CASE REPORT

Rhabdomyolysis with Acute Renal Failure in Falciparum Malaria: A Case Report

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ABSTRACT

Malaria is transmitted by the Plasmodium parasite, and often reported in Bangladesh in patients with a history recent travel to an endemic zone. Malaria is endemic in 13 of 64 districts in Bangladesh. About 14 million people are at risk. Prompt diagnosis and treatment is essential in preventing mortality. Severe malaria represents a medical emergency because it may rapidly progress to complications and death without prompt and appropriate treatment and almost exclusively caused by Plasmodium falciparum. The incidence of imported malaria is increasing and the case fatality rate remains high despite progress in antimalarial treatment. Clinical deterioration usually appears 3-7 days after onset of fever. Complications involve the nervous, respiratory, renal, and/or hematopoietic systems. Metabolic acidosis due to renal failure is a common systemic complication. We are reporting here a case of severe malaria in a 30-year-old man who presented with fever, myalgia, and reduced urination for two days.

Keywords: *Rhabdomyolysis, Acute renal failure, Falciparum malaria, Bangladesh*

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INTRODUCTION

Malaria is one of the most burden diseases among all infectious diseases. It is transmitted by the bites of infected female *Anopheles* mosquitoes.[1] In the year 2015, about 212 million cases of malaria occurred worldwide. Most of the cases in 2015 were in the WHO African Region (90%), followed by the WHO South-East Asia Region (7%) and the WHO Eastern Mediterranean Region (2%). Progression to severe and fatal disease is significant but not entirely confined to *Plasmodium falciparum* infections. High mortality is always associated with severe malaria. From a clinical perspective, there is a continuum from asymptomatic malaria to uncomplicated illness through to severe and lethal malaria.[2] In severe malaria, the prompt administration of an effective antimalarial drug, preferably by a parenteral route, is essential. Artesunate (i.v. or i.m.) is the treatment of choice, followed by Artemether (i.m.) and Quinine (i.v. or i.m.).[2]

Acute renal failure is a common complication in severe malarial infection which can be the resulted from multiple mechanisms: hypovolaemia, excessive haemolysis, disseminated intravascular coagulation or impaired microcirculation due to a high level of parasitized erythrocytes.[3] Rhabdomyolysis is an uncommon way of inducing renal failure in malaria infection. The diagnosis is based on high serum level of muscular enzymes; Creatine Phosphokinase (CPK) and clinical symptoms like myalgias. To our knowledge, very rarely few cases of rhabdomyolysis complicated by acute renal failure during malaria infection have been described.[4,5]

CASE REPORT

A 30-year old man was admitted in our hospital with one week history of intermittent high grade fever which appeared every alternate days, yellowish discoloration of his eyes and severe body ache and

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decreased urination for two days. He denied any itching, cough, dysuria, diarrhea, melaena, convulsions, blood transfusion and contact with any sick patient. The patient had no history of chronic diseases, drug, or alcohol abuse, contact with heavy metals, trauma, severe exercise, seizures, and use of medications, snakebite, or other recent infectious diseases. He did not have any travelling history to any endemic zone for malaria in the past one year; however, he had frequent travel history to endemic zones.

