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Malaria acute kidney injury in a child with glucose-6-phosphate dehydrogenase deficient child: a case report

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Abstract

Introduction: Malaria is a major public health problem worldwide especially in sub-Saharan Africa. Glucose 6 phosphate dehydrogenase (G6PD) deficiency offers protection from severe malaria in African children. Acute kidney injury a severe complication of malaria is expected to be rare in G6PD deficient individual.

Aim: We report a case of malarial AKI in a four year old boy with G6PD deficiency.

Methods: G.U.E. was referred to University of Uyo Teaching Hospital (UUTH), Uyo with history of passage of coke-coloured urine, fever and yellowness of the eyes. On physical examination he was febrile; temperature 38.3^{0}C, severely pale, jaundiced and had generalized oedema. His packed cell volume was 12%; haemoglobin genotype was AA; G6PD was deficient, positive malaria parasites on blood film and elevated serum urea and creatinine levels (49mmol/L and 1,064 µmol/L respectively). Renal ultrasonography was normal. He had 2 sessions of haemodialysis and the renal function improved. He was transfused and also received antimalarial

Conclusion: Individuals with G6PD deficiency can still develop severe and life threatening forms of malaria

Keywords: Malaria, Acute Kidney Injury, Glucose 6 phosphate dehydrogenase (G6PD) deficiency, Children, Uyo

Introduction

Malaria continues to be a major public health problem worldwide,[1] causing 7% of under-five mortality globally.[2] The main thrust of the mortality occurs in Africa[3] and in Nigeria, 300,000 deaths out of about 100million malaria cases occur every year.[4] The lethality of the plasmodium falciparum specie results from complications such as cerebral malaria, hypoglycaemia, acute renal failure, jaundice and haemoglobinuria estimated to occur in about one percent of episodes.[5,6]

Glucose 6 phosphate dehydrogenase (G6PD) is an essential enzyme that protects red blood cells, the host cells of plasmodium falciparum, from oxidative damage by the generation of glutathione. Mutations in this enzyme produce an X-linked deficiency state which affects over 400 million people globally.[7,8] The most common variant of this deficiency in sub-Sahara Africa is G6PD A-.[7] Several studies have linked G6PD A- deficiency to protection from severe malaria in African children.[7,9-10] This has also been corroborated in several reports from Nigerian studies.[11-15]

Acute kidney injury complicating malaria occurs in patients with heavy parasitaemia or acute intravascular haemolysis.[16] We report a case of a four year old boy with G6PD deficiency that had severe malaria complicated by acute renal failure in a Paediatric Emergency Unit of a tertiary hospital in southern Nigeria.

Case Report

G.U.E. was a four year old male who presented at the Paediatric Emergency Unit of the University of Uyo Teaching Hospital (UUTH), Uyo on referrral from a peripheral hospital with a passage of coke-coloured urine of 12 days, fever and yellowness of the eyes of 10days, generalized body swelling of 5days and reduced urine output and vomiting of 4days Urine was coke-coloured with no dysuria or change in frequency of urination or straining on mictuirition. The coke coloured urine lasted for two days after which the child developed a high grade, intermittent fever associated with chills and rigors but no convulsions.

Yellowness of the eyes was noticed on the same day. There was no change in the intensity of the jaundice. There was associated right sided upper abdominal pain but no pale stools.

Five days after onset of fever, he developed generalized body swelling which started with a facial swelling that regressed as the day progressed, later involved the legs and abdomen. Reduced urine output was also noticed with a frequency of once in the day and once at night as against three times in the day and twice at night during the pre-morbid state. Vomiting started a day later. It was postprandial, non-projectile and non-bilious. He vomited four times a day, average volume of 50millilitres per motion. There was no frequent stooling.

He was managed at two peripheral hospitals where he received a number of drugs and injections of which the names are unknown, before referral to UUTH.

This was his first hospitalization. He had had no previous blood transfusions. Other aspects of the history were not contributory.

General physical examination revealed an acutely ill looking boy, febrile with a temperature of 38.3°C, severely pale, jaundiced, peri-orbital oedema and pedal oedema up to mid-leg, not in respiratory distress and no signs of dehydration. His anthropometric measurements were within normal limits. Respiratory and cardiovascular systems examination didn't reveal any abnormalities. Abdominal examination showed a tender and smooth hepatomegaly of 10cm. There was no demonstrable ascites.

