Fatal Fulminant Legionnaires’ Disease Complicated with Rhabdomyolysis, Acute Kidney Injury, and Non-Occlusive Mesenteric Ischemia: An Autopsy Case Report

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Patient: Male, 72-year-old
Final Diagnosis: Acute kidney injury • Legionnaires’ disease • nonocclusive mesenteric ischemia • rhabdomyolysis

Symptoms: —
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology • Infectious Diseases • Nephrology

Objective: Unusual clinical course
Background: Legionnaires’ disease is one of the most common types of community-acquired pneumonia. It can cause acute kidney injury and also occasionally become severe enough to require continuous renal replacement therapy (CRRT). Non-occlusive mesenteric ischemia (NOMI) is a condition characterized by ischemia and necrosis of the intestinal tract without organic obstruction of the mesenteric vessels and is known to have a high mortality rate.

Case Report: A 72-year-old man with fatigue and dyspnea was diagnosed with Legionnaires’ disease after a positive result in the Legionella urinary antigen test. Pneumonia confirmed by chest radiography and computed tomography. He developed acute kidney injury, with anuria, rhabdomyolysis, septic shock, respiratory failure, and metabolic acidosis. We initiated treatment with antibiotics, catecholamines, mechanical ventilation, CRRT, steroid therapy, and endotoxin absorption therapy in the Intensive Care Unit. Despite ongoing CRRT, metabolic acidosis did not improve. The patient was unresponsive to treatment and died 5 days after admission. The autopsy revealed myoglobin nephropathy, multiple organ failure, and NOMI.

Conclusions: We report a fatal case of Legionnaires’ disease complicated by rhabdomyolysis, acute kidney injury, myoglobin cast nephropathy, and NOMI. Legionella pneumonia complicated by acute kidney injury is associated with a high mortality rate. In the present case, this may have been further exacerbated by the complication of NOMI. In our clinical practice, CRRT is a treatment option for septic shock complicated by acute kidney injury. Thus, it is crucial to suspect the presence of NOMI when persistent metabolic acidosis is observed, despite continuous CRRT treatment.

Keywords: Acute Kidney Injury • Legionnaires’ Disease • Mesenteric Ischemia • Rhabdomyolysis

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**Background**

*Legionella pneumophila* was first reported in 1976 at the American Legion Convention in Philadelphia, PA, USA [1]. Legionnaires’ disease accounts for 2% to 9% of community-acquired pneumonia cases and is one of the most severe forms of pneumonia, as evidenced by its high mortality rate [2]. Legionnaires’ disease can be complicated by acute kidney injury (AKI) and rhabdomyolysis, and a high mortality rate has been reported [3].

Non-occlusive mesenteric ischemia (NOMI), first reported in 1958, is a condition characterized by intestinal ischemia and irreversible necrosis, which occurs as a result of circulatory disturbance, but without arterial or venous occlusion [4]. While NOMI is commonly triggered by cardiac surgery or hypotension [5], diagnosing NOMI is challenging owing to the absence of characteristic symptoms, therefore delaying treatment initiation. This delay is concerning, as NOMI is a serious disease associated with a high mortality rate, despite multidisciplinary treatment that includes clinical therapy with vasodilators and surgical resection of the necrotic intestinal tract.

Here, we report a case of Legionnaires’ disease complicated by AKI, rhabdomyolysis, high lactic acid levels, and metabolic acidosis even after continuous renal replacement therapy (CRRT), which, upon autopsy, was found to be further complicated by NOMI.

**Case Report**

A 72-year-old man presented to our hospital with fatigue for 7 days and exertional dyspnea for 3 days. He had a history of smoking, but his drinking history was unknown. He reported

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<th>Table 1. Laboratory data of patients on admission.</th>
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* 10 L/min of supplemental oxygen via reservoir mask ABG – arterial blood gas; PT – prothrombin time; aPTT – activated partial thromboplastin time; TP – total protein; Alb – albumin; T-Bil – total bilirubin; AST – aspartate aminotransferase; ALT – alanine transaminase; LDH – lactate dehydrogenase; γ-GTP – gamma-glutamyl transpeptidase; CK – creatine kinase; eGFR – estimated glomerular filtration rate; BNP – B-type natriuretic peptide; CRP – C-reactive protein.
going on a spa trip a week prior to the presentation. His medical history was significant for hypertension, hyperlipidemia, and a stroke 10 years prior, which was treated with a ventriculoperitoneal shunt. His medications included candesartan, amlodipine, and pitavastatin.

