

## Clinical Features of Mycoplasmal Pneumonia in Adults

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We have examined 221 cases of mycoplasmal pneumonia in adults during the past 17 years. During this time epidemic waves occurred every three to four years. The incidence of disease was highest in patients 20 to 30 years of age. The most common clinical features were cough, fever, sputum, and rales. The most characteristic feature was a persistent cough which lasted about three to four weeks. Roentgenographic examinations showed a variety of patterns, but the most consistent feature was a feathery shadow, appearing in the lower field of either or both of the lungs. Lung function tests showed peripheral airway impairment. Although roentgenographic examination provided useful information, it could not be used as a pathognomic feature of mycoplasmal pneumonia. Tetracyclines were most effective for eliminating clinical symptoms, whereas the macrolides provided the best response based on roentgenographic evaluations.

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### INTRODUCTION

*Mycoplasma pneumoniae* causes primary atypical pneumonia and upper respiratory disease in young and adolescent children and in young adults [1,2,3,4].

Although mycoplasmal pneumonia generally follows a mild course, severe clinical symptoms may occur. In some patients, infection produces high fever and a persistent cough, and the agent may reside in the respiratory tract for a long period of time. Secondary bacterial pneumonia and exacerbations of chronic respiratory disease may occur or sequelae such as central nervous system disturbances, cardiovascular diseases, and hepatitis may be seen in spite of the administration of effective antibiotics [2,3,4,5].

This paper reviews the epidemiology, clinical manifestations, and complicating features of the disease, the roentgenographic, microbiologic, and serologic findings, and the results of chemotherapy obtained in 221 adults with mycoplasmal pneumonia.

### MATERIALS AND METHODS

We have examined 605 cases of atypical pneumonia in adults during the period ranging from 1965 through 1981 at the University Hospital, Nagasaki University School of Medicine. Of these, 221 (36.5 percent) were diagnosed as having mycoplasmal pneumonia and were selected for study on the basis of physical examination (clinical signs and symptoms), and by positive microbiological, serologic, chest X-ray, and pulmonary function test findings. Of 221 patients studied, 105 (47.5 percent) were diagnosed by positive *M. pneumoniae* cultures, and the remain-

TABLE 1

Clinical Effects of Antibiotics in Mycoplasmal Pneumonia, 414 Cases, Including Cases in Children

Antibiotics	Doses (in Adults)			No. of Cases	Mean Duration of Fever (days)	Mean Duration of Cough (days)
	Amount of Dose	Doses per Day	No. of Days			
Macrolides	200-400 mg	3	7-14	218	2.6	10.2
Tetracyclines	500 mg <sup>a</sup>	3	7-14	52	2.3	9.0
Aminoglycosides	<sup>b</sup>	1	4-7	13	3.2	9.0
Penicillins	1-2 g	3-4	4-7	28	4.8	10.5
Cephemes	1-2 g	1-2	4-7	83	5.5	9.9
Chloramphenicol	1-2 g	3-4	7-14	10	5.0	8.0
Non-treatment	-	-	-	10	5.8	15.7

<sup>a</sup>Doxycycline, 100-200 mg, once a day, 7-14 days<sup>b</sup>GM, 40-80 mg; DKB, 100-200 mg; SM and KM, 1-2 g

ing patients had fourfold or greater rises in specific, complement fixation antibody titers. Procedures used for isolation [6], complement-fixation [6], chest X-ray [6], and pulmonary function tests [7] have been reported previously. In brief, oropharyngeal swabs were inoculated directly onto agar and also into broth media [8]. Broth cultures were subcultured to agar medium following the first signs of growth or at weekly intervals for two weeks. Agar cultures were observed periodically for development of typical colonies and identification of *M. pneumoniae* was determined by the growth (disc) inhibition test [9]. Blood was obtained during the acute and convalescent stages of infection, and serum was tested for the presence of specific antibody by the complement-fixation test. Front and lateral chest X-rays were taken during the initial examination and evaluated for the appearance and location of pulmonary disease in a blind manner by five different pulmonary disease specialists. Pulmonary function tests were performed on 17 patients during the acute and convalescent stages using a flow curve recorder. The antibiotic therapy regimen used is given in Table 1.

