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Rhabdomyolysis: A Rare Extrapulmonary Manifestation of Mycoplasma Pneumoniae Infection in Adults - A Case Report

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Abstract *Mycoplasma pneumoniae* can be responsible for up to 40% of cases of Community-Acquired Pneumonia (CAP). The *M. pneumoniae* infection causes a variety of pulmonary and extrapulmonary manifestations. Rhabdomyolysis is a rare and life-threatening extrapulmonary complication of the *M. pneumoniae* infection, requiring early recognition, prompt supportive management, and treatment with appropriate antibiotics. We describe this case in 60-year-old male who present to the Accident and Emergency (A&E) with a 4-day history of dyspnea and generalized weakness. Further, investigations showed positive mycoplasma IgG and IgM serology. He was admitted to the ICU to undergo emergency dialysis for rhabdomyolysis-driven anuric acute kidney injury. **Case Summary:** Here, we present a case of a 60-year-old male with a 4-day history of dyspnea and generalized weakness. His past medical history was positive for high blood pressure and dyslipidemia, for which he was taking amlodipine, hydralazine, metoprolol, clonidine, and statin, however, was not compliant with his medication. He denied any recreational drug use. His lab work showed BUN 44, Cr 5.4, AST 1500, ALT 473, K 6.9, anion gap 23, and unrecordable CK levels (>160,000). His CXR and CT scan showed right-middle zone consolidation. Investigations showed positive mycoplasma IgG and IgM serology. He was admitted to the ICU to undergo emergency dialysis for rhabdomyolysis-driven anuric acute kidney injury and was started on azithromycin for *Mycoplasma pneumoniae*. Further probing of his past medical history revealed that he had a similar episode a few years ago where he developed rhabdomyolysis requiring dialysis for a total of 3 months, at which point he was likewise positive for mycoplasma. Given the new information, other causes of rhabdomyolysis such as inflammatory myositis and statin-induced myositis were ruled out based on diligent history-checking, examination, and opinions from rheumatologists. We were thus left with mycoplasma-induced rhabdomyolysis as the most likely cause. The patient clinically improved but remained dialysis-dependent and was discharged with outpatient dialysis. **Discussion**: Rhabdomyolysis is a pathological condition causing necrosis of the skeletal muscles and release of intracellular toxins into the bloodstream. The clinical sequelae of rhabdomyolysis can vary from asymptomatic disease to myalgia, electrolyte derangement, and life-threatening renal failure requiring dialysis. Rhabdomyolysis commonly results from ischemia, trauma, high temperature, exertion, drugs, and infections. Among infections, *M. pneumoniae* is a rare yet important cause of rhabdomyolysis. In our case, the clinical history, imaging findings, positive serology, and clinical response to the appropriate antibiotic regimen support meant that Pneumoniae was the cause of the rhabdomyolysis. Only a handful of cases report rhabdomyolysis as an extrapulmonary manifestation of *M. pneumoniae* infection. The severity of Rhabdomyolysis in these cases was variable, with the highest CK levels reported by Kaler et al. (49,578) responding to hydration. Our case is unique, as the CK levels were higher than the reference lab values (>160,000) and led to anuric renal failure requiring immediate dialysis. Antibiotics should be started promptly, considering the increasing incidences of macrolide resistance in *M. pneumoniae*. **Recommendations**: This case highlights the importance of maintaining a high clinical suspicion for rare extrapulmonary manifestations of *M. pneumoniae* such as rhabdomyolysis. Clinical history, examination, and appropriate investigations, especially mycoplasma serology, should be used to establish a diagnosis. The severity of rhabdomyolysis might vary and can range from less severe disease to anuric renal failure requiring dialysis. Appropriate antibiotics against the mycoplasma infection with consideration to macrolide resistance may lead to a better outcome.

Keywords: *Rhabdomyolysis, Mycoplasma Pneumoniae, infectious disease, antibodies, Creatine Kinase*

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1. Introduction

Mycoplasma pneumoniae is one of the few mycoplasma species known to be pathogenic to humans. However, it is one of the most common causes of atypical pneumonia among humans [1,2]. It can be responsible for up to 40% of cases of community-acquired pneumonia in certain age groups [3]. It commonly affects the respiratory tract and causes clinically significant pneumonia in 3 to 10% of cases [4]. However, it causes an array of extrapulmonary manifestations in up to 25% of cases [5]. The extrapulmonary manifestations can include cardiovascular, neurological, digestive, dermatological, hematological, musculoskeletal, sensory, and urogenital complications [6]. Rhabdomyolysis is a complex medical condition characterized by rapid injury or damage to the skeletal muscles, leading to the extracellular spill of intracellular components that can, in turn, lead to life-threatening complications [7]. Rhabdomyolysis is a rare complication of *M. pneumoniae* that has been infrequently reported in the literature. Here, we present an unusual case of a gentleman who presented with severe hyperkalemia and acute renal failure requiring dialysis secondary to rhabdomyolysis induced by the *M. pneumoniae* infection.

