CASE REPORT

Tubulointerstitial Nephritis Associated with Legionnaires’ Disease

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Abstract

A 47-year-old man was admitted to our hospital for community-acquired pneumonia complicated with acute renal failure. Legionella pneumophila serogroup type 1 was grown in BCYE (buffered charcoal yeast extract) agar for sputum culture. Although his respiratory illness responded to intravenous erythromycin therapy, renal failure worsened and necessitated hemodialysis. Renal biopsy showed profound tubulointerstitial nephritis. After initiation of steroid therapy his renal function improved and he was discharged thereafter. These findings suggest that in Legionnaires’ disease with acute renal failure, tubulointerstitial nephritis should also be considered and steroid therapy may be an effective modality for the renal complication.

Key words: acute renal failure, renal biopsy

Introduction

Tubulointerstitial nephritis and acute renal failure in association with infectious diseases has been occasionally reported in diseases, such as Yersiniosis, Leptospirosis, Chlamydial and viral infection (1).

Although Legionnaires’ disease was also reported to be one of the infectious causes associated with tubulointerstitial nephritis worldwide (2), no such case in Japan has been reported.

We recently treated a case with Legionnaires’ disease who also developed acute renal failure which is histologically revealed to be tubulointerstitial nephritis. This may be the first such case reported in Japan.

Case Report

A 47-year-old man was brought to the emergency department in Okinawa Miyako Hospital since he was found lying down near the stairway of his home.

He had consumed alcohol regularly for many years. He had acute pancreatitis 3 years previously. One day before admission he was doing well and had played golf with his friends. In the morning on the day of admission he complained of fatigue and chills. He had severe generalized myalgia. And then he was found by his family lying down and brought to our hospital. He had no headache, cough, dyspnea, palpitation, chest pain, vomiting, abdominal pain, diarrhea, gross hematuria, or seizure.

On examination, he looked sick and drowsy. His blood pressure was 98/60 mmHg, pulse rate 147/min, respiratory rate 54/min, and temperature 39.8°C. Extremities were cyanotic with diffuse mottling. Neck was supple. Crackles were heard over the left lung base. Jugular venous pressure and heart sound was normal. He had hepatomegaly but no splenomegaly. Extremity muscles were tender. Neurological examination showed generalized muscle weakness and hyporeflexia without focal deficits.

Laboratory findings were leukocytes 9,300/mm³ with normal differentials, hemoglobin 16.5 g/dl, platelets 106,000/mm³, blood urea nitrogen 17 mg/dl, creatinine 2.2 mg/dl, sodium 124 mEq/l, potassium 3.0 mEq/l, chloride 83 mEq/l, calcium 8.4 mg/dl, phosphate 6.1 mg/dl, aspartate aminotransferase 1,509 IU/l, alanine aminotransferase 100 IU/l, alkaline phosphatase 98 IU/l, lactate dehydrogenase 2,713 IU/l, gamma-glutamyl transpeptidase 644 IU/l, creatine phosphokinase 13,637 IU/l, total bilirubin 2.7 mg/dl, direct bilirubin 2.5 mg/dl, glucose 95 mg/dl, total cholesterol 83 mg/dl, prothrombin time 13.9 seconds (standard 12.0), activated partial thromboplastin time 46.1 second (standard 29.7), and C-reactive protein 26.5 mg/dl. Serology for hepatitis B, C and HTLV-1 was negative. Arterial blood gas analysis showed pH 7.46, PCO₂ 20 mmHg, PO₂ 68 mmHg, HCO₃ 14 mEq/l, and oxygen saturation 94%. Chest film showed left lower lung infiltrates (Fig. 1). His sputum looked like orange jelly. Sputum Gram’s stain showed no visible bacteria.

Diagnosis of community-acquired pneumonia was suggested and intravenous erythromycin 3 g per day and cefotaxime 3 g/
Legionellosis and Acute Renal Failure

Figure 1. Initial chest X-ray.

On the following day his respiratory condition got worse so that endotracheal intubation was performed and mechanical ventilation was initiated. Since oliguric acute renal failure also developed and poorly responded to rehydration and large-dose furosemide, hemodialysis was started thereafter. The level of creatine phosphokinase was 26,021 IU/l on the second hospital day.