## RESULTS

### *Patients, Age and Sex*

The age of the patients ranged from 15 to 82 years. One hundred sixty-five patients (74.6 percent) were less than 40 years old, and only nine cases (4.0 percent) more than 60 years old; 107 of the patients were men and 114 were women.

### *Incidence of Disease*

Although respiratory tract infections have been reported to be more prevalent during the fall and winter months [10], our study showed no significant seasonal variation. The time of the peak incidence of mycoplasmal pneumonia varied with the geographic location. Epidemics generally lasted from six to eight months. In Nagasaki city, periodic outbreaks occurred in 1966, 1970, 1973, 1975-1976, and 1980; the peak incidence of hospitalized patients occurred between January and August, 1980. In Sasebo, the peak incidence occurred between November 1976 and March 1977, and from February to December 1980, and in Fukue, from January to July, 1980.

*Clinical Findings*

The clinical signs and symptoms of patients with mycoplasmal and non-mycoplasmal pneumonia are shown in Fig. 1. All patients with mycoplasmal pneumonia produced a characteristic cough which was particularly severe at night and often persisted for three to four weeks, even after the resolution of abnormal roentgenographic findings. Fever ( $>37^{\circ}\text{C}$ ) was present in 207 patients (93.7 percent); 45.3 percent had fever greater than  $39^{\circ}\text{C}$ , and 76.4 percent had fever about