2. Case Summary

This is a case of a 60-year-old male who presented to the Accidents & Emergency (A&E) department with worsening exertional dyspnea and generalized weakness. The onset of symptoms were 4 days ago when he started feeling tired and developed shortness of breath upon exertion. Four days later, his symptoms progressed to generalized weakness of the body and dyspnea at rest. His past medical history was positive for hypertension, hypercholesterolemia, and a hospital admission a few years ago due to Acute Kidney Injury (AKI) secondary to Rhabdomyolysis requires dialysis. He used to occasionally drink alcohol and denied using any illicit substance, including cocaine. His current medication includes amlodipine, hydralazine, metoprolol, clonidine, and low-dose statin. He admitted that he was not compliant with his medications, and he confirmed that he did not take statin for more than a month.

His observations in the A&E were as follows: temperature 97.8 F, pulse 73 bpm, respiratory rate 20/min, blood pressure 121/70, and oxygen saturation 95% at room air. He was anuric on presentation. The results of the laboratory tests are summarized in Table 1. A chest x-ray was also performed that showed right-middle zone consolidation. An electrocardiogram (EKG) revealed sinus rhythm with peaked T-waves.

The derangement of laboratory tests with significantly elevated AST, ALT, uric acid, BUN, creatinine, chloride, potassium, and CK favored the diagnosis of rhabdomyolysis leading to anuric acute renal failure with hyperkalemia and high anion gap metabolic acid (HAGMA). Given the patient's hyperkalemia and anuric renal failure, he was transferred to the intensive care unit (ICU) for emergency dialysis. During his stay in the ICU, besides receiving dialysis, he was given treatment for hyperkalemia with sodium zirconium silicate (lokelma), calcium gluconate, and insulin/dextrose solution.

Table 1. Laboratory test results on initial presentation

Test name	Results	Reference range
Plasma sodium (mmol/L)	129	135-145
Plasma potassium (mmol/L)	6.9	3.4-5.0
Chloride (mmol/L)	92	95-108
BUN (mg/dL)	44.0	8-25
Creatinine (g/day)	5.40	0.8-2.4 (male)
Uric Acid (mg/dL)	16.4	4.0-8.5
Phosphorus (mg/dL0	16.6	2.5-4.5
Magnesium (mg/dL)	3.3	1.7-2.2
AST (units/L)	1500	10-40 (male)
ALT (units/L)	473	10-55 (male)
Creatine Kinase (CK) (units/L)	> 160,000	60-400 (male)

His blood workup came back positive for mycoplasma IgM antibodies. He was initially treated for community-acquired pneumonia with empiric broad-spectrum antibiotics including Zosyn (Piperacillin and Tazobactam Injection) and IV ceftriaxone. Given his x-ray findings of right-mid-zone consolidation and positive mycoplasma IgM antibodies suggesting a current/recent *M. pneumoniae* infection, he was switched to PO azithromycin and responded well to treatment.

The additional blood tests for HIV, hepatitis B and C, legionella, sputum cultures, blood cultures, and autoimmune screen were negative. Additional consultation with the rheumatology department was also arranged. Given the severity of his rhabdomyolysis, negative autoimmune screen, and lack of myopathy on physical examination, myositis (inflammatory myositis, polymyositis, and dermatomyositis) was less likely. Statin-induced myositis was also unlikely because even though he was on a low-dose of statin, he was not compliant with his medication, and he admitted to not taking it for more than a month. For more investigation, muscle biopsy was discussed with the patient however patient refused the procedure.

A closer analysis of his previous hospital admission revealed that he had a similar presentation several years prior when he likewise developed rhabdomyolysis requiring dialysis and was IgM positive for mycoplasma. He ws not on statin medication at that time. Based on the available evidence and response to treatment, a diagnosis of *M. pneumoniae*-induced rhabdomyolysis was made. He made good clinical recovery and saw a steady decline in his CK levels (>160,000, > 43,894, > 20,266). His kidney function and potassium levels improved, and the need for dialysis also became intermittent. He was discharged with a scheduled follow-up with the renal team to arrange outpatient dialysis sessions.

