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Int J Case Rep Images 2025;16(1):101–105.
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Myoglobin cast nephropathy long after an unevaluated febrile episode with no clinical evidence of rhabdomyolysis: A rare cause of reversible AKI—A case report

Rajesh Jayaraman, Balan Louis, Rajendran Tholappan, Vel Arvind Subramanian

ABSTRACT

Introduction: Rhabdomyolysis/myoglobin cast nephropathy constitutes a rare yet a reversible cause of acute kidney injury (AKI) in the critical care setting. We hereby report a case of a full-blown myoglobin cast nephropathy that occurred weeks after an unevaluated febrile illness but with a completely normal urine and serum biochemistry pertaining to myoglobin during the presentation.

Case Report: A 45-year-old man presented with features of AKI. Three weeks before the presentation he had an unevaluated febrile illness. His renal biopsy revealed strongly positive immunohistochemical-staining myoglobin with no other discernible cause. All the urinary and serum biomarkers pertaining to rhabdomyolysis, such as urine free myoglobin and creatine phosphokinase (CPK-MB), were negative. The patient responded completely to urine alkalinization and hydration.

Conclusion: Rhabdomyolysis is a rare yet a potentially reversible cause of AKI in the critical care settings. Our case ascertains the fact that a full-blown myoglobin cast nephropathy/AKI can still occur days to weeks after a febrile illness. Our study also stretches the clinical importance of suspecting a full-blown myoglobin cast nephropathy despite all the markers in urine and serum proving to be negative.

Keywords: Myoglobin cast nephropathy, Negative urine myoglobin, Post-febrile status, Reversible AKI

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Received: 31 March 2025
Accepted: 30 April 2025
Published: 03 June 2025

How to cite this article

Jayaraman R, Louis B, Tholappan R, Subramanian VA. Myoglobin cast nephropathy long after an unevaluated febrile episode with no clinical evidence of rhabdomyolysis: A rare cause of reversible AKI—A case report. Int J Case Rep Images 2025;16(1):101–105.

Article ID: 101507Z01RJ2025

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doi: 10.5348/101507Z01RJ2025CR

INTRODUCTION

Acute kidney injury (AKI) can occur in patients who have rhabdomyolysis and, less commonly, in patients with hemolysis. It is caused by the non-protein heme pigment that is released from either myoglobin or hemoglobin and is toxic to the kidney. Myoglobin is released from muscle in patients with traumatic or nontraumatic rhabdomyolysis, whereas hemoglobin is released from hemolyzed red blood cells. Both myoglobin and hemoglobin are filtered by the glomerulus into the

urinary space where they are degraded, thus releasing heme pigment. Tubular obstruction, direct toxicity to tubular epithelial cells, and presumably vasoconstriction and the resultant outer medullary ischemia are some ways by which the heme pigments cause nephrotoxicity [1, 2]. We hereby report a rare case of late-onset full-blown myoglobin cast nephropathy long after an unevaluated febrile illness that subsequently improved dramatically with volume replacement and urine alkalinization. Most cases of myoglobin cast nephropathy have a deranged biochemistry in the form of elevated CPK-MB and lactate dehydrogenase (LDH) along with urinary positivity of myoglobin at the time of presentation. In our case, the aforementioned biochemistry was entirely normal while presenting with severe AKI.

CASE REPORT

A 45-year-old male presented to us with a history of a week of mild swelling of legs, vomiting, tiredness, and a few episodes of diarrhea. There was no history of any infection, nephrotoxic drug intake. There were no major clinical symptoms of volume loss like lightheadedness, dizziness, etc. He did not have any symptoms suggestive of urinary tract obstruction. Clinical examination was normal except for a mild pedal edema. His blood pressure was 150/90 mmHg.

A past history revealed was a three-day duration of fever approximately 20 days before the date of presentation to us. The fever was low grade, without rigor, not associated with profuse diaphoresis. The fever was more during the evening hours, never associated with any degree of body pain or bone pain. There was no change in the color of the urine. The fever was said to have subsided with over-the-counter antipyretics. There were no other constitutional symptoms.

Blood, serum, and urine biochemistry done immediately revealed the following. His serum creatinine was 9.1 mg/dL, intact parathyroid hormone was 276 pg/mL, urine routine and microscopy were normal. Urine spot protein–creatinine ratio was 1.9. His fasting and post-prandial blood sugars and HbA_{1c} were normal. His serum tested negative for cytoplasmic anti-nuclear cytoplasmic antibody, perinuclear-anti nuclear cytoplasmic antibody, and anti-glomerular basement membrane antibodies. The ultrasound showed normal-sized kidneys with increased echoes. After two successive sessions of hemodialysis, renal biopsy was done with no further delay.

