EJCRIM
European Journal
of Case Reports
in Internal Medicine

A CASE OF LEGIONELLA PNEUMONIA WITH RHABDOMYOLYSIS, WITH EXTREMELY HIGH CREATININE KINASE WITHOUT ACUTE KIDNEY INJURY IN AN ADULT

Sangam Sangam[1], Sehrish Malik[2], Franc Hodo[1], Bhawesh Patel[1], Victoria Bengualid[3], Shorabh Sharma[1]

[1] Division of Internal Medicine, St. Barnabas Hospital, New York, USA
[2] CUNY School of Medicine, New York, USA
[3] Division of Infectious Diseases, St. Barnabas Hospital, New York, USA

Corresponding author's e-mail: ssangam@sbhny.org

Received: 25/05/2024
Accepted: 27/05/2024
Published: 04/07/2024

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Informed consent was obtained from the patient for this case study.

How to cite this article: Sangam S, Malik S, Hodo F, Patel B, Bengualid V, Sharma S. A case of Legionella pneumonia with rhabdomyolysis, with extremely high creatinine kinase without acute kidney injury in an adult. *EJCRIM* 2024;**11**:doi:10.12890/2024_004539

ABSTRACT

Legionella pneumophila is a bacterium that usually causes pulmonary disease but can rarely present with extrapulmonary manifestations, such as rhabdomyolysis. This is a case of Legionella infection with significant rhabdomyolysis but a lack of acute kidney injury.

A 38-year-old male with a history of epilepsy presented to the emergency department after a seizure episode with confusion, fever, emesis and bruises. He also complained of a productive cough and scant haemoptysis for the past two months. Chest X-ray showed retrocardiac and left upper lobe opacities; urine was positive for Legionella antigen and myoglobinuria. Creatinine phosphokinase was 242,488 U/l and creatinine was 0.5 mg/dl. The patient was managed with oxygen therapy, aggressive IV hydration and IV azithromycin, and later IV levofloxacin until his symptoms resolved.

Rhabdomyolysis may be a sign of Legionella infection. Rapid testing of Legionella antigen, especially in populations at risk, may be crucial for timely diagnosis and treatment. Kidney function may be preserved in the early stages of disease, but early treatment with antibiotics and aggressive hydration are an effective way to prevent deterioration in kidney function.

KEYWORDS

Legionella pneumonia, rhabdomyolysis, creatine kinase, CPK, acute kidney injury

LEARNING POINTS

- Legionella pneumonia is difficult to distinguish from bacterial pneumonia, therefore rapid Legionella testing, particularly in areas with high rates of incidence, is important for targeted therapy.
- Legionella pneumonia with rhabdomyolysis with extremely high CPK levels is usually associated with AKI but preserved kidney function is possible and early diagnosis and treatment can lead to decreased mortality and morbidity in severe cases.

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

INTRODUCTION

Legionella pneumophila is a common cause of atypical pneumonia, also known as legionnaires' disease. Legionnaires' disease manifests as fever, fatigue, chills, cough, diarrhoea, vomiting and confusion. It accounts for approximately 10% of cases of community-acquired pneumonia[1], and may require intensive care admission and major organ support. Only a minority of patients with risk factors in the setting of an outbreak develop legionnaires' disease, which includes older age, immunocompromised state, smoking and chronic disease such as respiratory, cardiovascular or kidney disease[2]. Legionnaires' disease may rarely present with extrapulmonary manifestations.

Rhabdomyolysis is caused by muscle necrosis and releases intracellular muscle components in the bloodstream, such as creatinine phosphokinase (CPK) and myoglobin. The severity of rhabdomyolysis is often defined by elevations in CPK levels, which are nephrotoxic and can result in renal failure. Rhabdomyolysis is more commonly caused by exertion but drugs, seizures, substance abuse and accidents can also cause it[3]. Legionella infection is a rare but recognised cause of rhabdomyolysis and can progress to renal dysfunction. A triad of legionnaires' disease, rhabdomyolysis and renal failure has been cited 22 times since 1980[4]. In these cases, renal failure is important to recognise so timely interventions can be implemented, such as hydration or dialysis, to avoid mortality[5].

Here, we present a case of a 38-year-old male with a medical history significant for epilepsy who developed Legionnaires' disease with severely elevated CPK levels of 242,488 mcg/l and myoglobinuria consistent with rhabdomyolysis but did not develop an acute kidney injury.

