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INSIDIOUS CARDIAC CHANGES IN PATIENTS WITH MYCOPLASMA PNEUMONIAE INFECTIONS.

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Aim: To investigate the cardiac influence of *Mycoplasma pneumoniae*.
Materials: 23 mycoplasmal pneumonia patients (age range, 3 to 77 years) and 31 bacterial pneumonia patients (age range, 1 to 94 years).
Methods: Cardio-thoracic ratio (CTR) on chest radiographs on admission and one month after treatment.
Results: In mycoplasmal pneumonia patients, the CTR on admission was 46.1±3.8% and the CTR after treatment was 42.9±3.8% ($p< 0.0001$). The CTR after treatment in the bacterial pneumonia patients did not change.

Conclusion: After treatment, a significant decrease in the CTR was observed in the mycoplasmal pneumonia patients. The pathogenesis of cardiovascular involvement associated with *Mycoplasma pneumoniae* infection has not been elucidated. However, this study showed that cardiac injury might occur without any subjective heart symptoms. Even if patients have no complaints, there may be cardiac involvement especially in the left ventricle in mycoplasmal pneumonia patients.

Key words: CTR, *mycoplasma pneumoniae*, cardiac injury

INTRODUCTION

Mycoplasma pneumoniae is a frequent cause of respiratory tract infections. Nonrespiratory complications may involve skin, joints, central nervous system, heart, liver, kidneys or blood. Cardiac complications involve second-degree heart block, complete heart block, pericarditis, myocarditis and congestive heart failure. These complications are serious diseases that frequently require intensive care during the acute phase. The incidence of carditis of patients with *Mycoplasma pneumoniae* infection has been reported to be 2-9%. Although cardiac injury due to *Mycoplasma pneumoniae* infection has been reported, some patients with no obvious heart symptoms or physical signs, abnormal electrocardiographic or chest radiographic findings, might still have some cardiac injury. Therefore in this study, we measured the cardiothoracic ratio (CTR) on chest radiographs in various mycoplasmal pneumonia patients to identify any insidious cardiac injury.

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METHODS

Subjects

We enrolled 84 pneumonia patients admitted in our hospital between Feb. 1995 and Apr. 2001 retrospectively. These patients demonstrated fever and pulmonary infiltration on chest radiograph compatible with pneumonia. We defined these patients as the bacterial pneumonia patients demonstrating pneumonia due to *Streptococcus pneumoniae* or *Hemophilus influenzae*. Responsible pathogens in the bacterial pneumonia patients were determined by sputum culture, meeting the criteria for group 4 or 5 on Geckler classification. The mycoplasmal pneumonia patients were determined by at least a four-fold titer rise or value over 1:320 titer in a passive agglutination test (SERODIA-MYCOII manufactured by Fujirebio INC. Japan) for serum antibodies against *Mycoplasma pneumoniae* and absence of other pathogens. Cases of old pulmonary lesion on chest radiographs were excluded. Patients with heart failure, chronic respiratory failure or other organ disease were also excluded. Finally, the mycoplasmal pneumonia patients contained 23 patients and the bacterial pneumonia patients contained

31 patients. The mycoplasmal pneumonia patients were composed of 14 males and 9 females (25.7±21.0 years), and the bacterial pneumonia patients were composed of 20 males and 11 females (51.7±26.9 years) (Table 1). Six patients in the mycoplasmal pneumonia patients had pleural effusion and only one patient had both pleural effusion and pericardial effusion. Corticosteroids were prescribed in three patients.

