Pigment cast nephropathy; time to revisit the diagnosis

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ABSTRACT

Pigment cast nephropathy is one of the most severe complications of rhabdomyolysis. It is an important cause of renal failure requiring renal replacement therapy. We report the case of a 23-year-old man who presented with short febrile illness with hyperpyrexia and altered sensorium. Non-contrast CT-brain and CSF analysis were normal. He later developed petechial rashes with thrombocytopenia followed by frank hematuria and worsening renal functions. A kidney biopsy was performed, which revealed findings of myoglobin cast nephropathy.

Implication for health policy/practice/research/medical education:
In this study we report a case of a 23-year-old man who presented with hyperpyrexia, altered sensorium and developed deranged renal function. A kidney biopsy was performed, which revealed findings of myoglobin cast nephropathy. Pigment cast nephropathy is a rare disorder and is often misdiagnosed. Our case was unique as he had varied clinical presentation with an underlying pigment cast nephropathy. A timely diagnosis and management lead to a good outcome in this case.


Introduction

Pigment cast nephropathy is a syndrome complex associated with an abrupt decline in the renal function as a result of the toxic action of pigments on the kidney (1). The major endogenous pigments responsible for this condition are myoglobin (released during rhabdomyolysis), hemoglobin (released during intravascular haemolysis) and bile (released into the circulation during cholestasis). Rhabdomyolysis induced pigment nephropathy accounts for 7%-15% of all cases of acute kidney injury (AKI) (2).

Rhabdomyolysis is typically characterised by muscle pain, red to brown urine due to myoglobinuria and elevated muscle enzymes, including creatine kinase in the blood. Here, we report the case of a patient presenting with fever and myalgia who later began passing red-brown coloured urine with a special focus on his blood picture and renal biopsy findings. A 23-year-old male presented with fever of 2 days duration, which was high grade, intermittent and associated with chills and rigors. There was no evening rise of temperature or associated night sweats. Additionally, he also complained of profound myalgia and severe prostration. The patient denied any past history of similar complaints or any medical/surgical illness. There was no history of recent travel to any endemic areas or use of any recreational drugs. However, he had undergone unaccustomed physical exertion about four days prior to admission.

On examination, the patient was febrile, had tachycardia but was normotensive. Though the patient had myalgia, there was no muscle tenderness associated with it. His general and systemic examination findings were within normal limits. He was managed symptomatically and was evaluated for tropical infections which in turn were all negative. The following day he developed hyperpyrexia (106°F) complicated with seizure and altered sensorium with neck stiffness. Non-contrast CT-brain and CSF
were ruled out. Subsequently anti-hypertensive (needed for hypertension) measures to preserve renal function, including vigorous rehydration (7). Treatment for rhabdomyolysis, at least initially, is mainly supportive, focusing on the management of the ABCs (airway, breathing and circulation) and measures to preserve renal function, including vigorous rehydration (7).

Pigment cast nephropathy is one of the most severe complications of rhabdomyolysis. Approximately 10% of patients with rhabdomyolysis develop pigment cast nephropathy. This condition is characterized by the presence of pigment casts in the urine, which are typically seen in cases of myoglobinuria. The casts are formed in the glomeruli and may lead to renal injury if left untreated. The management of pigment cast nephropathy involves the use of anti-inflammatory agents and supportive care to prevent further renal damage.

In conclusion, rhabdomyolysis is a serious condition that requires prompt diagnosis and treatment to prevent irreversible renal damage. Early recognition of the condition and prompt management with anti-inflammatory and supportive care can help minimize the risk of developing pigment cast nephropathy and other complications. Further research is needed to better understand the pathophysiology of rhabdomyolysis and develop novel therapies to prevent renal injury in this condition.
Light microscopy reveals features of acute tubular injury with loss of brush border, sloughing of the tubular epithelial cells and presence of myoglobin casts in the tubular lumen. These casts are composed of round granules lining up in chains or aggregating in clusters. Their colour ranges from pink to red brown (orangiophilic tinge) with hematoxylin and eosin stain (Figure 1A), bright magenta on PAS stain and appear polychromatic on trichrome stain (Figure 1B). IHC staining with antibody specific to myoglobin is strongly positive (Figure 1D) in these casts. No specific finding is noted on immunofluorescence microscopy; however, electron microscopy reveals globular myoglobin casts having an electron dense core with a less intense periphery with an absent substructure.

The differential diagnosis of pigment cast is hemoglobin cast and RBC cast in this setting, bile cast remains another entity produced under different circumstances (usually associated with high serum bilirubin levels >20 mg/dL). Differentiating myoglobin, hemoglobin and RBC casts on light microscopy is very difficult. Presence of ghost RBC’s within the cast gives a clue to the presence of RBC cast. Other than it no single feature can confidently distinguish these casts. Therefore, herein lies the importance of immunohistochemical test. The specific antibodies to both hemoglobin and myoglobin are now commercially available but not widely used. In our case we could confidently distinguish between these casts based on the positivity for myoglobin stain. However one should remember that coexistence of both hemoglobin and myoglobin casts is a remote possibility. Another thing to remember is that Perls Prussian blue staining, which is used to detect presence of iron in the tissue cannot identify the haemoglobin casts as this stain identifies the Fe$^{3+}$ iron molecule and not Fe$^{2+}$ which is present in hemoglobin cast (9). Bile casts which are seen in bile cast nephropathy, are yellow brown in colour and appear dark green and emerald green on Hall’s and Fouchet’s stains respectively (10).

Most of the patients with myoglobin pigment cast nephropathy recover their kidney function if the underlying cause can be treated, although renal replacement therapy may be required. It has a relatively good prognosis depending upon the underlying cause. However, a long term follow up is needed to ascertain the burden of pigment induced nephropathy to chronic kidney disease incidence in the future.

Conclusion

Our patient had delayed effect of heatstroke. Hematologic disorders like hemolysis and thrombocytopenia are commonly seen such cases (11). Although rhabdomyolysis is a rarely reported complication in heatstroke, it should be considered in patients who present with severe myalgia and markedly elevated creatine kinase levels. IHC remains the gold standard to classify and diagnose the cases of pigment cast nephropathy. Timely diagnosis and treatment leads to a good outcome in this otherwise potentially fatal disease.

Authors’ contribution

AWK and TJ reviewed the sample, reported pathology results and wrote the paper. SKP was the treating physician of the patient, followed up the case and helped in writing the draft. All authors read and signed the final paper.

Conflicts of interest

There is no conflict of interest in this study.
Ethical considerations
Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the author. The patient gave the consent to publish as a case report.

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References