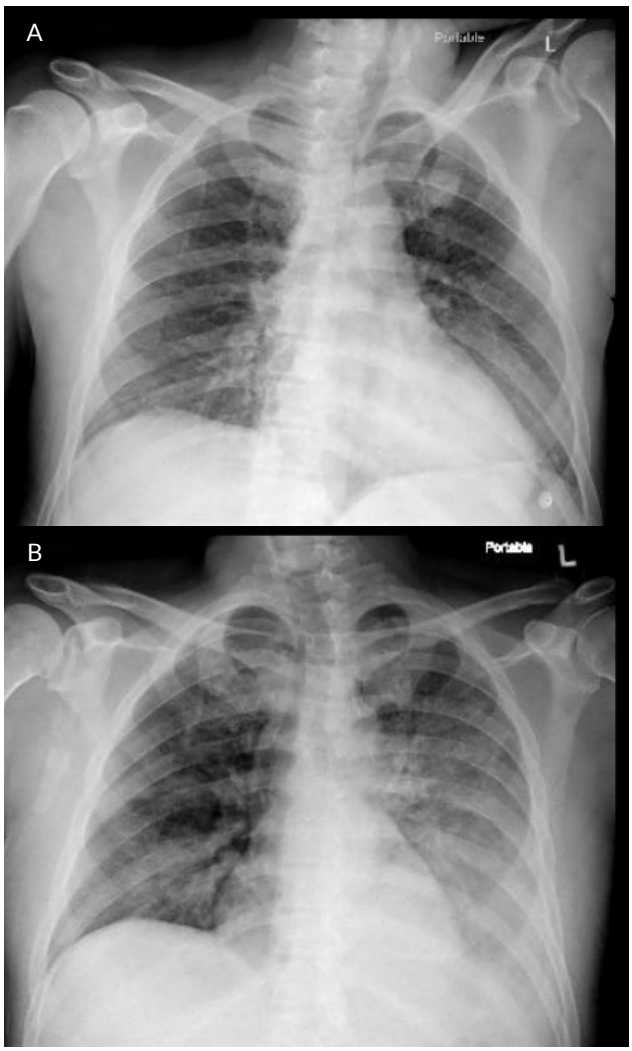

Figure 1. Chest X-ray on day 1 in the emergency department vs chest X-ray on day 6.

CASE DESCRIPTION

A 38-year-old male with a history of epilepsy was brought to the emergency department after a seizure episode and a fall in his bath. The patient presented with confusion, fever and episodes of vomiting one day before admission. The patient also reported a productive cough since his release from prison two months previously and scant haemoptysis for the last few days. On examination he was febrile (40.2°C), tachycardic (111 bpm), tachypnoeic (22/min) and hypoxemic (SpO_2: 92% on room air). Furthermore, he appeared confused and had multiple bruises on his face and shoulders.

IV fluids, IV azithromycin, IV cefepime and IV vancomycin were promptly started. Two sets of blood cultures were drawn before initiating antibiotic therapy. Consequently, the patient's mental status improved rapidly. A urine toxicology screen was performed and returned negative. The blood alcohol level was undetectable.

Initial laboratory tests revealed leukocytosis with lymphopenia, thrombocytopenia (69,000/µl), hyponatraemia (128 mEq/l), elevated CPK (749 U/l), normal serum creatinine (0.7 mg/dl) and elevated alanine transaminase (ALT, 43 U/l) and aspartate aminotransferase (AST, 64 U/l) *(Tables 1 and 2)*. A chest X-ray revealed retrocardiac and left upper lobe opacities, indicating pneumonia *(Fig. 1)*. A non-

Test	Normal range	Emergency department	Day 5	Day 8
WBC (10^3/µl)	4–10	10.7	5.0	6.0
Platelets (10^3/µl)	150–450	79	48	151
Haemoglobin (gm/dl)	11.2–15.7	15.6	13.9	13.3
Red blood cells (10^6/µl)	3.93–5.22	4.87	4.34	4.19

Table 1. Complete blood count for the hospital stay.