On the fourth hospital day, laboratory results showed growth of Legionella bacteria in BCYE (buffered charcoal yeast extract) agar for sputum culture and later it was identified as Legionella pneumophila serogroup type 1. Cefotaxime was discontinued. Oral rifampicin 300 mg per day was added to erythromycin.

His respiratory condition gradually improved. He was extubated on the 12th hospital day. However, renal failure still persisted in spite of recovery of respiratory illness. We performed renal biopsy on the 23rd hospital day. Histologically, focal tubular degeneration, atrophy and loss was present (Fig. 2). The interstitium around these damaged tubules was infiltrated by lymphocytes, plasma cells and some neutrophils. Tubulitis was found with lymphocytes invading beneath the tubular basement membrane and between tubular epithelial cells. Of the 8 glomeruli studied, 7 appeared normal, 1 showed sclerosis. Electron microscopy showed no specific tubular changes. No Legionella organism was noted by electron microscopy. The above findings were compatible with tubulointerstitial nephritis. After we started prednisolone 40 mg per day, urine volume responded gradually and serum creatinine decreased thereafter. He was discharged on the 35th hospital day (Fig. 3).

Fluorescent antibody tests against Legionella pneumophila type 1, which were performed on acute and convalescent days (first day and 30th day), revealed a more than four-fold rise (1:40–1:512).

Discussion

Although severe renal dysfunction associated with Legionnaires’ disease has been occasionally reported worldwide (Table 1), no case in Japan has apparently been reported. The mechanism of renal failure associated with Legionnaires’ disease is probably multifactorial. Among possible factors, those associated with dehydration or shock, rhabdomyolysis, endotoxemia and direct microbial toxicity were considered. Histologically, renal biopsy usually shows tubulointerstitial nephritis and/or acute tubular necrosis (3). Existence of Legionella bacteria was found by electron microscopy in one report (4). Recent reports on the mechanism of renal dysfunction point to direct renal toxicity from the Legionella organism or a systemic manifestation of Legionnaires’ disease (4).

Various infectious diseases can cause renal dysfunction such as tuberculosis, yersiniosis, leptospirosis, chlamydial and viral infection. The pathophysiology seems almost the same as Legionnaires’ disease.

Rhabdomyolysis is sometimes seen in severe cases with Legionnaires’ disease and could be an etiologic factor for the renal dysfunction in the present case. However, the renal histology in our case showed mainly a tubulointerstitial nephritis pattern. Tubulointerstitial nephritis can be caused by a variety of exogenous factors including medications. Although our patient had been given rifampicin and erythromycin for his pulmonary disease, renal dysfunction developed before the initiation of these medications and no allergic signs such as rash or eosinophilia were noted, therefore drug-induced tubulointerstitial nephritis was not the likely etiology for his renal dysfunction.
Figure 3. Clinical course. EM: erythromycin, RFP: rifampicin, PSL: prednisolone, CTX: cefotaxime, HD: hemodialysis, Cr: creatinine, BT: body temperature.

Table 1. Summary of 45 Reported Cases of Legionnaire’s Disease and Acute Renal Failure

<table>
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<tr>
<th>No. of patients</th>
<th>Dialysis</th>
<th>Outcome (Death)</th>
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Therapy for Legionnaires’ disease consists of early administration of large-dose intravenous erythromycin and occasionally oral rifampin (5). The mortality rate is around 15% even with correct diagnosis and therapy (6). Delayed treatment or missed diagnosis may lead to a higher mortality (around 80%) (7). Cases complicated with acute renal failure are reported to have increased mortality (53%) (4).

Therapy for tubulointerstitial nephritis in general is controversial, in part due to the lack of randomized controlled trials. Some investigators recommend the use of glucocorticoid, while others support only conservative treatment. In the present case, we administered oral prednisolone since earlier resolution of renal failure was considered to be life-saving and inexpensive. Certainly, more investigations are necessary to determine the optimal management of tubulointerstitial nephritis.

In conclusion, we report a case with Legionnaires’ disease who also developed acute renal failure caused by tubulointerstitial nephritis. When acute renal failure develops in a case with Legionnaires’ disease, tubulointerstitial nephritis should also be considered as one of the differential diagnoses.

References

1) Brenner BM. Brenner and Rector’s The Kidney. Fifth ed. W. B. Saunders