Acute Renal Failure and Nephrotic Syndrome Associated with Mycoplasma Pneumoniae Pneumonia

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A 67-year-old man developed severe hypoxemic pneumonia and acute renal failure with nephrotic syndrome, associated with Mycoplasma pneumoniae infection. Antibody- or immune complex-mediated mechanisms appeared likely, since there was apparent deposition of immunoglobulin (IgM) and complement components (C1q, C3) in the glomeruli, although light microscopy of renal biopsy tissue revealed minor glomerular abnormalities with tubulointerstitial change. The initial antibiotic treatment was not appropriated, therefore possibly allowed the progression of the disease. Early diagnosis and appropriate therapy are essential to the management of Mycoplasma pneumoniae infection (Kitakanto Med J 2005; 55: 41–44)

Key Words: mycoplasma pneumoniae, bronchiolitis, acute renal failure, nephrotic syndrome

Introduction

Mycoplasma pneumoniae (M. pneumoniae) is one of the leading causes of community-acquired pneumonia occurring in pediatric patients and young adults. Extrapulmonary manifestations of M. pneumoniae infection may notably involve cardiological, neurological, gastrointestinal and hematological system, but renal involvement is rare. Though some renal diseases associated with M. pneumoniae infection have been reported. They include glomerulonephritis, IgA nephritis, interstitial nephritis and nephrotic syndrome. Here we report a case of M. pneumoniae infection presenting acute renal failure with nephrotic syndrome.

Case Report

A 67-year-old man with no previous case history visited near a hospital complaining of cough, sputum and fever on 12 September 2003. Although oral antibiotic therapy was administrated, his condition worsened, and chest radiograph revealed infiltrative shadow in the left upper lung field. He was admitted to the hospital on 16 September and flomoxef, cefazidine, panipenem/betamipron and clindamycin was intravenously administered sequentially. However, he complained of progressive dyspnea and a room air arterial blood gas revealed severe hypoxia with Pco2 of 34.6mmHg, Paco2 of 47.5mmHg. The chest radiograph of 25 September revealed fine nodular interstitial pattern in the bilateral lung field (Fig.1). Computed tomography (CT) of the chest revealed fine centrilobular nodules throughout the bilateral lung (Fig.2). He was admitted to another hospital on 26 September.

Fig.1 Chest radiograph showing fine nodular interstitial pattern in bilateral lung field.
Despite of treatment with the simultaneous intravenous administration of meropenem 1.0 g daily and clindamycin 1.2 g daily, chest radiograph demonstrated an increase in density. As with slight edema of the legs, hematuria and proteinuria were observed with the aggravation of renal function. Meropenem and clindamycin were discontinued. The drug lymphocyte stimulation test (DLST) of cefazidime, meropenem and clindamycin was negative. The complement fixing (CF) antibodies for M. pneumonia (titre \( > 640 \)) were positive and treatment with clarithromycin and minocycline were instituted on 29 September.

He was referred to our hospital once again on 2 October. His body temperature was 36.9°C, pulse rate 90 beats/min, and blood pressure 158/85 mmHg on examination. Coarse crackle was audible on the bilateral lung, and moderate edema and skin rash of the legs were observed. Laboratory investigations showed blood urea nitrogen as 34 mg/dl, serum creatinine 2.7 mg/dl, serum total protein 5.9 g/dl, albumin 2.4 g/dl, and urinary excretion of protein 4.0 g/day. Nephrotic syndrome was diagnosed by these findings. White blood cell count was 8300/µl, and C-reactive protein 2.5 mg/dl. Serum complement factor C4 was
11.9mg/dl (low), CH₅₀ 19.7U/ml (low), and serum C₁q 5.7µg/ml (high). The M. pneumonieae CF antibody titre had risen to 2560 and the acute serum cold agglutinin titre was 1: 2048. Sputum culture was normal flora, antinuclear antibodies were negative, and the anti-streptolysin titre was normal. A definite diagnosis of M. pneumonieae infection was made serologically, thus, treatment with clarithromycin was continued. On 23 October, a percutaneous renal biopsy was performed, although there were apparent improvement in clinical symptoms, the readings of chest radiograph, and renal function. Light microscopy of renal biopsy tissue revealed minor glomerular abnormalities, with tubulointerstitial change (Fig.3). Immunofluorescence revealed coarse granular deposits of immunoglobulin (IgM) and complement components (C₁q, C₃) in capillary walls and mesangium (Fig.4). The patient recovered from the pneumonia in 8 days after administration of clarithromycin. He was discharged on November 7, and proteinuria was no longer present on 14 January 2004.