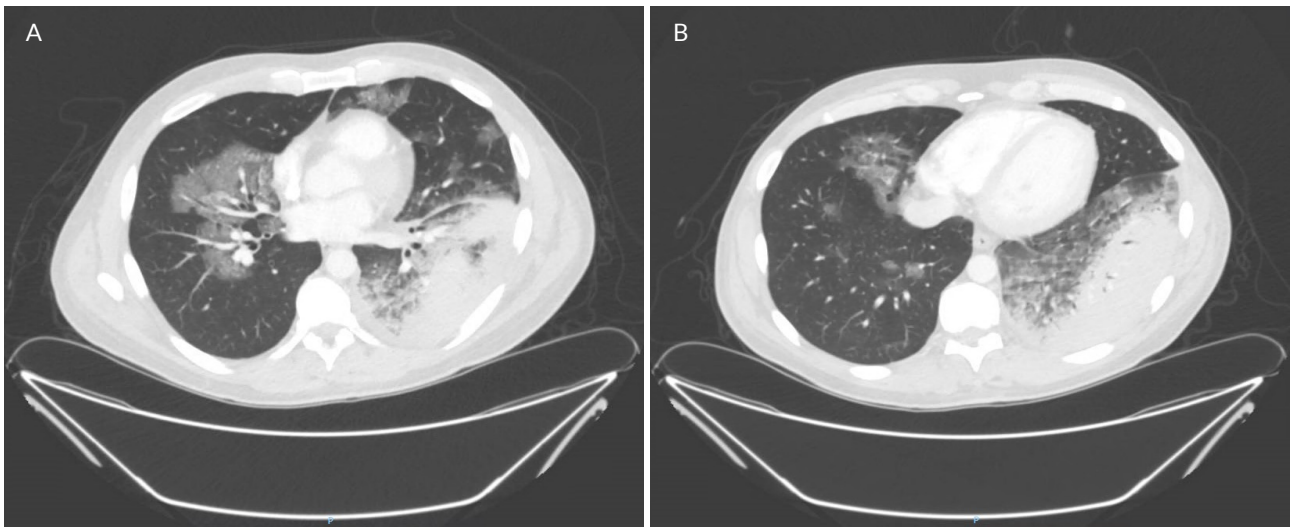

Figure 2. A CT scan of the thorax showing extensive dense consolidation of the left lower lobe with small left-sided effusion.

contrast computed tomography (CT) scan of the head and cervical spine ruled out any acute intracranial abnormality, spinal fracture or subluxation, but demonstrated a minimally displaced left nasal bone fracture with associated perinasal soft tissue swelling. A CT scan of the maxillofacial area confirmed the findings.

The patient was admitted with a preliminary diagnosis of community-acquired pneumonia. He was started on aggressive IV hydration due to high CPK levels, and airborne precautions were in place until tuberculosis could be ruled out given the history of recent incarceration, haemoptysis and upper lobe infiltrates. Urinalysis, urine culture, sputum culture and three acid-fast bacilli tests were performed. Oral and maxillofacial surgery was consulted for the nasal bone fracture, and the patient's anti-epileptic medications (oxcarbazepine and levetiracetam) were also resumed. The screening antigen test for urine Legionella returned positive, leading to infectious disease consultation. Cefepime and vancomycin were discontinued, and antibiotics were narrowed down to azithromycin. IV hydration was continued due to rising creatine kinase levels.

On the second day the patient developed haematuria, diarrhoea, chills, cough and hypoxia requiring oxygen supplementation, raising concern for extrapulmonary manifestations of Legionella. Urinalysis was positive for blood with no red blood cells. A CT scan of the chest revealed extensive dense consolidation of the left lower lobe with small left-sided effusion. It also demonstrated multiple foci of discrete ground glass opacification in the left upper lobes, lower lobes and right middle lobes *(Fig. 2)*. An ultrasound of the abdomen and echocardiogram did not reveal any notable findings. A respiratory BioFire® panel and COVID-19 antigen polymerase chain reaction tests showed negative results.

On the fifth day, the patient's CPK levels reached their peak at 240,880 U/l, without a concurrent rise in creatinine (0.8 mg/dl). ALT (317 U/l) and AST (1925 U/l) also peaked on the same day. IV azithromycin was changed to IV levofloxacin on day five due to possible rare treatment failure as the

Variables	Normal range	Emergency department	Day 5	Day 8
Sodium (mEq/l)	135–145	128	128	135
Potassium (mEq/l)	3.5–5.3	3.0	3.7	4.2
Chloride (mEq/l)	96–108	98	99	105
Glucose (mg/dl)	70–99	145	129	91
Urea nitrogen (mg/dl)	8–23	14	9	8
Creatinine (mg/dl)	0.6–1.2	1.1	0.8	0.5
Calcium (mg/dl)	9.2–11.0	8.1	7.4	7.9
ALT/SGPT (IU/l)	4–36	43	317	268
AST/SGOT (IU/l)	8–33	64	1925	1469

Table 2. Basic metabolic panel for hospital stay.