Table 1. Characteristics of mycoplasmal and bacterial pneumonia patients on admission

	Mycoplasma (n=23)	Bacteria (n=31)	*p*
Male/Female	14/9	20/11	0.78
Age (years)	25.7±21.0	51.7±26.9	0.0003
WBC ($x10^2/mm^3$)	59.0±20.5	99.9±30.1	<0.0001
neutro (%)	61.8±15.0	71.0±15.7	0.04
eosin (%)	4.0±3.6	1.9±3.5	0.05
lymp (%)	26.1±12.5	20.2±14.4	0.1
CRP (mg/dl)	4.2±5.3	10.8±7.5	0.001
LDH (IU/L)	272.7±141.2	187.6±43.7	0.01
CTR (%)	46.1±3.8	46.3±5.0	0.9

〈Study design and methods〉

Two doctors measured cardiac diameters, thoracic diameters and calculated the cardio-thoracic ratio (CTR) on chest radiographs on admission then again almost one month after treatment. Cardiac and thoracic diameters were measured on postero-anterior chest radiographs. Transverse heart diameter was measured on each of the radiographs by taking the sum of the horizontal distance from the midline to the most prominent part of the left heart border and the horizontal distance from the midline to the most prominent part of the right heart border. Maximal thoracic diameter was measured as the maximal horizontal distance between the internal margins of the chest wall(1). We then compared certain variables between the mycoplasmal pneumonia and the bacterial pneumonia patients. The percentage change in CTR after treatment was calculated in each group. In addition, we measured the maximal computed tomographic cross-sectional area of bilateral ventricles in 5 mycoplasmal pneumonia patients by NIH image system before and after treatment.

〈Statistical analysis〉

We analyzed the patient's baseline variables by unpaired T test after confirming the normal distribution by F test. The ratio of male and female was analyzed by chi-square test. CTR before and after treatment were compared by paired T test after confirming the normal distribution by F test. The correlation between percentage changes in CTR and other parameters were analyzed by Peason's correlation coefficient. A $p< 0.05$ value was considered significant. The data are expressed as means±SD.

RESULTS

We showed various parameters of the two groups in table 1. In the bacterial pneumonia patients, the average patient age was older than that in the mycoplasmal pneumonia patients (51.7±26.9 vs 25.7±21.0 years ; p=0.0003). In the bacterial pneumonia patients, WBC and CRP values were significantly higher than those in the mycoplasmal pneumonia patients. The titer ranged from 1:160 to 1:10240 (mean; 1:1572±2398). In the mycoplasmal pneumonia patients, LDH was significantly higher than that in the bacterial pneumonia patients (272.7±141.2 vs 187.6±43.7 ; p=0.01). CTR on admission did not differ in the two groups. However, after treatment, a significant decrease in CTR was observed in the mycoplasmal pneumonia patients but not in the bacterial pneumonia patients (Figure 1). In the mycoplasmal pneumonia patients, the cardiac diameter before treatment was larger than that after treatment (11.4±2.2 vs 10.7±1.9 cm; p=0.0001), but the thoracic diameter

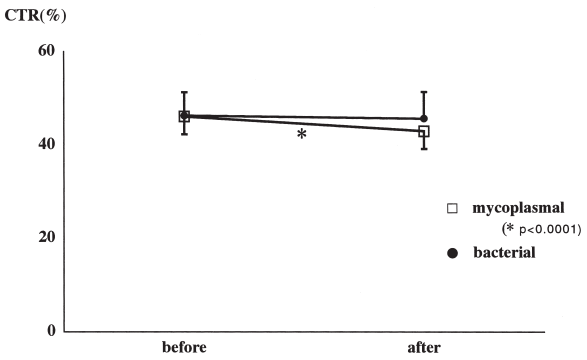

Fig. 1. Change in CTR after treatment in the mycoplasmal and bacterial pneumonia patients. After treatment, a significant decrease in CTR was observed in the mycoplasmal pneumonia patients.

did not change (24.8±4.6 vs 25.0±4.4 cm; p=0.18). The change in the cardiac diameters after treatment was 0.7±0.8 cm in the mycoplasmal pneumonia patients, and 0.2±0.9 cm in the bacterial pneumonia patients. The cross-sectional area of the left ventricle in mycoplasmal pneumonia patients significantly decreased after treatment (44.1±12.0 vs 37.8±14.7 cm^2; p=0.04). In the mycoplasmal pneumonia patients, there was no correlation percentage change in the CTR with other parameters (Table 2). We did not obtain any abnormal findings including ST-T change or arrhythmia on electrocardiograph.