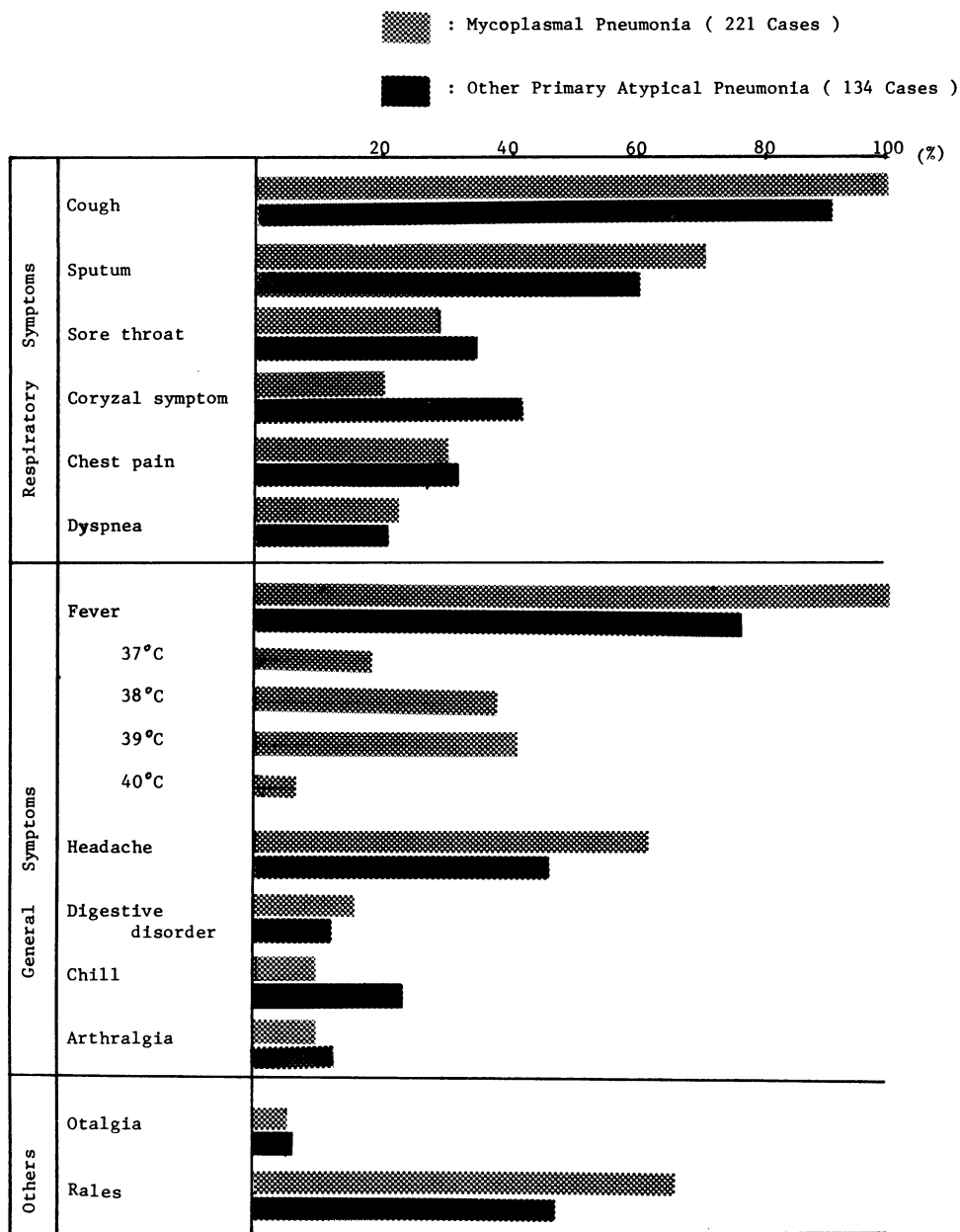


FIG. 1. Signs and symptoms of adult patients with mycoplasmal pneumonia.

38°C. Sputum was ejected in 70.5 percent of the patients, dry or moist rales were found in 66 percent, headache developed in 62 percent, dyspnea was present in 22 percent, and chest pain was described in 30 percent of the cases. Although myringitis has been associated [11] with mycoplasmal pneumonia in children, it was present in only 5 percent of our adult patients. Thus, the salient features of mycoplasmal pneumonia in our study were a cough, sputum ejection, fever, and headache. Coryza, chest discomfort, sore throat, and arthralgia were characteristic of atypical pneumonias of other etiology.

#### *Laboratory Studies*

Leucocyte counts remained within the normal range in most cases (60 percent) but leucophilia (13 percent) occurred in some. However an increased erythrocyte sedimentation rate was seen in 64 percent and C-reactive protein was positive in approximately 90 percent of the cases.

#### *Roentgenographic Findings*

The Brolin classification of disease was used to evaluate the chest X-ray patterns in the study group. Fifty-two percent of the patients showed an alveolar pattern, 9 percent an interstitial pattern, and 29 percent had a mixed alveolar and interstitial pattern on initial examination. Seventeen cases (8.3 percent) developed pleural effusion and three cases had atelectatic changes. Patterns of disease were most commonly seen in the lower lung fields. The right lung lower field was most commonly involved, followed by the left lower field and then the middle field. Frontal and lateral chest X-ray examination revealed a preferential occurrence in region segments 3, 4, 5, 8, and 10 on the right side lung and region segments 3 and 10 on the left side. Forty-five cases (20 percent) had bilateral abnormalities.

#### *Lung Function*

The lung function tests were performed during the acute and convalescent stages of disease in 17 adult patients (seven men and ten women) with acute mycoplasmal pneumonia. The forced expiratory volumes per second percent (FEV 1.0 percent) during the acute stage were decreased in 15 of 17 cases, and six of the cases had a severe decrease in FEV of 1.0 percent. The V75/HT and V50/HT values were also reduced during the acute stage but showed quick recoveries after treatment. The V25/HT values of all patients examined on admission were lower than the predicted values. Based on follow-up studies of V25/HT values, impairment of small airways was seen during the early stages of mycoplasmal pneumonia. The change of maximum mid-expiratory flow (MMF) was similar to that of V25/HT. The MMF value was lowest five to six days after onset and then it gradually returned to normal. Based on the FEV 1.0 percent, V50/HT, V25/HT, and MMF data, lung function impairment in patients with mycoplasmal pneumonia involved both the high and low lung volumes.