His vital signs on admission were as follows: temperature, 40.4°C; blood pressure, 140/92 mmHg; heart rate, 87 beats per min; respiratory rate, 40 breaths per min; and oxygen saturation, 93% after 10 L/min of supplemental oxygen via reservoir mask. Physical examination revealed weakened and diminished breath sounds on the right side but no crackles. His abdominal findings were unremarkable. There was no tenderness or muscular defense. The results of laboratory test results on admission are presented in Table 1.
Chest radiography revealed decreased permeability of the right lower lung fields. Computed tomography (CT) of the chest indicated extensive consolidation of the right lower lobe (Figure 1). An abdominal CT scan revealed neither intestinal edema nor ascites. The sputum and blood cultures were negative for significant pathogens. A *Legionella* urinary antigen test was positive. The patient was diagnosed with *Legionella pneumophilia* pneumonia, complicated by rhabdomyolysis and AKI.

The patient was immediately intubated with mechanical ventilation, owing to severe hypoxia, and was administered levofloxacin, piperacillin/tazobactam, and steroid pulse therapy (methylprednisolone, 1000 mg/day). Six hours later, he was treated for septic shock with noradrenaline infusion because of the gradual worsening of his blood pressure.

On day 2, the patient developed anuria, and renal dysfunction worsened, with serum creatinine, blood urine nitrogen, and potassium levels of 6.4 mg/dL, 67 mg/dL, and 7.0 mEq/L, respectively. Metabolic acidosis also worsened, with a serum pH of 7.123, HCO₃⁻ levels of 15.2 mEq/L, and lactate levels of 2.9 mmol/L. CRRT was subsequently started.

On day 3, sputum examination by bronchoscopy was positive for Gimenez stain, and the culture was positive for *Legionella*. Azithromycin was administered, along with polymyxin B-immobilized fiber column direct hemoperfusion (PMX-DHP).

On day 4, the patient developed paroxysmal atrial fibrillation, disseminated intravascular coagulation, thrombocytopenia (platelet count, 71,000/ul), elevated fibrinogen degradation products (60 µg/mL), and was treated with a continuous infusion of heparin. The patient’s respiratory failure gradually worsened, with the progression of the pneumonia shadow on chest radiography (Figure 2).

On day 5 of hospitalization, despite continued CRRT, his metabolic acidosis persisted, and his blood pressure decreased further. The patient did not respond to the multidisciplinary treatment and died (Figure 3).
An autopsy was performed 12 h after death (Figure 4). Autopsy revealed pneumonia in the right lower lobe and diffuse alveolar damage during hyaline membrane formation in all lobes of both lungs. The autopsy also revealed cortical necrosis in the kidney and myoglobin cast in the distal tubules. Additionally, necrosis of the centrilobular tissue of the hepatic lobule, as well as of the adrenal gland, spleen, and pancreas, were observed.

Non-contiguous necrosis, but no organic changes and thromboembolism, was observed throughout the small and large intestines. No vegetation was observed in the heart of the patient. Therefore, we definitively diagnosed Legionnaires’ disease, with myoglobin nephropathy, multiple-organ failure, and NOMI.

**Discussion**

Here, we report a case of Legionnaires’ disease with rhabdomyolysis and AKI in a patient who developed NOMI. Legionnaires’ disease was treated with antibiotics, severe respiratory failure was treated with mechanical ventilation, septic shock was treated with catecholamines and PMX-DHP, and AKI was treated with CRRT; however, his condition did not improve, and he died. The autopsy revealed diffuse alveolar damage, myoglobin cast nephropathy due to rhabdomyolysis, and NOMI.

A PubMed Mesh search using the terms “Legionella”, “autopsy”, and “adult” yielded 3 published cases after the year 2000 [6-8]. Most autopsy cases of *Legionella* pneumonia refer mainly to pulmonary lesions but none to the kidneys or the gastrointestinal tract.

Legionnaires’ disease is sometimes associated with rhabdomyolysis or AKI, and kidney pathology reveals acute tubulointerstitial nephritis or myoglobin cast nephropathy. AKI due to Legionnaires’ disease is caused by rhabdomyolysis, the direct nephrotoxicity of *Legionella* bacteria, inflammatory cytokines,
and decreased renal blood flow due to hypotension [9]. There have been many case reports on Legionella, rhabdomyolysis, and renal failure [10-12], and the complication rate of AKI due to Legionnaires’ disease is 13% to 15%, with a mortality rate of 40% to 53% [2,13]. Additionally, 33% to 50% of patients who have Legionnaires’ disease complicated with rhabdomyolysis have AKI [2]. Renal pathological findings in Legionnaires’ disease include (from most frequent to least frequent) acute tubular necrosis, acute tubulointerstitial nephritis, and myoglobin casts [13-16]. Our patient had Legionnaires’ disease, rhabdomyolysis, and AKI, and the renal autopsy revealed acute tubulointerstitial nephritis and myoglobin casts. These findings were considered to be one of the causes of AKI.

