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Case Report

Cerebral Malaria Associated with Acute Renal Failure in a Sudanese Patient: Case Report

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ABSTRACT

Malaria is a common health problem especially in the tropics. Cerebral malaria is a worse complication of the disease with unknown pathophysiology. In this scenario, a Sudanese housewife was brought to the emergency room after a sudden fall in the ground, she was in coma. Investigations revealed sever falciparum malaria, thrombocytopenia and features of acute renal injury. Quinine was prescribed in addition to antithrombotic, diuretics and supportive medications. In the following day she developed aspiration pneumonia and a fourth generation antibiotic was prescribed. One day later she looked very ill, jaundiced with features of Disseminated Intravascular Coagulation (DIC). Her general condition was not improving, and then she was arrested and died. Multiple organs failure associated with sever malaria was considered as the cause of death.

Keywords: Malaria; Cerebral malaria; Coma; Acute renal injury

INTRODUCTION

Malaria is an international devastating disease affecting over 40% of the world's population. According to the World Health Organization (WHO), globally there were 229 million malaria cases in 2019 in 87 malaria endemic countries. Malaria case incidence reduced from 80 in 2000 to 58 in 2015 and 57 in 2019 globally. The WHO African Region estimated 215 million cases in 2019, accounted for about 94% of cases. Globally, Malaria deaths, reduced steadily over the period from 2000 to 2019, from 736,000 in 2000 to 409,000 in 2019 [1]. Incidence of severe malaria is approximately two million cases with nearly 430,000 deaths annually [2]. It is considered as medical emergency affecting multisystem with different clinical manifestations varying between adults and children with cerebral involvement, kidney dysfunction, and acidosis are independent predictors of mortality in both adults and children [3,4]. Also there are prognostic indicators with the strongest association with death in children with severe malaria to be Acute Kidney Injury (AKI) [5]. Malaria is caused by the obligate intra or more of the four malaria species *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae* [6]. Severe malaria is mostly caused by *Plasmodium falciparum* infection, However, *Plasmodium vivax* and *Plasmodium knowlesi* are also known to lead to severe and fatal disease [7]. Severe malaria is defined as acute malaria with signs and symptoms of organ dysfunction and/or high level of parasitemia and is associated with high mortality rate [8]. Cerebral Malaria (CM) is defined as asexual *Plasmodium falciparum* parasitemia and deep coma with no other coma etiology evident [9,10]. The exact pathophysiology for CM is unknown, but it is associated with parasitized red blood cell sequestration in brain capillaries, this sequestration may lead to impaired or alert perfusion and local release of inflammatory factors. CM may be fatal within few hours of onset of coma, and unarousable coma has a high mortality (20% or more) even when treatment and intensive care facilities are available. The prognosis is worse if CM is associated with Acute Renal Failure (ARF) [11-14]. The WHO criteria for severe malaria include Acute Renal Failure (ARF) which is common among adults living in low malaria transmission areas who acquire malaria [15]. ARF is associated with mortality in severe malaria [16]. Malarial ARF is commonly found in non-immune adults and older children with falciparum malaria, and since the precise mechanism of malarial ARF is not known, several hypothesis including mechanical obstruction by infected erythrocytes, immune-mediated glomerular and tubular pathology, fluid loss due to multiple mechanisms and alterations in the renal microcirculation, have been proposed [17]. Severe malaria in Sudan is usually due to *Plasmodium falciparum*, however, cases due to *Plasmodium vivax* have been described [18].