On examination, his initial vital signs were pulse 130 bpm, BP: 90/60 mmHg, RR-30 breaths/min, and T-102°F on Day-0. He appeared pale, icteric; there were bleeding spots in his noses and bleeding spots over his chest. His capillary refill time was 3s. He had severe prostration. He would cry out of pain whenever his proximal muscle groups were touched. There was no lymphadenopathy. His systemic examination revealed hepatomegaly and splenomegaly. His chest was clear on examination. His GCS was 12 and he did not have any neck stiffness or any flapping tremors. On admission, his initial WBC count (7000/ul) and haemoglobin (13.1 g/dl) were with in normal limits; however, platelet count was low (30,000/ul). A comprehensive metabolic panel revealed, blood glucose 4.6 mmol/l, creatinine of 1.96 mg/dl, serum electrolytes revealed Na^+ 133mmol/l, K^+ 4.4 mmol/l, Cl^- 99 mmol/l initially. In addition, the hepatic panel showed serum bilirubin of 16.8 mg/dl and ALT-72 U/L. Other investigations revealed: Reticulocyte count: 2%, CRP-48mg/dl, CPK-911u/l, LDH 614 U/l. On Day 1, an initial ICT for Malaria was positive for both P. Vivax and P. Falciparum which was then repeated twice to reconfirm it (Fig. 1). Parasite count and venous lactate was not done. Urinalysis was positive for blood 3+, bilirubin 2+, protein 1+, urobilinogen 1+ and the red blood cell was 49-99/ HPF, WBC 9-19 / HPF. The chest X-ray was normal. On the Day 1, his urine output further declined and became very dark (Fig. 2). The IEDCR was contacted; the patient was supplied with three doses intravenous artesunate to be given at 2.4 mg/kg/dose at 0, 12 and 24 hours. The first dose was given on 1815 hours on Day1, 2nd dose on 0615 hours on Day 2 and 3rd dose on 1815 hours on Day 2 (Fig. 2). After receiving the 2nd dose, the patient's orientation to time place and person deteriorated at 1415 hours on Day 2 with a GCS of 10. On 1900 hours Day 2, his metabolic panel revealed, creatinine: 3.48 mg/dl, an arterial blood gas analysis showed pH 7.3, PO_2 45 mmHg, PCO_2 24.1 mmHg, $HCO3^-$ 11.5 mmol/l, BE 14.9 mmol/l. Further blood test revealed: haemoglobin 11.7 g/dl, SO_2^- 77%. Serum electrolytes were Na^+ 131 mmol/l, K^+ 6.8 mmol/l, Ca^{++} 0.67 mmol/l, Cl^- 106 mmol/l. On Day 2, further hydration and correction of electrolytes was intended and urgent dialysis was being arranged for the patient. The patient was treated with 10% Calcium gluconate IV, nebulized salbutamol for the correction of hyperkalaemia. The patient's blood pressure dropped to 80/50 mm of Hg and he was resuscitated with IV fluids. The urine output decreased to 0.3ml/kg/hour. The urine color appeared dark red as shown in Fig. 3. He was also given IV sodium bicarbonate to correct the acidosis. Despite all efforts the patient died 0845 on Day 3.

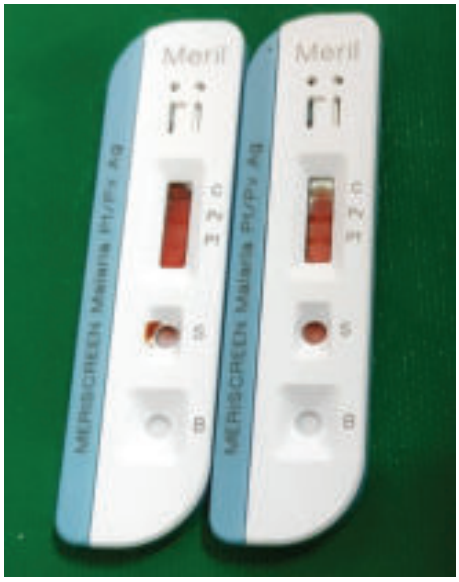

Fig. 1: *Immunochromatographic tests (ICT) done on the bed side showing ICT positive for both Plasmodium falciparum and Plasmodium vivax.*

