ORIGINAL ARTICLE

BLACK WATER FEVER (BWF) FOLLOWING QUININE THERAPY, IN A 6 YEAR OLD NIGERIAN: A CASE REPORT FROM THE RAINFOREST SOUTH EASTERN NIGERIA

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Abstract

Introduction: Black Water Fever (BWF) is a syndrome characterized by intravascular haemolysis, haemoglobinuria and acute renal failure. It is an uncommon complication of Plasmodium Falciparum malaria in our environment. BWF is a rare manifestation of Falciparum Malaria characterized by sudden intravascular haemolysis followed by fever and haemoglobinuria. We present a rare case of Black water fever (BWF) with a typical presentation of fever, vomiting, and abdominal pain; with eventual passage cola colored urine, jaundice and oliguria after receiving intravenous quinine infusion. Case Presentation: AM is a 6–Year old female who presented with a 3-week history of fever, abdominal pain and vomiting. Examination revealed Pyrexia and Hepatosplenomegaly. A diagnosis of malaria was made based on blood smear for thick and thin film. She passed cola coloured urine and had oliguria 6 days after admission. Quinine infusion was stopped and artesunate commenced. She was transfused with red cells. After six days she made adequate urine, cola coloured urine stopped and her haemoglobin concentration was 9 g/dl. Conclusion: Quinine, which can be procured over the counter, is used injudiciously in managing both complicated and uncomplicated malaria and these could precipitate BWF. A high index of suspicion, early diagnosis based on clinical features and certain laboratory investigations can help manage the child promptly and avert the numerous morbidities and fatality that follow it.

Keywords: Black Water Fever; Malaria; Fatality

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Introduction

Malaria is responsible for almost a third of under 5 mortality and is associated with a tenth of maternal deaths in Nigeria with 63% of hospital attendance in Nigeria health care facilities. [1]

Malaria affects more than 240 million people, over 40% of the world’s population, in more than 100 countries in the tropics, from South America to the Indian peninsula. [2]

One child dies of malaria somewhere in Africa every 20 seconds and there is one malaria death every 12 seconds somewhere in the world. Malaria kills in one year what Acute Immune Deficiency Syndrome (AIDS) killed in 15 years, if 5 million have died of AIDS; 50 million have died of malaria. It has several complications of which BWF is among. [1]

BWF (Black water fever) is a syndrome characterized by intravascular haemolysis, haemoglobinuria and acute renal failure.

It is an uncommon complication of Plasmodium Falciparum malaria in our environment. The overall incidence in Nigeria is unknown but the frequency may be more than reported. [3] Mortality rate is about 18% and morbidity is high because about 90% of patients have suffered from various degrees of renal failure among which 47% of them require dialysis. [4]

BWF is a complication of treating severe malaria with Quinine Sulphate based antimalarial therapy and those which are derivatives of amino-alcohol family such as halofantrine and mefloquine. [1,5] It can also occur in non-immune or semi-immune individuals who were treated with quinine preparations. [5]

It is a possible sequel in children suffering from Glucose-6-Phosphate Dehydrogenase deficiency.

It typically presents with passage of darkish brown or cola coloured urine in addition to the usual features of malaria such as fever, headache, nausea and vomiting as well as abdominal pain. [6]

Case Presentation

A 6–Year old girl who presented via the children emergency ward with a 3-week history of fever, vomiting, abdominal pain and passage of cola coloured urine and oliguria 6 days after admission.

Patient was apparently well until 3 weeks prior to presentation when patient suddenly developed fever. Fever was high grade, intermittent, worse at night with associated chills and rigor. There was no history of pain on urination, ear discharge, pain on swallowing or body rash. Patient was also noticed to have started vomiting some hours after the fever. About the same time, she also complained of abdominal pain which was generalized and did not radiate to any other part of the body. For these symptoms, she was taken to a private hospital where some injections and infusions were given but to no avail, necessitating referral to Enugu State University of Technology Teaching Hospital.

Examination revealed Pyrexia and hepatosplenomegaly. A diagnosis of malaria was made based on blood smear for thick and thin film.

Six days into admission, mother noticed passage of cola coloured urine, leg and facial swelling that regresses as the day goes by and oliguria. These symptoms started
after she was placed on intravenous quinine. There is no history of passage of cola coloured urine in the past. Her genotype (blood type) is AA.

Delivery was by spontaneous vertex and she cried immediately after birth, weighed 3.4 kilograms and had no jaundice at birth.

Patient had no immunization at all. There was no family history of jaundice, sickle cell anaemia or passage of cola coloured urine.

Examination then revealed an acutely ill looking child, well nourished with facial puffiness, febrile (38.9°) in no obvious respiratory distress, icteric, pale, and bilateral pedal edema up to the ankle with splenomegaly and hypertension (Blood pressure of 110/80, normal for age is 90/56). Laboratory investigations showed haemoglobin concentration of 5mg/dL, Total white blood cell count of 2.5 x10⁹/L, Neutrophils of 36%, Lymphocytes of 63% and Monocyte of 1%. Blood film showed fragmented red cells and Malaria Parasite (moderate). White blood cells and platelets appear normal. Bedside urine analysis showed Bilirubin (moderate), Urobilinogen (mild), Ketones nil, Glucose nil, pH 6 and Specific Gravity of 1.020. G6PD Assay was negative (Non Reactive). Urine Microscopy yielded red blood cell (mild), Epithelial cells (mild), Crystals of Amorphous phosphate (moderate) and no cast.