3. Discussion

Rhabdomyolysis is a rapid-onset clinical condition resulting from damage to skeletal muscles, leading to their

breakdown. In turn, this leads to the spilling of toxic intracellular components into the extracellular space. These toxic substances include myoglobin, aldolase, creatine kinase (CK), lactate dehydrogenase, and electrolytes such as potassium. Symptoms can range from asymptomatic disease to life-threatening complications such as hyperkalemia, acute renal failure, and disseminated intravascular coagulation (DIC) [7]. The most common causes of rhabdomyolysis include prescription medication, drugs, alcohol abuse, trauma, neuromuscular disorders, and immobility [8]. Infections are an infrequent cause of rhabdomyolysis, with the most common being influenza A and B, HIV, EBV, legionella, herpes, staphylococcus aureus, salmonella, clostridium, and streptococcus pyogenes [7]. *M. pneumoniae* is not commonly attributed as an infectious cause of rhabdomyolysis in adults. A literature review suggests that it has only been reported as a cause of rhabdomyolysis in a handful of cases, making it an extremely rare extrapulmonary manifestation of *M. pneumoniae* in adults [9-17].

The extrapulmonary manifestations of *M. pneumoniae* are attributed to three of its pathogenic actions: (1) a direct response where the bacterium is present at a site and inflicts direct damage by stimulating the production of inflammatory cytokines; (2) an indirect response where the bacterium triggers the formulation of immune complexes of autoimmunity that helps target distant organs or the body system; and (3) a vascular response where the bacterium causes damage to the organs by promoting vascular occlusion [6]. The pathogenesis of rhabdomyolysis due to *M. pneumoniae* is poorly understood, but an indirect immune response is likely the key mechanism, with increased production of tumor necrosis factor-α causing damage to muscles [6].

Creatine Kinase (CK) is an enzyme found in the heart and skeletal muscles. When the muscles break down, CK can leak from the intracellular space into the bloodstream. The level of CK is an important predictor of the severity of rhabdomyolysis, as higher CK levels suggest an increased risk of acute renal failure [7]. In the available literature, the levels of CK due to *M. pneumoniae* infection in adults range from 792 U/L (11) to >40,000 U/L [9] (Table 2). To the best of our knowledge, the levels of CK in our case are the highest reported as a result of *M. pneumoniae*-induced rhabdomyolysis in adults. This makes our case unique.

Table 2. Available literature on the levels of CK in *M. pneumoniae*-induced rhabdomyolysis in adults

Study	CK levels (U/L)
Rothstein and Kenney [9]	> 40,000
Decaux et al [10]	2,900
Daxbock et al. [11]	792
Gupta et al [12]	77,700
Khan et al [13]	14,220
Gosselt et al. [14]	3,017
Kalet et al. [15]	39,125
Gulenay et al. [16]	7,646
Ojbindra et al. [17]	2,537

The treatment for *M. pneumoniae* infection includes the use of antibiotics classes such as macrolides, fluoroquinolones, and tetracycline. As *M. pneumoniae* lacks a cell wall, it is intrinsically resistant to all antibiotics that target bacterial cell walls, including penicillin and cephalosporin [18]. As occurred in our case, the patient was initially given broad-spectrum penicillin and cephalosporin-based antibiotics as empiric treatment for community-acquired pneumonia. However, once the diagnosis of *M. pneumoniae* was established, he was switched to a macrolide and showed a good response to treatment. Nonetheless, attention should be paid to the increasing incidence of macrolide resistance among those with *M. pneumoniae.* In some research, more than 90% of *M. pneumoniae* strains isolated from the Chinese population were resistant to macrolide antibiotics [18]. In our case, none of the culture results came back positive for *M. pneumoniae*, so establishing antibiotic sensitivity was not possible. Since the diagnosis was based on positive IgM antibodies, treatment with first-line antibiotics for *M. pneumoniae* (macrolides) was initiated with a good response. Nevertheless, the selection of antibiotics should always be guided by culture results wherever possible to avoid antibiotic resistance.

4. Conclusion and Recommendations

- *M. pneumoniae* is an important cause of atypical pneumonia and should always be considered as a diagnosis when investigating cases of community-acquired pneumonia.
- It most commonly affects the respiratory tract but can cause an array of extrapulmonary manifestations. Rhabdomyolysis is a rare but recognized complication of *M. pneumoniae* infection and should be recognized early.
- Rhabdomyolysis symptoms range from asymptomatic disease to severe hyperkalemia and acute renal failure requiring dialysis. Therefore, prompt recognition and early treatment of this potentially life-threatening complication are crucial.
- The diagnosis of *M. pneumoniae* infection is based on history and clinical examination, and it should be supplemented by a thorough workup including chest imaging (such as x-ray), cultures (sputum and blood), and mycoplasma serology to detect mycoplasma antibodies.
- *M. pneumoniae* is intrinsically resistant to antibiotics targeting cell walls such as penicillin and cephalosporin. Macrolides are the first-line antibiotics. However, there is an increasing incidence of macrolide resistance among cases of *M. pneumoniae* infection. Therefore, macrolide resistance should always be considered in such cases.

Statement of Competing Interests

We have no conflicts of interest to disclose for this manuscript; All authors declare that they have no conflicts of interest.

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