#### *Complicating Infections*

Mixed infections due to *H. influenzae*, *M. pneumoniae*, and *S. aureus* occurred in 27 adults with mycoplasmal pneumonia. Respiratory viruses were also responsible for other mixed infections. In a different study, influenza virus, parainfluenza virus, respiratory syncytial virus, and adenovirus were diagnosed in children with mycoplasmal pneumonia.

### *Chemotherapy*

The clinical effectiveness of various antibiotics for treatment in children and adults with mycoplasmal pneumonia was also examined. Efficacy was based on reduction in the duration of fever and cough and in the resolution of chest roentgenography. The mean duration of fever was 2.6 days in patients treated with macrolides, 2.3 days with tetracyclines, 3.2 days with aminoglycosides, 4.8 days with penicillins, and 5.5 days with the cepheems.

The duration of fever in patients treated with the penicillins and cepheems were similar to that of the untreated control group. The mean duration of cough in patients treated with macrolides was 10.2 days and was 9.0 days for either the tetracyclines or the aminoglycosides (Table 1). Improvement of disease shown by chest X-ray (90 percent resolution) occurred in 49.8 percent of the patients one week after treatment with macrolides and in 87.0 percent of the patients after two weeks of treatment. Following tetracycline therapy, 26.4 percent of the patients improved after one week and 73.3 percent after two weeks. The aminoglycosides produced improvement in 94.7 percent of the patients at the end of two weeks of treatment. The improvement rate among patients given the penicillins or cepheems was less than 50 percent after two weeks of treatment. Treatment with the tetracyclines markedly reduced or eliminated colonization of the mycoplasma from the respiratory tract within the first week, whereas colonization persisted a little longer in patients given the microlides.

## DISCUSSION

*Mycoplasma pneumoniae* disease commonly occurs in children and young adults [1,2,3,4] but has also been reported in older subjects [2,5]. In our study, we examined over the past 17 years 221 patients, aged 15 to 82, with mycoplasmal pneumonia. During this time we noted periodic epidemic peaks every three to four years. Each epidemic period continued for six to eight months. These epidemic peaks were also noted by Lind [13] and Ponka [12]. There was no seasonal variation in the incidence of disease in our study. A persistent cough, which occurred throughout the night and lasted three to four weeks, was the most characteristic feature of the disease. Other features were fever, rales, headache, sputum ejection, and dyspnea. Myringitis was seen in only a few of the adult patients. Patients with non-mycoplasmal but atypical pneumonias presented with coryzal symptoms, sore throat, and chills in our study.

Chest X-ray examination did not reveal any special specific or pathognomic features [2,3,12]. X-ray shadows were predominantly of the alveolar pattern or were mixed with interstitial patterns of disease in our study. Rosmus et al. [14] reported the development of roentgenographic findings in mycoplasma pneumonia which were characterized by a diffuse reticular pattern, followed by acinar involvement, and finally by a return to a reticular, interstitial pattern. There was very little change in the patterns of roentgenography during the time course of infection. A pleural effusion pattern was seen in 17 cases and an atelectatic pattern in three cases. Shadows occurred most frequently in the lower fields, in the frontal regions of segments 4 and 5 and in segment 10. In all cases, it was important to discriminate between mycoplasmal pneumonia and other respiratory diseases. Differential diagnosis for pulmonary tuberculosis was especially difficult and required particular caution.

It has been shown previously that mycoplasma infections impair the function of

ciliated epithelial cells and produce inflammation of airways spreading to respiratory bronchioles [2,3,10,15]. We have shown that lung function was impaired both at high and at low lung volume based on significant reduction in V50/HT, V25/HT, and MMF values. These results reflect the pathologic alteration of the small airways [7].

Most *M. pneumoniae* infections show a mild course. However, at times, infections can cause severe sequelae involving the liver, pancreas, or central nervous system, or infections can be complicated by secondary infections with other bacterial or viral agents [2,3,4,16]. Moreover, the agents can persist for long periods. Therefore, it is important to carry out proper therapy of *M. pneumoniae* infections. In our study, the tetracycline therapy was the most effective in reducing colonization and clinical disease, whereas the macrolides were more effective in resolution of roentgenographic manifestations.

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