CASE REPORT

A 55-year-old Sudanese housewife was brought to the emergency room after a sudden fall on the ground, at presentation she was unconscious, had mouth bleed and convulsions. Her son claimed that, the condition started 3 to 4 days ago with intermittent onsets

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of fever, vomiting and diarrhea, but she didn't have a medical intervention during that time. According to her son, the patient had no past history of diabetes, hypertension, asthma or heart disease, and she didn't have a similar complain before. Her family history was clear except for diabetes mellitus, drug history was negative and the patient had not known allergy to any drug. On examination the patient looked ill, not pale, not jaundiced and unconscious. Her BP was 80/50. Chest, abdomen and CNS examinations showed no remarkable findings. ECG was performed and investigations requested at that time included CBC, blood film for malaria, renal function test, serum calcium, serum magnesium and brain CT. Brain imaging showed an edema, while laboratory results revealed sever Falciparum malaria associated with thrombocytopenia and hypomagnesemia (Table 1).

Quinine infusion 600 mg in 500 ml 10% dextrose was immediately prescribed, together with Ceftriaxone injection 1 gm, Pantodal infusion, Paracetamol, Phenytoin, Dopamine in addition to NG feeding. The patient was scheduled for input and output chart starting from that day and received 2 liters of IV fluids in the emergency room. Then the patient was transported to the Intensive Care Unit (ICU), where thigh stockings were applied as a prophylactic anti-thrombotic agent. In day two in the ICU; chest examination revealed scattered cryptic wheezes, and she was still unconscious but no convulsions. Her blood pressure was 80/55 and temperature 37.7°C, a diagnosis of aspiration pneumonia was reported. In this day urine analysis was performed; the chemistry showed Glycosuria (+) and free hemoglobin (++), while urine microscopy showed 4-6 Pus cells and 14-16 RBCs/HPF. Previous medications were continued in this day with the addition of Cefroxime, Metronidazole and Potassium chloride. In addition, 250 µl Heparin PD was used in this day as prophylactic anti-thrombotic agent. Total input was 2300 ml/24 hrs while the total output was 2060 ml/24 hrs. In day three in the ICU the patient looked very ill, febrile and not jaundiced. Chest examination revealed cracks and her BP was 90/60, and she developed Disseminated Intravascular Coagulation (DIC). Laboratory investigations in this day showed

Table 1: Baseline laboratory results.

Parameter	Result	Reference range
B. Urea	43 mg/dl	10-50
S. Creatinine	1.5 mg/dl	0.5-0.9
S. Sodium	134 mmol/l	135-145
S. Potassium	3.3 mmol/l	3.5-4.5
S. Magnesium	1.75 mg/dl	-
Blood film for malaria	*P. Falciparum* rings seen (Hyperparasitemia)	-
WBC	10.1 × 103/µl	40-11
RBC	4.99 × 106/µl	3.8-4.8
HGB	14.9 g/dl	12-15
HCT	43.30%	36-46
MCV	86.8 fl	78-100
MCH	29.9 pg	27-32
MCHC	34.4 g/dl	31.5-35
PLT	59 × 103/µl	150-450
LYM%	10	20-40
MXD%	9	1-15
NEUT%	81	40-80
RDW-CV	13.30%	11-16

Table 2: Laboratory results in day III.

Parameter	Result	Reference Range
B. Urea	106 mg/dl	10-50
S. Creatinine	4.0 mg/dl	0.5-0.9
S. Sodium	143 mmol/l	135-145
S. Potassium	6.4 mmol/l	3.5-4.5
WBC	10.5 × 103/µl	4-11
RBC	4.36 × 106/µl	3.8-4.8
HGB	13.1 g/dl	12-15
HCT	38.60%	36-46
MCV	88.5 fl	78-100
MCH	30 pg	27-32
MCHC	33.9 g/dl	31.5-35
PLT	30 × 103/µl	150-450
LYM%	8	20-40
MXD%	2	1-15
NEUT%	90	40-80
RDW-CV	15.10%	11-16
T. Billirubin	1.4 mg/dl	0.3-1.1
D. Billirubin	1.1 mg/dl	0.1-0.4
Total protein	5.6 g/dl	5.8-8.2
Albumin	2.8 g/dl	3.3-5
ALP	85 µ/l	30-120
AST	615 µ/l	<35
ALT	784 µ/l	<34
CRP	160 mg/l	<5

abnormal renal function test; elevated liver enzymes, C-Reactive Protein (CRP) and lowered Platelets count (Table 2).

