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Case Report

A rare nexus: G6PD deficiency's uncommon affiliation with rapidly progressive renal failure through the prism of pigment nephropathy

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ABSTRACT

Acute kidney injury (AKI) with evidence of hemolysis is associated with tropical infections. However, pigment-induced AKI can happen with relatively uncommon genetic causes of hemolytic anemia, i.e., glucose 6-phosphate deficiency (G6PD). We share our experience of one such patients whose clinical presentation was rapidly progressive glomerulonephritis. On evaluation, she had a history of usage of some drugs and with G6PD estimation revealing deficient status even during the episode while other tests such as Coomb's test and bone marrow biopsy was normal. The kidney biopsy revealed diffuse tubular injury with presence of several coarse granular/pigmented casts in tubular lamina. She was managed with hemodialysis and showed complete recovery. Thus, in tropical countries G6PD deficiency although is not common, should be considered among patients who presented as rapidly progressive renal failure (RPRF) and having history of precipitating factors for G6PD deficiency and a detailed hemolytic work-up needs to be carried out as an important cause of preventable recurrent AKI in tropical countries.

Keywords: RPRF, Pigment nephropathy, Renal biopsy, G6PD deficiency

INTRODUCTION

Pigment nephropathy is an abrupt decline in renal function as a consequence of the toxic action of endogenous hem-containing pigment on the kidney. Such pigments include myoglobin, released from skeletal muscle in rhabdomyolysis, and hemoglobin, released during intravascular hemolysis.[1,2] Both myoglobin and hemoglobin are freely filtered by glomeruli and when oxidized, release their heme moiety into the urinary space.[3] However, within the nephron, excess heme pigments may cause renal vasoconstriction, tubular obstruction, increased oxidative stress and inflammation.[4] In this discussion, we're focusing on a case of pigment nephropathy that initially presented as rapidly progressive renal failure but was subsequently revealed to be linked to G6PD deficiency following thorough investigation.

CASE REPORT

A 20-year-old female from Bhandara visited GMCH Nagpur's OPD with a 10-day history of fever, which started gradually, was of moderate intensity, and occurred without chills or rigors. Additionally, the patient reported reduced urine output for the past three days. The patient had previously attempted local remedies for the fever, which were ineffective. Further inquiry into the patient's symptoms revealed no abdominal pain, burning during urination, cough, breathlessness, or any underlying medical conditions. During the examination, the patient exhibited signs of pallor and icterus. However, there were no indications of cyanosis, clubbing, lymphadenopathy, or pedal edema. The jugular venous pressure (JVP) was within the normal range. Further systemic examination revealed bilateral basal crepitations. Assessments of the

central nervous system, cardiovascular system, and abdominal region did not reveal any notable abnormalities. To investigate the underlying cause, routine blood and urine tests were conducted, yielding the following results (Table 1).

Table 1: Lab tests.

Tests	Values
Hb	4.9 gm%
TLC	18000
Platelets	1.47 lac
Total protein	6.9 gm
Total albumin	6.9 gm%
ALT	28 u/l
AST	54 u/l
ALP	57 u/l
Urea	158 mg%
Creatinine	12.9 gm%
Na	137 mmol/l
K	3.6 mmol/l
Fever profile (HRP2, scrub, widal, dengue)	Negative
CRP	11.3 mg/dl
LDH	>1200 u/l
Ferritin	>300 ng/ml
Triglyceride	99 gm%
Total cholesterol	95 gm%
HDL	28 gm%
LDL	47 gm%
Urine	
Total protein	284.86
Creatinine	78
P/c	3.62 mg/dl

USG (abdomen + pelvis) revealed kidney size of right 10.3×4.1cm and left of 11.4×4.7 cm along with mild ascites and mild pleural effusion. Peripheral blood examination suggestive of few schistocytes. After reviewing the patient's clinical history and investigations, we arrived at a diagnosis of rapidly progressing renal failure. We also looked for ANCA, C3, C4 which was insignificant. Subsequently, hemodialysis was initiated along with blood transfusion. Patient received total of 10 dialysis along with 4 blood transfusion. Patient responded to hemodialysis and recovery was accessed with the help of urine output and kidney function test. The patient needed to be hospitalized for a total of 30 days. We scheduled a renal biopsy to determine the underlying cause of the renal failure (Figure 1-3).

Following the kidney biopsy results, we shifted our focus towards investigating hemolysis as a potential cause of this pigment nephropathy. The patient's workup for hemolysis commenced, with the peripheral blood examination revealing only hypochromic anemia along with few schistocytes. Sickling test was negative, we proceeded with direct and indirect Coombs tests, both of which also yielded negative results. Additionally, the ANA test was negative. Subsequently, the patient's G6PD enzyme levels were assessed and found to be reduced. G6PD (quantitative)-165 u/10^{12} RBCs (202-558). Finally, we kept diagnosis as G6PD deficiency induced pigment nephropathy leading to rapidly progressive renal failure.

