Case Report

A Case of Fatal Myocarditis Associated with *Mycoplasma pneumoniae* Pneumonia

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Mycoplasma pneumoniae is a common cause of respiratory tract infections. *M. pneumoniae* infection frequently manifests with extrapulmonary symptoms such as central nervous system complications, skin or mucosal involvement, and gastrointestinal problems. However, cardiac complications associated with *M. pneumoniae* are rarely reported. We report the case of a 47-month-old girl who died of fulminant myocarditis associated with *M. pneumoniae* pneumonia. **(Korean J Pediatr Infect Dis 2009;16:92-96)**

Key Words : *Mycoplasma pneumoniae*, Myocarditis, Pneumonia

Introduction

Mycoplasma pneumoniae is a frequent respiratory pathogen among children as well as adults. It is the most common pathogen responsible for community acquired pneumonia in children over 5 years of age. Besides community acquired pneumonia, the infection affects the upper and lower respiratory tracts, leading to upper respiratory tract infection, bronchiolitis, tracheobronchitis, bronchitis. It is also associated with asthma exacerbations[1].

Interestingly, many patients with *M. pneumoniae* pneumonia show the extrapulmonary manifestations which are sometimes of greater severity and clinical importance than the primary pulmonary manifestations. Among these extrapulmonary complications, central nervous system (CNS) complications and skin or mucosal involvement are most common[2, 3].

However, cardiac complications associated with *M. pneumoniae* are relatively uncommon. Cardiac involvement has been reported in rates of from 1 to 8.5% of persons with serological evidence of infection, and is more common in adults than in children[1].

We describe the case of a 47-month-old girl who died of fulminant myocarditis associated with *M. pneumoniae* pneumonia.

Case report

A 47-month-old, previously healthy girl presented with fever and productive cough. The symptoms started three days prior to presentation, the fever increased up to 39℃, and spiked three to four times a day, and the cough was worsening. On admission, the vital signs revealed a heart rate of 120/min with a blood pressure of 110/52 mmHg, a respiratory rate of 36/min, and a

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body temperature of 38.7℃. On physical examination, the patient did not appear very ill, rales and wheezing were not heard, however, the breathing sounds were decreased at left lower lung field. The heart rate was regular and no heart murmur was detected. The other physical findings were unremarkable.

The laboratory findings showed a complete blood count with a white blood cell count of 3,360/mm^3 (55% segment form, 36.8% lymphocytes), a hemoglobin concentration of 11 g/dL, a hematocrit of 31.4%, and a platelet count of 146,000/mm^3. The C-reactive protein was 3.33 mg/dL (normal 〈0.5 mg/dL), and the electrolytes and other chemistry laboratory data were normal.

The results of the venous blood gas analysis were pH 7.427, pCO_2 35.5 mmHg, pO_2 69.7 mmHg, HCO_3^- 22.9 mmol/L, and O_2 saturation 94.2%. The anti-mycoplasma antibody titer was below 1:40. No aerobic or anaerobic bacteria were isolated on the blood culture. A chest x-ray showed haziness at the left lower lung field with small pleural effusion (Fig. 1A).

Ampicillin/sulbactam (150 mg/kg/day for ampicillin) was administered as empirical treatment for possible bacterial infections. On the third hospital day the patient was afebrile and the respiratory symptoms resolved. On the 4th hospital day, the blood test showed a white blood cell count of 5,600/mm^3 (68.7% segment form, 19.8% lymphocytes), the CRP of 1.90 mg/dL and the mycoplasma antibody titer of 1:80. A chest x-ray showed decreased haziness at the left lower lung field (Fig. 1B).

On the evening of the 4th hospital day, a high fever was temporarily developed up to 39.4℃, which was spontaneously subsided in the next morning. On the evening of the 5th hospital day, the heart rate suddenly increased to 176/min with a blood pressure of 93/57 mmHg, the respiratory rate increased to 56/min, and the body temperature of 36.7℃ with an O_2 saturation of 97%. In addition, there were significant abnormalities on laboratory findings: increased white blood cell count and CRP values; metabolic acidosis (pH 7.293, pCO_2 18.5 mmHg, pO_2 49.3 mmHg, and HCO_3^- 8.8 mmol/L); coagulopathy (PT 4.13 INR and aPTT 116 sec); and increased liver and cardiac enzymes (Table 1). A mild cardiomegaly was suggested without a definite increase of perihilar infiltration at the left lower lobe in chest x-ray (Fig. 1C).