Serum urea and electrolyte revealed normal values, safe for slightly raised urea.

Abdominal ultrasound showed kidneys which appeared enlarged measuring about 9.8 x 3.5 cm (R) and 10.4 x 4.6 cm (L). (Normal range 7.8 x 1.2 cm (R) and 8.1 x 1.3 (L)) There was prominent pyramid of the (L) kidney.

Intravenous quinine infusion was thus stopped and intravenous artesunate commenced. She was transfused with packed red cells. Intravenous fluid was given with frusemide and input and output chart commenced. After six days patient started making adequate urine 1.8 ml/kg/hour, the cola coloured urine stopped and her post transfusion haemoglobin concentration was about 9 g/dL. The enlarged spleen resolved and so was the jaundice. She was subsequently discharged.

**Discussion**

Black water fever is an uncommon complication of *Plasmodium Falciparum* characterized by fever, haemoglobinuria and haemoglobinuria. [6] It has been postulated that malaria parasitized red blood cells undergo antigenic alteration that make them susceptible to immune mediated destruction in the spleen due to the production of auto antibodies against such cells.[7] This derangement could also affect non-parasitized red cells thus leading to severe anaemia.[7]

Black water fever have been described by Hippocrates and Gilles de Corbeil in ancient Greek philosophy.[8] It was first coined in 1819 by English surgeon and then in Africa by a Sierra Leonean doctor John Farrell Eason in 1884.[9]

BWF has become exceptional since 1950, when quinine was replaced by chloroquine. The disease reappeared in 1990 following the re-utilization of quinine because of malaria resistance to chloroquine.[10]

Although the cascade is triggered by the administration of quinine (as noted in our patient), halofantrine and mefloquine have also been implicated. These drugs have
similar amino-alcohol molecules as quinine. [10]

The clinical presentation of BWF is typical with attendant intravascular haemolysis. Olga et al [11] in Cuba noted a patient with fever, headache and vomiting with malaria parasitaemia who later passed cola coloured urine, had jaundice and renal failure after administration of quinine. She did well after quinine was stopped, red cells transfused and haemodialysis instituted. Our patient had similar features of intravascular haemolysis with early signs of renal failure but improved after she was transfused with red cells and quinine changed to artesunate. Khandewal [12] and co-workers in their series used aretemesine derivative in managing their patient with BWF with tremendous improvement. Haemodiagnosis was not done in this index case because the serum creatinine was still within normal range, besides; the early signs of renal failure were reversed by renal challenge using intravenous fluids (normal saline).

It is conceivable that Glucose 6-Phosphate Dehydogenase deficient individuals who took oxidant drugs may subsequently develop haemoglobinuria and jaundice. [13] This is least possible in our patient who is a female with a non reactive G6PD assay. More so she had malaria which was treated in a private setting and had quinine which possibly triggered the haemolysis. The dark coloured urine, the anaemia which was corrected by blood transfusion and development of renal insufficiency are clear features of BWF.

Massive haemolysis and associated haemoglobinuria had been reported in two adults with sickle cell anaemia and pernicious anaemia. Nevertheless our patient is not a known case of sickle cell anaemia. When haemoglobin precipitates in the kidney, renal impairment can result and this would lead to rise in blood urea and creatinine levels. Our case has normal creatinine levels. This can be explained by the fact that cola coloured urine and early signs of renal failure were tackled promptly in our series and thus renal parenchymal involvement was averted. Oumar [14] and colleagues in his report of three patients with black water fever also noted two cases that had mild renal insufficiency in form of oliguria.

It is very pertinent for paediatricians who manage cases of malaria to be aware these complications and reserve the use of quinine only for patients with severe malaria as quinine apart from causing other side effects can trigger BWF.

Fortunately, the emergence of Artemesine combination therapy (ACT) in the management of malaria will go a long way to curb this malady.

Conclusion

Black water Fever is a rare but deleterious disease which is seen in malaria endemic region. Quinine which can be procured over the counter is used injudiciously in managing both complicated and uncomplicated malaria and these could precipitate BWF.

High index of suspicion, prompt management of this condition and proper use of quinine will help a great deal in curbing this menace. Evolution is usually favorable in the paediatric population so far adequate care is provided.
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Competing Interest: The authors hereby declare that we have no competing interests.

Authors’ Contribution

All the authors made substantial intellectual contributions to this study. CJM was involved in the conception, design, and data collection, interpretation of results, preparation of the manuscript, revision of the article at various stages and preparation of the final draft. Other authors made substantial contributions in the design, data collection, and interpretation of the results, preparation of the manuscript, revision and preparation of the final draft.

Consent: An informed consent was granted by the care giver.

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