Table 2. The coefficiency of various parameters to the change of CTR (before CTR-after CTR) in mycoplasmal

	r	*p*
Age (years)	-0.03	0.89
SpO_2(%)	-0.11	0.67
LDH(IU/L)	0.24	0.31
GOT(IU/L)	0.33	0.14
GPT(IU/L)	0.35	0.13
CRP(mg/dl)	-0.11	0.65
Mycoplasma CF titer	-0.19	0.40

DISCUSSION

Cardiac injury in *Mycoplasma pneumoniae* infection has been reported, including pericarditis, myocarditis and complete AV block(2-11). In this study, although severe heart failure and chronic respiratory failure cases were excluded, CTR of chest radiograph in the mycoplasmal pneumonia patients significantly decreased after treatment although definite heart dysfunction was not suspected. Though CTR on admission did not differ between the two groups, CTR after treatment was smaller in the mycoplasmal pneumonia patients than in the bacterial pneumonia patients. Though CTR on admission had already increased in the mycoplasmal pneumonia patients, the difference in CTR before treatment in the two groups might have been canceled by the age difference. In the mycoplasmal pneumonia patients, the cardiac diameter before treatment was larger than that after treatment, but the thoracic diameter did not change. Therefore, the change in CTR was not due to respiratory fluctuation of the thorax, and the increased CTR on admission was thought to be due to cardiac dilatation.

Next, we should consider whether we can ignore changes in the heart diameter due to the cardiac cycle. In previous reports(1), the difference in cardiac diameter in systole and diastole was 0.4±0.4 cm. In this study, the change in cardiac diameter after treatment was 0.7±0.8 cm in the mycoplasmal pneumonia patients. We considered that the CTR change was not due to the cardiac cycle but due to the enlargement of the heart diameter during *Mycoplasma pneumoniae* infection. And the computed tomographic left ventricle cross-sectional area in 5 mycoplasmal pneumonia patients significantly decreased after treatment although the right ventricle did not change. Therefore, we considered that the increase in CTR in the mycoplasmal pneumonia patients resulted from the enlargement of the left ventricle and asymptomatic myocarditis occurred in the left ventricle. The high value of LDH in the mycoplasmal pneumonia patients might reflect cardiac dysfunction, as we did not recognize differences on pulmonary or hepatic disorder in both groups.

The pathogenesis of cardiovascular involvement associated with *Mycoplasma pneumoniae* infection has not been elucidated. There are three possibilities. First, cardiovascular involvement is caused by direct invasion of *Mycoplasma pneumoniae* into the heart. Second, *Mycoplasma pneumoniae* infection may cause heart injury due to an autoimmune response. Third, an increased tendency for blood coagulation and intravascular thrombosis has been noted(12). In this study, since the change in CTR was not related to serum antibodies against *Mycoplasma pneumoniae* , the mycoplasma antibody titer did not reflect cardiac injury. The results are not shown in this paper, the expansion of pulmonary infiltration was not consistent with the increase in CTR. In mycoplasmal pneumonia, an increase in the level of IL-1β was reported. Recently, correlation IL-β and TNF-α to myocardial damage has been reported(13). These cytokines might cause cardiac damage in *Mycoplasma pneumoniae* infection. In addition, there was the report that immunomodulatory therapy with intravenous gammaglobulin might be effective during the acute stage of myocarditis(13). Further investigation is warranted. This study showed that cardiac injury, especially in

the left ventricle, might occur without any subjective heart symptoms. Even if patients have no complaints, there may be cardiac injury in mycoplasmal pneumonia patients.

Abbreviations: CTR: cardio-thoracic ratio

SpO_2: oxygen saturation by pulse oximeter

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