The antibiotics were changed to cefotaxime (150 mg/kg/day) and roxithromycin (7 mg/kg/day) due to the

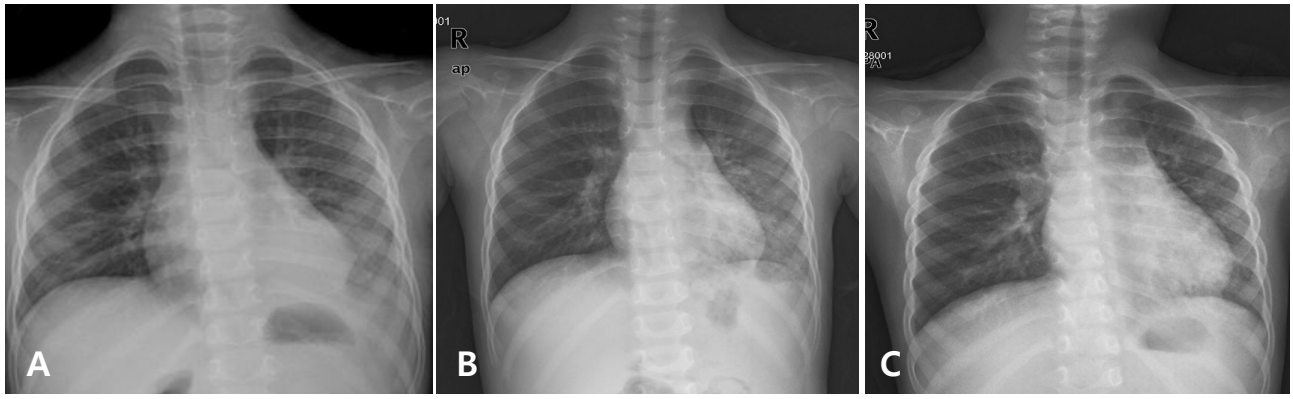

Fig. 1. The chest x-ray findings showed haziness at left lower lung field with small amount of pleural effusion on admission (A), decreased infiltration on the 4th hospital day (B), and mild cardiomegaly without change in pulmonary infiltration on the 5th hospital day (C).

impression of a worsening pneumonia or sepsis. Sudden onset of generalized tonic seizures and vomiting was developed. After a few minutes, asystole were observed on the EKG monitoring. Ventricular tachycardia and ventricular fibrillation were detected during the cardiopulmonary resuscitation. Unfortunately, the patient died, in spite of the cardiopulmonary resuscitation efforts including cardioversion, bicarbonate, and inotropics.

A few days later we noted that PCR of nasopharyngeal aspiration for *M. pneumoniae* was positive. Reverse-transcriptase PCR assays for other respiratory viruses including RSV, adenovirus, influenza virus, parainfluenza virus, and enterovirus were all negative. Under the suspicion of fulminant myocarditis, the serum samples kept in the refrigerator were tested for cardiac enzymes. Abruptly elevated levels of cardiac enzymes were noted for sample of five hours prior to the resuscitation on the 5th hospital day, whereas the levels of cardiac enzymes were within normal limits on the 4th hospital day (Table 1).

Discussion

Fatal cardiac complication associated with *M. pneumoniae* infection is thought to be very rare, especially during the childhood. This case describes a 47-month old girl who died of acute myocarditis associated with *M. pneumoniae* pneumonia.

M. pneumoniae infection is common in children and adolescents, and extrapulmonary complications frequently occur. The range of extrapulmonary manifestations varies widely, including neurological, cardiac, dermatological, musculoskeletal, hematological and gastrointestinal symptoms[1]. There are several proposed mechanisms thought to explain the pathogenicity of *M. pneumoniae*, including adherence to cells, fusion to cell membranes, cell invasion and cytotoxicity, immune response and cytokine production[1, 2, 4]. For cytoadherence, the initial event leading to colonization, infection and lung tissue damage[5]. For cell invasion, even though this is an extracellular pathogen, *M. pneumoniae* can penetrate cell membranes and invade cells[6]. Cytotoxicity occurs during close contact between *M. pneumoniae* and host tissue that allows local disruption and cytotoxicity through the release of enzymatic and cytolytic metabolites directly on to the cell[5, 7, 8]. Immune response and cytokine production is manifested by activation of the immune system : induction of

Table 1. Laboratory Findings during the Hospitalization

Laboratory data	HD #1	HD #4	HD #5	HD #5 (resuscitation)
WBC (/mm^3)	3,360	5,600	19,300	14,650
Hemoglobin (g/dL)	11	11	11.4	7.3
Platelet (×1,000/mm^3)	146	215	412	269
C-reactive protein (mg/dL)	3.33	1.90	9.05	5.41
HCO_3^- (mmol/L)	13	16	8.8	5
AST/ALT (IU/L)	41/16		377/34	285/66
Albumin	3.7		2.8	1.3
Mycoplasma Ab.titer	<1:40	1:80		
Creatine kinase (IU/L)		112	3,607	1,642
Creatine kinase-MB (ng/mL)		0.1	372.6	127
Troponin I (ng/mL)		<0.01	130.41	90.42
LDH (IU/L)		324	1,093	846

HD, denotes hospital day

B- and T- lymphocyte proliferation; secretion of major histocompatibility complex class I and II proteins; and release of multiple cytokines.