The viable glomeruli were normal in size. There was no segmental sclerosis, collapse of glomerular tuft or podocyte hyperplasia. Capillary lumen was patent with no double contouring in Jone's stain. There was no necrotizing lesion, no fibroid degeneration or crescent formation. Tubules portrayed a moderate degree of acute tubular injury along with the presence of linearly arranged strings of eosinophilic degenerated granular blobs within the tubular lumen (Figure 1). There was no interstitial inflammation or granulomas. Masson-trichrome staining depicted the casts more clearly (Figure 2). The tubular casts on immunohistochemistry over paraffin blocks stained positive for myoglobin (Figure 3).

Based on the biopsy report, an extended evaluation was done. There was no muscle injury in any form, no history of binge of alcohol consumption. There was no history suggestive of any poison consumption known to cause rhabdomyolysis. Serum phosphate and potassium were normal. There was no change in the color of the urine at any time during or shortly before the illness. There was no history of statin intake.

A thorough biochemical analysis pertaining to myoglobinuria and rhabdomyolysis was also done. Serum LDH was 273 (biological reference range: 120–300), serum haptoglobin was 168 mg/dL (30–200), urine myoglobin in spot sample was 21 μg/L or 21 ng/mL (1–1000), CPK-total 37.6 units/L (30–200), CPK-MB 3.08 ng/mL (<6.5), and urine free hemoglobin was absent.

Mutations pertaining to recurrent myoglobinuria including mitochondrial-DNA encoded cytochrome C oxidase-1 and 2 along with LP1N1 gene were found to be negative. The patient was then treated with adequate hydration and urine alkalinization. The serum creatinine rapidly decreased over two weeks to reach a value of 1.3 mg/dL. He was then discharged. A repeat biopsy done a month later revealed a completely normal tubular picture (Figure 4).

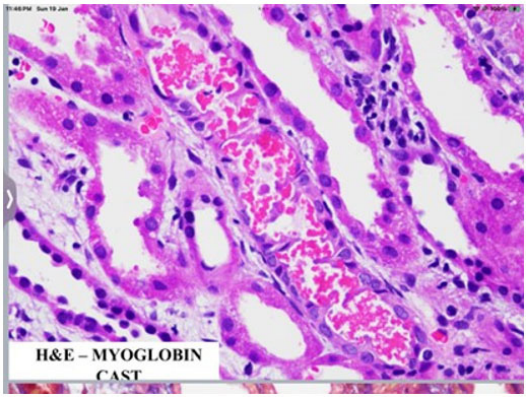

Figure 1: Plenty of reddish granular rounded ropy/aggregates of myoglobin casts in the tubules: H and E stain.

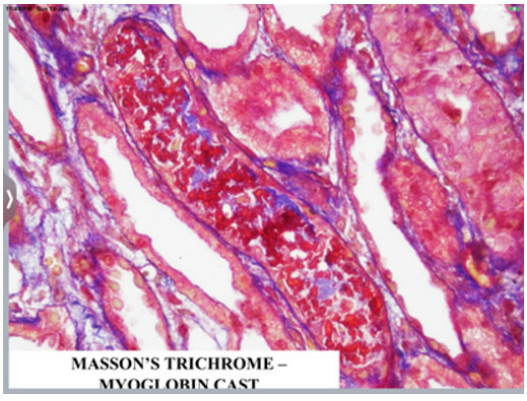

Figure 2: A better depiction of the casts using MT stain.

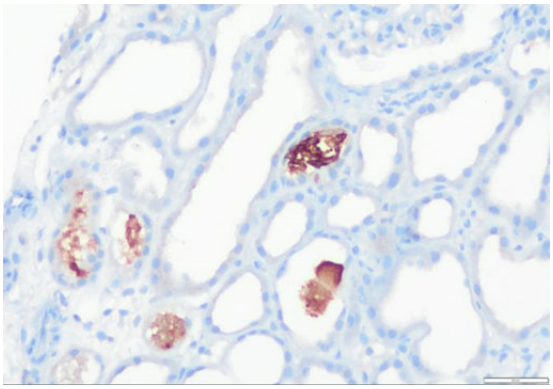

Figure 3: IHC on paraffin block showing positive staining of the casts for myoglobin.