A provisional diagnosis of acute kidney injury probably secondary to severe malaria to rule out a haemoglobinopathy was made. Investigations were ordered and significant results were a packed cell volume of 12%; haemoglobin genotype of AA; G6PD was deficient, positive malaria parasites on blood film; markedly deranged serum electrolytes, urea and creatinine levels (Table 1). Renal ultrasonography showed normal sonographic picture of both kidneys with good cortico-medullary differentiation.

A definitive diagnosis of severe malaria complicated by acute kidney injury in a G6PD deficient child was made. He was treated with intravenous artesunate followed by tablets artesunat/lumefantrine for three days plus haematinics. He was transfused with sedimented cells at a dose of 15mls/kg body weight. He had two sessions of haemodialysis with marked improvement in the serum electrolyte, urea and creatinine values (Table 1).

Table 1. Serum electrolyte, urea and creatinine values

Values	At presentation	After 1st dialysis	After 2nd dialysis	Follow up visit
Creatinine(μmol/L)	1,064	620	94	91
Urea(mmol/L)	49	39.2	11.7	6.9
Sodium(mmol/L)	121	140	146	138
Potassium(mmol/L)	5.5	3.7	4.8	4.5
Chloride(mmol/L)	92	95	110	107
Bicarbonate(mmol/L)	15	18	21	22

His packed cell volume improved to 21% after transfusion. Urine flow rate improved to 2.5ml/kg/hr after the second session of dialysis from 0.54ml/kg/hr on admission. Temperature settled by the third day and vomiting stopped on the seventh day of admission. Jaundice was only a tinge on discharge thirteen days after admission. On follow up two weeks after discharge, urea had returned to normal.

Discussion

Plasmodium falciparum is the most common specie of plasmodium that causes malarial disease in sub-Sahara Africa. It remains a major cause of morbidity and mortality worldwide especially in under five children.[2] The episodes can be acute and uncomplicated or present with severe and life threatening complications. Some of the complications include hyperpyrexia, prostration, acute renal failure, cerebral malaria, multiple convulsions, hyperparasitaemia, jaundice, haemoglobinuria, severe anaemia and respiratory distress.[4]

Red blood cell polymorphisms including haemoglobinopathies and G6PD deficiency are common in malaria endemic regions. Several studies[9-15] have demonstrated that they protect against severe forms of malarial disease. In Nigeria, where virtually all young children experience episodes of malaria, their presence offer a tremendous survival benefit when they prevent progression of acute uncomplicated malaria to severe life threatening disease.

The enzyme G6PD is involved in the production of reduced glutathione that protects red blood cells from oxidative stress. Deficiency of this enzyme invariably creates unfavourable intracellular environment, thus providing resistance against the malaria parasite.[17] Guindo et al [9] and Clark et al[10] from Mali and Gambia respectively, reported protection of G6PD A- deficient children from severe malaria. However, while Clark and coworkers[10] demonstrated this protection in both G6PD deficient male hemizygotes and female heterozygotes, Guindo *et al* [9] on the other hand reported a highly significant protection against severe malaria in hemizygous males but not in heterozygous females. In their study, the protection was principally evident against cerebral malaria which was the most frequent form of life threatening malaria. Several Nigerian studies[11-15] have also confirmed G6PD deficiency as offering protection from severe malaria in their children.

Acute kidney injury complicating plasmodium falciparum malaria is uncommon in sub-Sahara Africa where infection is mostly endemic.[18] The aim of this case report therefore is to showcase a G6PD deficient under five child who otherwise should be protected from severe and life threatening forms of falciparum malaria presenting with acute kidney injury . He presented with oliguria, a urine flow rate of 0.54ml/kg/hr and markedly deranged electrolytes, urea and creatinine values. Could it be that this child had a different allele or genotype of the G6PD enzyme? It's been suggested that other G6PD deficiency alleles are relatively common in some regions of West Africa.[10] We do not have facilities to type G6PD in our center which serves as a limitation. Further studies should look at carrying out quantitative G6PD assay and genotyping, routinely for all cases of severe malaria in our facility.

Conclusion

Acute kidney injury complicates falciparum malaria in our environment and patients with red blood cell polymorphisms like G6PD deficiency can still develop severe and life threatening forms of malaria.

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