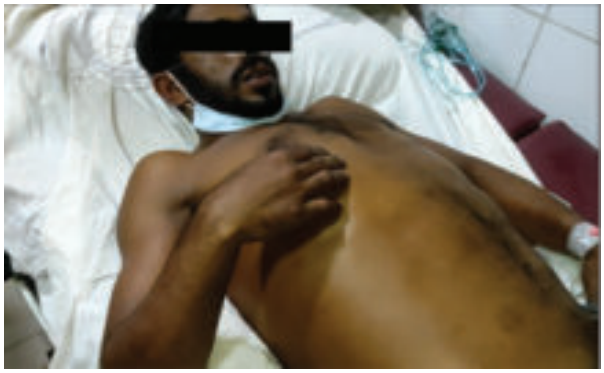

Fig. 2: *Patient on Day 2 at 14:15 hours.*

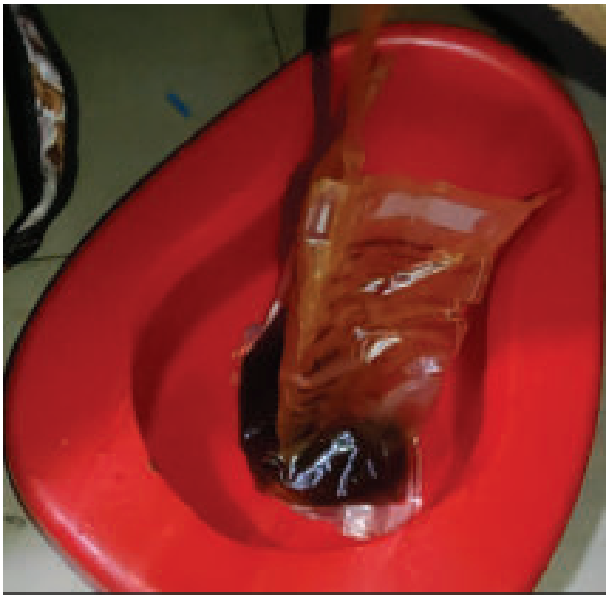

Fig. 3: *Patient's urine on Day2 at 18:15 hours.*

DISCUSSION

Malaria is an important public health problem in Bangladesh with significant morbidity and mortality. More than 95% of malaria cases in Bangladesh are reported from 13 highly endemic districts, where 11 million people are at risk.[6] An early and accurate diagnostic approach is essential for reduction of morbidity and mortality of malaria. Considered as the gold standard, microscopic examination of Giemsa-stain blood films is widely used because of its efficiency and low cost. However, the microscopic technique is time-consuming and requires equipment and trained personnel.[7] Immunochromatographic tests (ICT) render the non-microscopic methods for malaria diagnosis, thereby saving on training and time. These tests are easy to perform and require little training to interpret results.[8] Immunochromatographic rapid tests offer the possibility of more rapid non-microscopic method for rapid diagnosis.[9,10] In diagnosis of Falciparum malaria in Bangladesh, a study done by Ahmed MU et al. have revealed that "ICT Malaria Pf " had sensitivity and specificity of 94.2% and 100% respectively.[10] Both the studies found that Immunochromatographic rapid diagnostic tests were reliable.[9,10] Reducing the impact of malaria is key to the achievement of the Millennium Development Goals (MDGs), agreed by every United Nations Member States. In achieving the global goal rapid diagnostic test can play its role. Considering the limitations in the rural areas rapid diagnostic tests (RDTs) are very useful.[11] Harani MS et al. evaluated the sensitivity Ischaemic acute tubular necrosis is by far the most common cause of acute renal failure in *P. falciparum* malaria.[9] It is the result of hypovolemia, peripheral pooling of blood and blockage of microcirculation by parasitized red cells and non-specific effects of infection.

In this case, the patient had rhabdomyolysis that may be the actual reason of this acute renal failure. Many mechanisms may induce these muscle damages.[12] In this case, rhabdomyolysis could not be explained by usual causes (hyperthermia, crush syndrome, metabolic abnormality, drugs, or other infectious diseases). Thereafter, the responsibility of *P. falciparum* as the pathophysiological mechanism of the rhabdomyolysis was supposed. Only a few publications are available about rhabdomyolysis and *P. falciparum* infection.[4,5] The mechanism postulated to explain rhabdomyolysis is the sequestration of parasitized erythrocytes in striated muscle capillaries, inducing microcirculatory obstruction. *Plasmodium falciparum* may also induce myositis with myoglobinuria.[13] This mechanism may explain the muscle pain experienced by our patient and the high level of CPK.

We suggest that signs of rhabdomyolysis has to be sought in patients with acute renal failure and *P. falciparum* malaria infection, especially when muscle pain is present. Mild jaundice due to haemolysis in malaria is common. Severe jaundice due to haemolysis, hepatocyte injury, and cholestasis may occur in the setting of P. falciparum infection; this manifestation is more common among adults than children. Liver dysfunction together with renal impairment and other organ dysfunction portend a poor prognosis.[14] Our patient most likely developed jaundice because of severe haemolysis. Thrombocytopenia is also a common feature in malaria. Thrombocytopenia induced by malaria is due to shortened life span in the peripheral blood and, third, some interaction is present between platelets and malaria plasmodia or parasitized red cells.[15]

The possible cause of death in our patient was due to severe metabolic acidosis and acute renal failure. Acidosis is an important cause of death from severe malaria; it is caused by several factors, including: anaerobic glycolysis in host tissues where sequestered parasites interfere with microcirculatory flow, parasite lactate production, hypovolemia and

insufficient hepatic and renal lactate clearance.[14] The prognosis of severe acidosis is poor in Falciparum malaria.

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