

## CASE REPORT

# HEMATURIA: A RARE PRESENTATION OF G6PD DEFICIENCY

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## ABSTRACT

A young man presented to urologist with a history of passing red color urine after intake of some medications from the local doctor. On investigations he was having anemia, altered liver function tests, mild renal impairment, and evidence of hemolysis. Hematologist was involved who advised to get certain tests including G6PD estimation, which was found to be deficient. He was admitted and managed conservatively with antibiotics; intravenous fluids, anti-emetics and proton pump inhibitors. He improved within 3-4 days and was discharged. Thus teamwork amongst various specialties improved the diagnosis and management of such a rare presentation of a disease.

**Key words:** G6PD deficiency, Haemolysis, Renal failure, Haematuria.

## INTRODUCTION

Passing red color urine is a very common presentation to urologists and nephrologists and can be seen in a variety of clinical settings.<sup>1,2</sup> Red color urine may be due to hemoglobinuria, myoglobinuria, porphyria and hematuria.<sup>3</sup> It can be due to surgical or medical causes. Surgical causes usually include stones, and malignancies. Medical causes usually include urinary tract infection and glomerulonephritis. The case we are going to discuss, presented in a common way with red color urine but on investigations turned out to be a rare disease, Glucose 6 phosphate dehydrogenase (G6PD) deficiency.

A 22 years old college student presented to general practitioner with history of gross haematuria for the last two days. There was no history of lumbar pain, frequency, urgency or burning micturition. There was past history of intake of some medications for the skin problem three days back. The general practitioner referred the patient to urologist, who advised routine urine examination and abdominal ultrasonography. Urine examination revealed that it was of red color, pH 5.0, blood ++, protein ++, pus cells 15-16 /HPF, red blood cells numerous /HPF, urate crystals + + +. As there was no surgical cause of red color urine so he referred the patient to nephrologist. At that time patient was febrile, pale and jaundiced. He was normotensive. On laboratory investigations, Hb 8.5gm/dl, WBC's 11000x10<sup>3</sup>/μl, differential count (poly 48% lympho 47%, mono 3% eosino 2%), RBC's; 2.5x10<sup>6</sup> μl, total bilirubin 3mg/dl (direct 1.6 and indirect 1.4), ALT 167 U/L, AST 213 U/L, ALP 242 U/L, urea 80 mg/dl, creatinine 1.6 mg/dl, albumin 3.8gm/dl, Platelet count, prothrombin

time, and activated partial thromboplastin time were normal. The viral markers for hepatitis were negative. As the patient was having anemia due to hemolysis so hematologist was also consulted. He advised further tests for confirming hemolysis like reticulocyte count, which was 3% lactate dehydrogenase 5988 u/l (NR 50-380), indirect coomb's test which was negative and G6PD estimation which was deficient. Patient was managed with intravenous fluid, antibiotics, anti-emetic and proton pump inhibitor. He improved within three days. Investigations at the time of discharge showed serum bilirubin 0.8 mg/dl, ALT 86 U/l, AST 47 U/l. After one week of discharge urine examination showed blood fine traces, protein nil, RBCs 1-2 /HPF, pus cells occasional, serum bilirubin 0.4 mg/dl urea 29 mg/dl and creatinine 1.1 mg/dl.

## DISCUSSION

G6PD deficiency is a hereditary disorder. Its mode of transmission is X-linked recessive. It is the most common enzymatic disorder of red blood cells in humans, affecting 200-400 million people.<sup>4</sup> It occurs most often in the tropical and sub tropical zones of the Eastern Hemisphere.<sup>5</sup> For example, in Asia, 5.5% in South China<sup>6</sup>, 0-27% in India<sup>7</sup> and less than 0.1% in Japan<sup>8</sup>.

The gene for G6PD is located on X chromosome<sup>9</sup> and has been cloned and sequenced<sup>10</sup>. G6PD is expressed in males carrying a variant gene, while heterozygous females are usually clinically normal. G6PD deficient patients present in different forms like acute hemolytic anemia, neonatal hyperbilirubinemia and favism. WHO has classified the different G6PD variants according to the magnitude of haemolysis.<sup>11</sup>

Class- I variants have severe enzyme deficiency and have chronic hemolytic anemia.