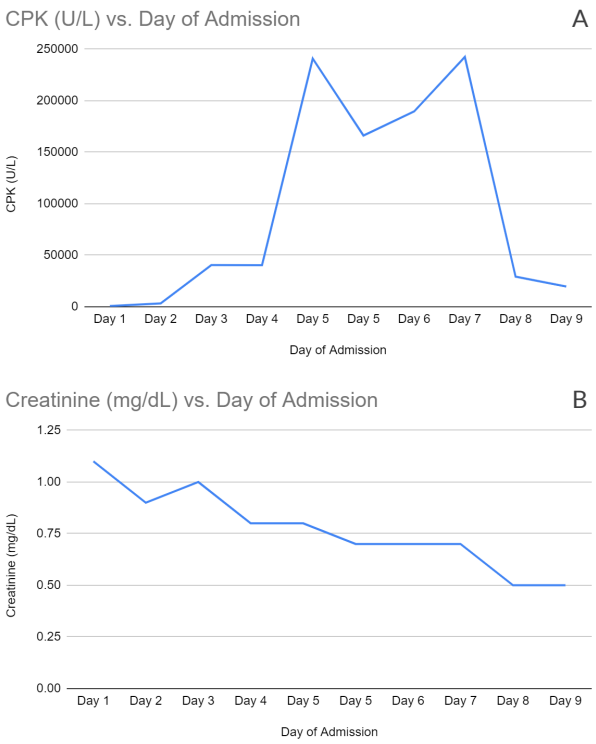

Figure 3. Time course of the trend of A) CPK level (U/l) and B) creatinine levels (mg/dl) throughout the hospital stay.

patient showed minimal improvement. He continued to require oxygen therapy along with aggressive IV hydration for extremely high creatine kinase levels. The final results of blood cultures were also available by the fifth day, indicating no detectable growth of microorganisms.

By the eighth day he became afebrile, with resolving symptoms and no longer needing supplemental oxygen. CPK levels (29,252 U/l) *(Fig. 3A)*, AST (1469 U/l) and ALT (268 U/l) started down-trending, and creatinine (0.5 mg/dl) *(Fig. 3B)* remained normal. The CPK levels rose again after the patient refused intravenous fluids on days six and seven, reaching a second peak of 242,488 U/l on day seven *(Fig. 3A)*. Subsequently, the levels fell sharply to 29,252 U/l on day eight as IV hydration was resumed, and the infection was resolved with antibiotics. He was discharged on the tenth hospital day after five days of treatment with levofloxacin.

DISCUSSION

This case of a 38-year-old male with Legionella pneumonia associated with rhabdomyolysis, without acute kidney injury, underscores the complexity in the management of this rare condition. Legionella is a common cause of community-acquired pneumonia in the United States[1]. However, the occurrence of Legionella-associated rhabdomyolysis is infrequent. Rhabdomyolysis is a condition characterised by the breakdown of muscle tissues, resulting in the release of myoglobin and creatine kinase into the bloodstream. The classic triad of symptoms comprising muscle pain, weakness and dark urine was observed in our patient, a presentation seen in fewer than 10% of cases[6].

Characteristic laboratory findings in rhabdomyolysis include elevated CPK levels, myoglobinuria and a positive urinalysis for blood, although with few to no red blood cells on microscopic examination. Additionally, elevated liver enzymes – particularly AST due to skeletal muscle breakdown – and electrolyte disturbances are also seen. Almost half the patients develop acute kidney injury (AKI)[6-8]. Our patient showed elevated CPK levels, myoglobinuria and elevated liver enzymes while the creatinine remained within normal range throughout the hospital stay.

Rhabdomyolysis often arises due to various causes including trauma, crush injuries, metabolic myopathies, disturbances in electrolyte levels, exposure to toxins, use of certain medications and infections. Among infectious agents, influenza, human immunodeficiency virus (HIV) and enterovirus are the common viral causes, while Legionella, followed by Streptococcus, Francisella and Salmonella account for the bacterial causes. Bacterial aetiologies are associated with significant mortality and morbidity, with 50% of the cases leading to acute renal failure and 38% culminating in fatalities[5].