The extensive sequence homology of the *M. pneumoniae* adhesin proteins and glycolipids of the cell membrane with mammalian tissues is a well-known example of molecular mimicry that may trigger autoimmune disorders that involve multiple organ systems through the formation of antibodies against substances such as myosin, keratin, fibrinogen, brain, liver, kidney, smooth muscle, and lung tissues[1].

Extrapulmonary complications of *M. pneumoniae*, such as central nervous system manifestations and arthritis, seem to occur more frequently in children[3, 9], but, *M. pneumoniae* associated carditis is known to be uncommon and more commonly described in adults than in children[1]. Ponka[10] reported that the mean age was 32 years among the patients with *M. pneumoniae* associated carditis. Carditis associated with *M. pneumoniae* may be caused by the following[1, 9, 11]. Direct invasion of the myocardium by the organism via either the lymphatic or circulatory systems or from the lower respiratory tract by contamination; or autoimmune mechanism; or increased tendency for intravascular coagulation association with *M. pneumoniae* infection.

Since the review by Ponka[10] in 1979, 21 additional cases of *M. pneumoniae* associated carditis have been published and were reviewed by Paz and Potasman in 2002[9]. In this review, pericarditis was the final diagnosis in 15 patients, myocarditis in 5 patients, and 1 patient had myopericarditis. A review of the radiologic findings in 19 cases revealed that 13 patients (68%) had pulmonary involvement. Pneumonia was observed in 9 patients (47%) and pleural effusions in 4 patients (21%). Six of these patients also had cardiomegaly. Five other patients had cardiomegaly without pulmonary involvement. Mycoplasma infection was confirmed by positive cultures of the pericardial fluid, tissue, or sputum in 9 cases. The final identification revealed 5 cases of *M. pneumoniae*, 3 cases of *M. hominis*, and 1 case of *Ureaplasma urealyticum* infection. The serologic diagnosis was made in 12 cases by use of complement fixation test, immunofluorescent antibody, enzyme-linked immunosorbent assay, or indirect agglutination assay. Echocardiographic studies showed pericardial effusions in all patients with pericarditis (n=15) and demonstrated a reduction of the left ventricular ejection fraction and/or wall motion abnormalities in 3 patients with myocarditis. Two patients with myocarditis had normal echocardiograms. Among the 22 patients, only a single patient died, most probably of respiratory failure due to severe bilateral pneumonia. In 15 cases, complete recovery was demonstrated without complications.

Ong et al.[12] reported a case of a 15-year-old boy who presented with sudden cardiac death, secondary to acute necrotizing eosinophilic myocarditis and his serum total anti-mycoplasma antibodies were increased, and all other viral studies were negative.

In this case, a 47-month-old, previously healthy girl was hospitalized for the treatment of pneumonia showed some clinical improvement during the hospital course. On the 4th hospital day, the patient suddenly developed fever, which subsided in the next morning. On the evening of the 5th hospital day, suddenly developed tachycardia, tachypnea, and metabolic acidosis and soon cardiac arrest and death.

It is assumed that the cause of sudden death was cardiac arrest due to fetal arrhythmia due to myocardial dysfunction caused by acute myocarditis which was strongly suggested by the markedly elevated cardiac enzymes. *M. pneumoniae* was considered the etiological agent of the pneumonia on the basis of the positive PCR

result for *M. pneumoniae* and negative results for other major respiratory pathogens and enterovirus. Put these results together, it is suggested that the patient had a *M. pneumoniae* pneumonia which was later complicated by acute myocarditis.

한글요약

마이코플라즈마 폐렴에 속발한 심근염으로 사망한 소아 1례

서울대학교 의과대학 소아과학교실

김대일 · 최진형 · 조은영 · 최영준 · 성지연 · 양미애 오지은 · 김소희 · 이준호 · 이진아 · 최은화 · 이환종

*Mycoplasma pneumoniae*는 소아 및 청소년에게 발병하는 폐렴의 주요한 원인균으로, 중추신경계, 피부나 점막, 소화기계 등의 합병증을 자주 동반하는 것으로 알려져 있다. 하지만 *M. pneumoniae*와 관련된 심장의 합병증은 비교적 흔하지 않은 것으로 알려져 있고 특히 소아에서는 드문 것 로 알려져 있다. 이에 저자들은 *M. pneumoniae* 폐렴으로 입원하여 치료 중에 속발한 심근염으로 사망한 47개월 여아에 관한 증례를 보고하는 바이다.

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