Discussion

Dumas et al³ first reported the association between M. pneumonieae infection and renal disease in 1976, describing two cases of pneumonia associated with membranoproliferative glomerulonephritis. Von Bonsdorff et al⁴ reported another case of similar histology. Vitullo et al² reported a case of acute proliferative glomerulonephritis associated with M. pneumonieae infection in which IgG, C₃ and mycoplasma antigen were deposited along the glomerular capillary walls and in the mesangium. Pasternack et al⁵ reported a case of acute tubulointerstitial nephritis associated with M. pneumonieae infection in which C₃ and mycoplasma antigen was deposited in the renal interstitium. Rare cases of mycoplasma pneumonia associated with IgA nephropathy⁶ or nephritic syndrome⁷ have been described previously. The authors concluded that the renal disease was caused by mycoplasma-induced immune complex nephritis.

Nineteen cases of M. pneumonieae-associated nephritis have been described previously, including 3 patients with nephrotic syndrome and 4 with tubular or tubulointerstitial nephritis.⁸ Campbell et al⁷ first reported the association between M. pneumonieae infection and nephrotic syndrome in adults, describing a case of pneumonia associated with rapidly progressive glomerulonephritis. In our patient, antibody-or immune complex-mediated mechanisms appear likely, since there was apparent deposition of immunoglobulin and complement components in the glomeruli. There were no underlying infections such as streptococcal organisms except for M. pneumonieae infection. Thus, mycoplasma-induced immune complex was considered to be the cause of the renal disease. However, light microscopy revealed minor glomerular abnormalities. A possible reason is that glomerular damage might have improved since renal biopsy was performed after apparent improvement in renal dysfunction. Another reason may be that this case might have been a case of nephrotic syndrome with a minimal change disease. A case of transient massive proteinuria associated with M. pneumonieae infection in children was reported by Akano et al⁹ describing the similarity to the clinical manifestation of nephrotic syndrome and the causal relationship between M. pneumonieae infection and transient renal injury. In our case, the renal dysfunction resulting from immune injury is associated with a major functional change of the glomerulus (usually an increase in protein permeability), but without light microscopic evidence of damage.

Although interstitial infiltration of lymphocytes was also observed, there was possibility of M. pneumonieae-associated or drug-induced tubulointerstitial nephritis. However, there were no findings suggesting drug-induced nephritis. As apparent deposition of Immunoglobulins, complements and mycoplasma antigen were not detected in the renal interstitium, hence the association between M. pneumonieae infection and tubulointerstitial nephritis is controversial. However, other possible causes of tubulointerstitial nephritis are excluded by the history, clinical findings, and course of the disease. Hence the most possible cause of tubulointerstitial nephritis is M. pneumonieae infection.

These findings suggest a causal relationship between M. pneumonieae infection and the acute renal failure, including glomerular and tubulointerstitial damage. It is not clear whether the pathogenesis of the renal dysfunction is due to immune mechanisms or to the direct action of the renal lesions.

Clinically infectious bronchiolitis is generally considered to be a pediatric disease, rarely being recognized in adults,¹⁰ as with the case of Bronchiolitis caused by the mycoplasma.¹⁰ Particularly, histology of acute M. pneumonieae induced bronchiolitis has been described in less than 20 autopsies and biopsy specimens.¹⁰-¹² In our case, the radiographic finding of pneumonia almost consisted of bronchiolitis pattern. The skin rash observed may be also due to M. pneumonieae.

There was apparent improvement in renal dysfunction and respiratory failure after adequate treatment of the mycoplasma infection was started. However, the initial antibiotic treatment was not appropriated, and therefore possibly allowed the progression of the disease, developing hypoxic severe pneumonia and
acute renal failure with nephrotic syndrome. There are also cases of fulminant mycoplasma pneumoniae infection with multiple organ failure\textsuperscript{13} and death due to acute respiratory distress syndrome.\textsuperscript{14} The management of M. pneumoniae infection is mandatory for early diagnosis and appropriate therapy.

References