Ultimately, we discharged the patient. After one month of follow-up, we obtained the following results. KFT with urea-34, creatinine-1.4 and urine protein to creatinine ratio 1.8 mg/dl, CBC with hemoglobin 8.9 gm%, TLC 8000 and platelets 2.3 lac.

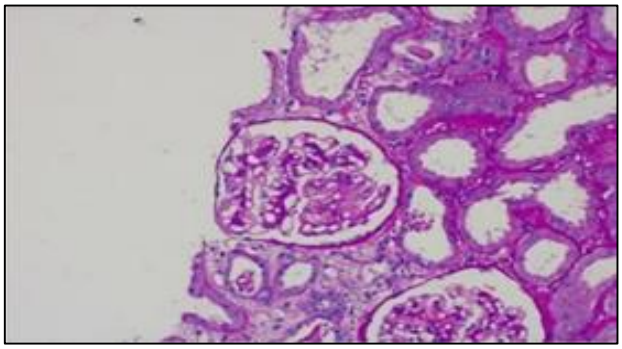

Figure 1: DIF studied do not show significant glomerular or extraglomerular immune deposits.

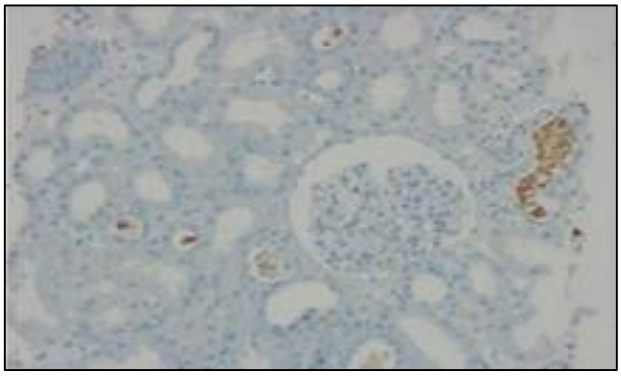

Figure 2: Diffuse severe glomerular tubular injury with presence of several coarse granular/pigmented cast (positive for hemoglobin by IHC) in tubular lumina is observed.

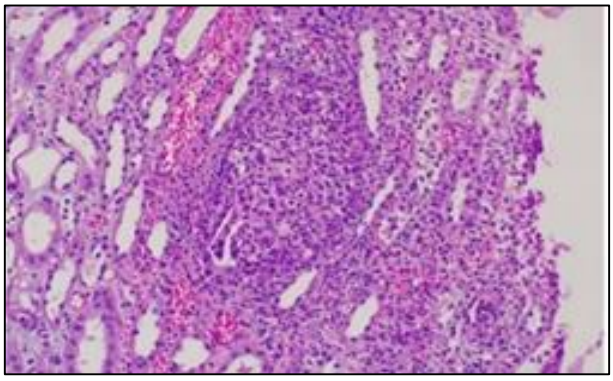

Figure 3: Dense interstitial neutrophilic infiltration forming area of neutrophilic tubulitis seen.

DISCUSSION

G6PD deficiency is a genetic disorder that affects the red blood cells, making them more susceptible to damage when exposed to certain triggers, such as infections, certain foods, or medications.[5] One of the lesser-known complications of G6PD deficiency is pigment nephropathy, a condition characterized by kidney damage due to the accumulation of pigments. G6PD is an enzyme that plays a crucial role in protecting red blood cells from oxidative stress. G6PD deficiency is an X-linked genetic disorder, primarily affecting males, but females who are carriers can also exhibit symptoms.[6] Deficiency results in the red blood cells being more vulnerable to damage and breaking down when exposed to certain oxidative stresses. This leads to hemolysis, where red blood cells are destroyed, and hemoglobin is released into the bloodstream. Pigment nephropathy occurs in individuals with G6PD deficiency when there is a significant release of hemoglobin and its breakdown products into the bloodstream due to hemolysis. Hemoglobin breaks down into heme, which further decomposes into bilirubin and free iron. This excess bilirubin and free iron can damage the kidneys. Furthermore, in some cases, heme may be filtered through the glomeruli into the renal tubules, causing direct damage to kidney tissue.

In our situation, taking into account the medical history of using fever medication could have triggered the development of G6PD deficiency.[7,8] This, in turn, may have contributed to hemolysis and subsequent kidney damage, ultimately resulting in pigment nephropathy.[9,10]

CONCLUSION

G6PD deficiency-induced pigment nephropathy is a rare but important complication of G6PD deficiency. It highlights the interconnectedness of genetic conditions and the potential for one disorder to exacerbate another. Timely diagnosis, careful management of G6PD deficiency, and appropriate treatment of pigment nephropathy are essential to mitigate kidney damage and ensure the best possible outcome for affected individuals.

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