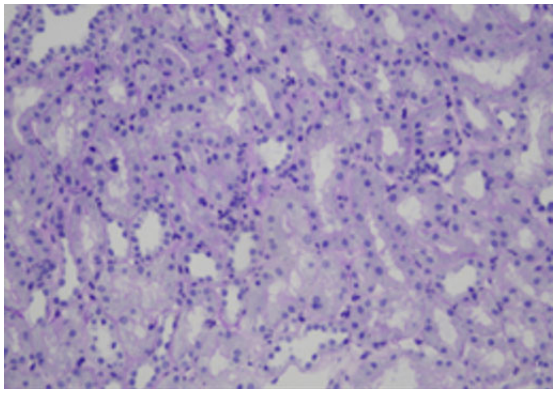

Figure 4: Biopsy done a month later revealed normal tubules.

DISCUSSION

Rhabdomyolysis constitutes to approximately 7–15% of acute kidney injury cases in the critical care setting [3]. Myoglobin has a shorter half-life (2–3 hours) due to its rapid excretion and metabolism. Myoglobinuria/myoglobin cast nephropathy has a multitude of etiology. The most common causes of rhabdomyolysis/myoglobinuria include trauma, medical drugs, illicit drugs and substance abuse, alcohol, prolonged immobility, etc.

Liapis et al. reported a distinctly different set of an etiological spectrum for rhabdomyolysis and myoglobin cast nephrology amongst the South Indian cohort [4]. This includes snake envenomation, severe exertion (the commonest) followed by various other causes that include alcoholism, sepsis, wasp sting, infections like scrub typhus, etc. In our case we did not find any evidence of any of the known etiologies enunciated above except for an unevaluated febrile illness that purportedly occurred three weeks before presenting to us.

Myoglobin casts are usually brownish granular in nature, while with Masson-trichrome staining they tend to exhibit an intense, bright-red hue. Myoglobin casts are hard to trace in certain renal biopsies if there is no major renal impairment [5]. But most of the cases presenting with a full-blown myoglobin cast nephropathy will have both clinical and biochemical evidence of rhabdomyolysis.

In our case, the patient neither had any feature suggestive of overt rhabdomyolysis at the time of presenting to us in a state of renal failure nor had enzyme elevations specific to skeletal muscle injury. Hemoglobin casts exhibit a striking similarity to myoglobin casts. A light microscopy might not be sufficient enough to distinguish them [6]. Rhabdomyolysis is the most common cause of pigment nephropathy and is followed by hemolysis. Myoglobin immunostain is very specific for myoglobin [6]. In our case immunostaining for myoglobin was strongly positive, thus confirming the diagnosis of myoglobin cast nephropathy.

Urine and serum myoglobin concentration are not found to be sensitive in detecting or predicting myoglobin cast nephropathy [7]. While the normal urinary myoglobin concentration is said to be less than 5 ng/mL, our patient had a level of 21 ng/mL in his spot urine sample. For myoglobin to produce a visibly altered Coca-Cola-colored or tea-colored urine, its concentration should be more than 250 μgm/mL [8]. Our patient had a very low concentration of urinary myoglobin and did not present with any of the features of the classical triad of rhabdomyolysis namely muscle pain, weakness and dark-colored urine. Yet he had a biopsy picture of severe tubular injury due to myoglobin casts.

Varadarajan et al. reported a case of malaria-related rhabdomyolysis and myoglobin cast nephropathy that was presumed to be compounded by the use of anti-malarial drugs as well, including chloroquine and atovaquone [9].

Kim et al. in 2017 reported a fatal case of rhabdomyolysis with acute renal failure complicated by severe fever with thrombocytopenia [10]. In this case, a 54-year-old female farmer got admitted with fever and diffuse myalgia. Laboratory findings revealed thrombocytopenia, leukopenia, azotemia, extremely elevated muscle enzyme levels and myoglobinuria that finally proved to be fatal.

Shukla et al. reported a case of fever, fasting, and rhabdomyolysis [11]. In this patient, genetic testing showed a homozygous pathogenic variant in Carnitine Pamitoyl transferase II gene resulting in its deficiency. This enzyme plays a vital role in the carnitine cycle involving the transport of long chain hydrophobic fatty acids from the cytosol into the mitochondrial matrix for the production of energy via β-oxidation. In our case, genetic testing proved to be negative and there was no family history of any similar illness.

To the best of our knowledge, ours is the first case to be reported as a late-onset myoglobinuria long after an unevaluated febrile illness in the absence of an overt myoglobinuria at the time of presentation. To the best of our ability, we could not trace out any such case that has been reported earlier in the literature with a similar picture of a severe and reversible myoglobinuric AKI weeks after a febrile illness that recovered completely. Our study stretches the clinical importance of suspecting a full-blown myoglobin cast nephropathy despite all the markers in urine and serum proving to be negative. As the

condition is potentially reversible if promptly diagnosed and treated, one would not rely on the concurrence of a positive serum and urine biochemistry pertaining to rhabdomyolysis to start the treatment, our study emphasizes.