Class- II variants have severe enzyme deficiency but there is usually an intermittent hemolysis.

Class-III variants have moderate enzyme deficiency with intermittent hemolysis, usually associated with infection or drugs.

Class-IV variants have no enzyme deficiency or hemolysis.

Class-V variants have increased enzyme activity.

Our patient most probably falls in class-II and III variants (G6PD Mediterranean and G6PD A-). Because in these classes patients are usually asymptomatic and remain in steady state but there is sudden destruction of the more deficient erythrocytes. This destruction of erythrocytes is triggered by drugs having redox potential, by selected infection and metabolic abnormalities (e.g. Diabetic Ketoacidosis). Acute hemolytic episode usually manifests with hematuria, pallor, jaundice and dark urine. Our patient also showed typical acute hemolytic episode. The patient consulted urologist who worked up on the basis of urological causes. When urological work up did not reveal any surgical cause, he referred the patient to the nephrologist. In our patient there were two probable factors for precipitation of hemolysis, one is intake of certain drugs which he took from some local doctors for his skin problem and other is urinary tract infection. There are various group of drugs like analgesics, sulphonamides, anthelmintics and antimalarials,<sup>12</sup> which precipitate hemolysis in G6PD deficient patients. These drugs<sup>13</sup> interact with hemoglobin and oxygen, leading to intracellular formation of H<sub>2</sub>O<sub>2</sub> and other oxidizing radicals. As these oxidants accumulate within enzyme deficient cells with low GSH level, hemoglobin and other proteins are oxidized, leading to loss of function and cell death. Infections play an important role in precipitating hemolysis in G6PD deficient subjects.<sup>14, 15</sup> Salmonella, E. coli,<sup>14</sup> beta hemolytic streptococci, rickettsia and viral hepatitis<sup>16</sup> are the precipitating agents. In some variants, G6PD level is absent in leucocytes. This leads to abnormal leucocytes function and such subjects are prone to develop infection, similar to chronic granulomatous diseases.<sup>17</sup> The probable mechanism for hemolysis due to infection is that the red cells are damaged by oxidants, generated by phagocytising macrophages.<sup>18</sup> In our patient, second probable mechanism for hemolysis was urinary tract infection. We don't know the exact cause of infection because his urine culture was negative. We treated him with antibiotics and he improved.

Hemolysis is diagnosed by two tests, Lactate dehydrogenase (LHD) and Haptoglobin. The combination of an increased serum LHD and a reduced

haptoglobin is 90% specific for diagnosing hemolysis.<sup>19,20</sup> In case of acute hemolysis, except raised bilirubin liver function tests should be normal. But in this case he has high value of ALT and AST, which favors that there is an associated pathology of liver for which he is under investigation by a gastroenterologist. In this case we have ruled out most probable causes of acute hepatitis like hepatitis B, C and E as HBsAg, HCV by PCR, which were negative, and anti HEV IgM by ELISA was negative. A case of hemolytic anemia was reported by Nirvan Mukerji which was precipitated by super infection of hepatitis D virus on hepatitis B virus function.<sup>21</sup>

This patient had mild renal failure, which was most probably due to volume depletion and heme pigment nephropathy. According to a study in USA<sup>22</sup> heme pigment nephrotoxicity is implicated in 10-15% of hospitalized patients with acute renal failure. The hemolysis of RBC's release alpha - beta dimers which are very small (M. Wt 34,000). These dimers are either bound by circulating heptoglobin or filtered by the glomerulus and appear in the urine as hemoglobinuria resulting in its red to brown color.<sup>23</sup> The hemoglobin which is filtered as dimer is taken up by renal tubular cells where they are degraded and passed in urine as hemosidrenuria. In our patient renal failure was of mild degree and it was managed conservatively with intravenous fluids, avoiding nephrotoxic drugs, without the need for dialysis.

## CONCLUSION

Rare diseases like G6PD deficiency can present in a very common way like hematuria. A high index of suspicion and multi-disciplinary approach improves the diagnosis and management of patients.

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