The triad of Legionella pneumonia, rhabdomyolysis and renal failure is a rare yet fatal complication with an established association. Legionella with rhabdomyolysis and AKI carries a high mortality rate (51% vs 15% without AKI)[2]. AKI is a common complication of rhabdomyolysis, occurring in almost 50% of the cases[6-8]. High CPK levels are correlated with an increased risk of AKI as evidenced by a 5-year prospective observational study conducted in 2003 by de Meijer et al.[9]. This study found that AKI occurred in 65% of patients with severe rhabdomyolysis admitted to the intensive care unit. Patients with AKI had significantly higher creatine kinase (CK) activity on admission and peak CK activity. The mean CK level was 38,351±35,354 U/l on admission and rose further in all patients (mean: 59,747±67,514 U/l). Also, patients with acute renal failure had a higher mortality rate of 59% vs 22% in those without it. This study concluded that serum CK levels correlated with the development of AKI.

Our case stands out as a rare instance of Legionella pneumonia with rhabdomyolysis and preserved renal function. While there are very few reported cases of Legionella pneumonia associated with rhabdomyolysis featuring extremely high CPK levels, none have reported preserved renal function. However, instances of preserved renal function are possible. For example, Soliman et al. described a case of Coxsackie B virus in a 14-year-old girl with rhabdomyolysis without renal failure[10]. Another case reported by Hansrivijit et al. described extremely high CK activity in non-traumatic rhabdomyolysis without AKI in a 22-year-old male. They concluded that factors such as young age, no concurrent cocaine use and adequate oral hydration may prevent AKI in rhabdomyolysis[4], mirroring the characteristics of our patient.

Legionella pneumonia is difficult to distinguish from bacterial pneumonia, posing a diagnostic challenge. This also underscores the importance of rapid legionella testing for targeted therapy, reducing unnecessary antibiotics and

decreasing morbidity and mortality. Early diagnosis in our patient was facilitated by urine Legionella screening on admission, leading to the initiation of antibiotic therapy with azithromycin, later switched to levofloxacin. Notably, our patient lacked co-morbidities such as hypertension, diabetes or prior renal disease, which could adversely affect renal function, serving as an additional protective factor.

REFERENCES

1. Koufakis T, Gabranis I, Chatzopoulou M, Margaritis A, Tsiakalou M. Severe Legionnaires' disease complicated by rhabdomyolysis and clinically resistant to moxifloxacin in a splenectomised patient: too much of a coincidence? *Case Reports in Infectious Diseases* 2015;**2015**:793786.
2. Soni AJ, Peter A. Established association of legionella with rhabdomyolysis and renal failure: a review of the literature. *Respir Med Case Rep* 2019;**28**:100962.
3. Sutarjono B, Alexis J, Sachidanandam JC. Legionella pneumonia complicated by rhabdomyolysis. *BMJ Case Rep* 2019;**12**:e229243.
4. Hansrivijit P, Yarlagadda K, Puthenpura MM, Cunningham JM. Extremely high creatine kinase activity in rhabdomyolysis without acute kidney injury. *Am J Case Rep* 2020;**21**:e924347.
5. Singh U, Scheld WM. Infectious etiologies of rhabdomyolysis: three case reports and review. *Clin Infect Dis* 1996;**22**:642–649.
6. Ma H, Bavishi A, Jain B. Legionella associated rhabdomyolysis: a case report. *J Medl Case Rep* 2023;**17**:258.
7. Veenstra J, Smit WM, Krediet RT, Arisz L. Relationship between elevated creatine phosphokinase and the clinical spectrum of rhabdomyolysis. *Nephrol Dial Transplant* 1994;**9**:637–641.
8. Safari S, Yousefifard M, Hashemi B, Baratloo A, Forouzanfar MM, Rahmati F, et al. The value of serum creatine kinase in predicting the risk of rhabdomyolysis-induced acute kidney injury: a systematic review and meta-analysis. *Clin Exp Nephrol* 2016;**20**:153–161.
9. de Meijer AR, Fikkers BG, de Keijzer MH, van Engelen BG, Drenth JP. Serum creatine kinase as predictor of clinical course in rhabdomyolysis: a 5-year intensive care survey. *Intensive Care Med* 2003;**29**:1121–1125.
10. Soliman A, Bisht S, Jeyamurugan K, Balasundaram P, Basak R. Severe rhabdomyolysis in a pediatric patient after Coxsackie B virus infection without acute renal failure: a case report. *Cureus* 2020;**12**:e7126.