Myoglobinuric AKI usually has a better prognosis [12]. The prognosis depends on the age of the patient at the time of presentation and coexisting comorbidities. Our patient was of middle age with no other comorbidities and he completely recovered with hydration, urinary alkalinization along with a few sessions of hemodialysis.

In a study done by Jansi Prema and Kurien [13], most of the 57 patients with rhabdomyolysis and myoglobin cast nephropathy who presented with a creatinine of more than 8 mg/dL recovered. Most of the patients in this cohort were young with no comorbidities.

CONCLUSION

Rhabdomyolysis/myoglobinuria and pigment-induced AKI are rare yet potentially treatable causes of AKI. They have a multitude of etiologies including several drugs, strenuous exercise, alcohol, and certain rare metabolic and genetic causes. Though some febrile illnesses have been described to cause rhabdomyolysis during the acute phase, our case proves that a full-blown myoglobin cast nephropathy/AKI can still occur days to weeks after a febrile illness. Our study stretches the clinical importance of suspecting a full-blown myoglobin cast nephropathy despite all the markers in urine and serum proving to be negative. As the condition is potentially reversible if promptly diagnosed and treated, a normal serum and urine biomarker study pertaining to rhabdomyolysis shall not deter the treatment process. Also, it concludes that urine and serum myoglobin are not sensitive in detecting or predicting myoglobin-cast nephropathy.

REFERENCES

1. Zager RA. Rhabdomyolysis and myohemoglobinuric acute renal failure. Kidney Int 1996;49(2):314–26.
2. Holt S, Moore K. Pathogenesis of renal failure in rhabdomyolysis: The role of myoglobin. Exp Nephrol 2000;8(2):72–6.
3. Najafian B, Fogo AB, Lusco MA, Alpers CE. AJKD atlas of renal pathology: Myoglobin cast nephropathy. Am J Kidney Dis 2017;69(2):e7–8.
4. Liapis H, Boils C, Hennigar R, Silva F. Myoglobin casts in renal biopsies: Immunohistochemistry and morphologic spectrum. Hum Pathol 2016;54:25–30.
5. Vanholder R, Sever MS, Erek E, Lameire N. Rhabdomyolysis. J Am Soc Nephrol 2000;11(8):1553–61.
6. Dvanajscak Z, Walker PD, Cossey LN, et al. Hemolysis-associated hemoglobin cast nephropathy results from a range of clinicopathologic disorders. Kidney Int 2019;96(6):1400–7.
7. Lappalainen H, Tiula E, Uotila L, Mänttäri M. Elimination kinetics of myoglobin and creatine kinase in rhabdomyolysis: Implications for follow-up. Crit Care Med 2002;30(10):2212–5.
8. Servonnet A, Dubost C, Martin G, et al. Myoglobin: Still a useful biomarker in 2017? [Article in French]. Ann Biol Clin (Paris) 2018;76(2):137–41.
9. Varadarajan R, Patel A, Salah H, et al. Myoglobin cast nephropathy diagnosed on renal biopsy in a patient treated for malarial infection. Case Rep Nephrol 2024;2024:6764335.
10. Kim MG, Jung J, Hong SB, et al. Severe fever with thrombocytopenia syndrome presenting with rhabdomyolysis. Infect Chemother 2017;49(1):68–71.
11. Shukla SG, Verma A. Fever, fasting, and rhabdomyolysis in an adult male. Neurol India 2020;68(1):182–4.
12. Chatzizisis YS, Misirli G, Hatzitolios AI, Giannoglou GD. The syndrome of rhabdomyolysis: Complications and treatment. Eur J Intern Med 2008;19(8):568–74.
13. Jansi Prema KS, Kurien AA. Etiological spectrum and histopathological diagnosis of rhabdomyolysis associated myoglobin cast nephropathy in South India. Indian J Nephrol 2021;31(1):22–6.

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Author Contributions

Rajesh Jayaraman – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Balan Louis – Design of the work, Analysis of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Rajendran Tholappan – Acquisition of data, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Vel Arvind Subramanian – Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission
The corresponding author is the guarantor of submission.

Source of Support
None.

Consent Statement
Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

ABOUT THE AUTHOR

Article citation: Jayaraman R, Louis B, Tholappan R, Subramanian VA. Myoglobin cast nephropathy long after an unevaluated febrile episode with no clinical evidence of rhabdomyolysis: A rare cause of reversible AKI—A case report. Int J Case Rep Images 2025;16(1):101–105.

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