Although various adjunctive therapies have been introduced in addition to antimicrobial therapy, the prognosis of sepsis remains poor. A previous study showed improved life expectancy when PMX-DHP was administered at the start of CRRT for septic shock complicated with AKI [17]. However, Surviving Sepsis Campaign guidelines (SSCG) 2021 do not recommend the use of PMX-DHP for septic shock, given the insufficient evidence regarding improvement in life expectancy. In the present case, PMX-DHP for septic shock may not have been the right choice, given that it did not improve life expectancy, and it should either been avoided or administered simultaneously with CRRT on day 2. High-dose methylprednisolone was initiated to treat withdrawal from shock, but the patient died on day 5. It is impossible to determine whether the short-term steroid treatment significantly impacted on the patient’s death.

Figure 4. Findings from the autopsy of the lung, kidney, and small and large intestines. (A) Lung showing massive consolidation in the right lower lobe (arrow). (B) Neutrophil cell infiltration within the alveoli observed in the right lower lobe (arrow). (C) Enlargement of the alveolar space and hyaline membrane formation in the upper right lobe (arrow). (D) Clear border between the pale renal cortex and the congestion in the medullary region (arrow). (E) Tubular epithelial cell desquamation and casts observed (arrow). (F) Immunohistological study using an anti-myoglobin antibody showing myoglobin casts in the distal tubules (arrow). (G) The entire lumen of the small and large intestines showing hemorrhagic necrosis. (H) The small intestine showing diffuse submucosal hemorrhage and nonobstructive mesenteric insufficiency (arrow).
in a short time. However, given that SSCG2021 recommends a dose of 200 mg/day of hydrocortisone for treating withdrawal from septic shock [18], it may have been more beneficial to choose hydrocortisone with a fixed volume in this case rather than high-dose methylprednisolone.

There have been no previous case reports of Legionnaires’ disease associated with NOMI. NOMI has a very poor prognosis, with a mortality rate of 56% to 79% [5]. The most common risk factors for NOMI are cardiac surgery and hemodialysis [19]; other factors include heart failure, atrial fibrillation, advanced age, and catecholamine use [20-22]. NOMI usually presents with gradually worsening abdominal pain and no other typical symptoms. Laboratory findings include elevated CRP, AST, LDH, and lactate levels, as well as metabolic acidosis. None of the biochemical findings are pathognomonic for NOMI and should always be considered together with clinical symptoms for a comprehensive diagnosis [23]. In the present case, hemodialysis, advanced age, arrhythmia, sepsis, and catecholamines were considered risk factors for developing NOMI. At the time of admission, there were no concerns of abdominal findings, such as abdominal pain, and the abdominal CT scan showed no intestinal edema or ascites that were suggestive of NOMI. Therefore, the patient was diagnosed not to have NOMI. After admission, he was placed on a ventilator for acute respiratory failure and had decreased consciousness. Therefore, we were unable to confirm his subjective symptoms and occurrence of NOMI. Despite using CRRT for AKI, metabolic acidosis was not corrected, and lactate levels remained elevated. These 2 findings, together with the autopsy results, led us to speculate that the patient had developed NOMI during admission. However, diagnosing NOMI based on blood tests alone while the patient is alive is challenging because elevated AST, CK, and LDH levels can also occur in rhabdomyolysis. In this case, elevated lactate levels and prolonged metabolic acidosis, even with CRRT, were probably the only findings that led us to suspect the development of NOMI.

Conclusions

Here, we report a fatal case of Legionnaires’ disease complicated by rhabdomyolysis, AKI, myoglobin cast nephropathy, and NOMI. Legionella pneumonia complicated by AKI is associated with a high mortality rate, which may have been further exacerbated by the complication of NOMI. In our clinical practice, CRRT is a treatment option for septic shock complicated by AKI. Thus, it is crucial to suspect the presence of NOMI when persistent metabolic acidosis is observed, despite continuous CRRT treatment.

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