nodules and thickening of bronchovascular bundles as being seen more commonly on CT than on chest radiographs (25 of 28 patients, 89%; 23 of 28 patients, 82%).

In our subjects, the most common chest CT finding of MpP was generalized bronchial wall thickening, seen in 97% of patients. However, many previous reports noted that most MpP patients had nodular shadows and patchy shadows around bronchial walls. This would correspond to the nodular opacities detected in only 9 patients (25%) in the present study. We considered generalized bronchial wall thickening to be more important than the other radiological findings of MpP.

The most widely reported radiological feature of MpP is centrilobular nodules in the lung parenchyma. Reittner et al reported nodules to more commonly be visualized on HRCT (22). In the present study, all patients underwent conventional CT with a slice thickness ranging from 5 to 7.5 mm. Lack of HRCT is a limitation of our study. Although conventional CT may show the nodules with some blurring, HRCT demonstrates the characteristic features very clearly.

MpP infection occurs via the sinopulmonary tract by droplet dissemination. The Mp organism attaches to cilia through the P1 protein and multiplies in the respiratory epithelial layer (23). Attachment to epithelial cilia is essential for Mp infection, a disease thought to progress and to manifest as
infection was uncertain. *H. influenzae* disease in segmental bronchi. However, pneumonia due to *H. influenzae* tends to show bronchial wall thickening (p = 0.0041, Fisher’s exact probability test), according to our observations. Lee et al reported HRCT findings of diffuse micro-nodular lung diseases (25). Their report did not include infectious diseases such as MpP and pneumonia due to *H. influenzae*. We found one case of pneumonia, due to *H. influenzae*, showing the micro-nodular pattern. However, the relation between bronchial wall thickening and *H. influenzae* infection was uncertain.

Dense coalescent consolidations with air bronchograms were more common in the CAP group and the difference was statistically significant. We consider the main site of inflammation to be the alveolar space rather than the bronchial epithelium, because most CAP organisms initially grow within the alveolar space.

In conclusion, the main aim of our study was to identify a means of rapidly distinguishing MpP from other pneumonias in daily clinical practice without waiting for serological Mp results. We consider bronchial wall thickening to be the CT finding which is most suggestive of diagnosis of MpP, as distinct from bacterial pneumonia. A diagnosis of MpP is anticipated to be more reliable, if supported by leukocyte counts whenever possible. However, the final diagnosis of MpP must be based on appropriate bacteriological and/or serological examinations.

References


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