Meroponium 1 gm was prescribed in this day after sepsis had been considered; in addition to fresh frozen plasma and platelet concentrate, While KCl and Heparin were stopped in this day. Before the implementation of this plan and in the mid of this day the patient was arrested; CPD was done for 30 minutes, but the patient didn't respond and died. This report was written after agreement of family representative who shared the patient's medical history with the researcher.

DISCUSSION

In this case if we look on the severity of the disease in relation to the total mass of infected red cells (which doesn't necessarily involve the observation of parasites on the peripheral blood) we can notice some sort of correlation. The symptoms started 4 days before the day of admission but as low grade illness and during this period the mass of infected RBCs developed gradually, till the day of admission when hyper parasitemia (>250,000 parasites/µl) had been observed on the peripheral blood film. This is in accordance with the development of cerebral manifestations. The amplification of parasitized red cell mass is related to the sequestration of infected cells, and considering the pathogenesis of CM, sequestration of red cells containing the mature forms of parasite in the microvasculature is thought to be a major mechanism of the disease [19]. The sequestration of PRBCs in the relatively hypoxic venous beds allows optimal parasite growth and prevents the PRBCs from being destroyed by the spleen [20]. It is the sequestered parasites that cause pathology in severe malaria, and the prognosis is related to the sequestered biomass [21,22]. The peripheral blood parasite

count is a relatively poor predictor of the size of this biomass. This clearly stated in a recent postmortem study of fatal falciparum malaria in adults, in which the median ratio of cerebral to peripheral blood parasitemia was 40 ranging from 1.8 to 1500 [23]. Another finding to be discussed is the relation between malaria and thrombocytopenia. In this case the baseline platelets count was 59 × 103/µl; which is not uncommon finding in acute malaria infections, as it has been estimated that near 80% of patients infected with *P. falciparum* develops thrombocytopenia during their infection [24]. Concerning the magnitude of parasitemia, in the baseline results the patient had hyper parasitemia associated with a PLTs count of less than 100 × 103/µl. This is in accordance with the correlation stated in Horstmann's study between low platelet counts and high count of malaria plasmodia in *P. falciparum* and *P. vivex* infections, as patients PLTs counts raised to threefold the initial value within 5 days after clearance of parasites [25]. Another previous study done by Leal-Santos et al. showed a consistent inverse association between parasitemia and the Platelets count [26], while here the PLTs count in day II was lower than the first time, but unfortunately the level of parasitemia was not performed after the day of admission. Malarial Acute Renal Failure (MARF) defined as a serum creatinine concentration >2651 M (3 mg/dl), and plasma Creatinine is considered as the best prognostic marker in subsequent needs for kidney replacement therapy and outcome [27,28]. Up to 40% of patients with severe *P. falciparum* malaria can have acute kidney injury and mortality can be as high as 75% if renal replacement is delayed in malaria endemic countries [29,30]. In this case; the baseline serum Creatinine level was 1.5 mg/dl, while in day III it raised to 4.0 mg/dl, which indicates the development of Acute Renal Failure (ARF). Other laboratory findings in that day showed hyperkalemia, hypoalbuminemia, slight jaundice and elevated transaminases (Table 2). These findings are in accordance with several studies in which all of the above findings plus anemia and hyponatremia significantly associated with ARF in sever malaria [31-33]. Several studies reported risk factors for AKI associated with severe malaria lead to increased mortality rate such as hyperbilirubinemia, leukocytosis, oliguria or anuria and electrolytes disturbances. Hyponatremia is frequent in malaria-associated AKI, occurring in 30%-50% of cases while hyperkalemia is associated with hemolysis and acidosis [34-37]. Other authors have looked at the risk factors associated with the development of ARF and mortality in sever malaria, for example Vannaphan et al. who found jaundice, anemia, hypoalbuminemia, hyponatremia, hyperkalemia, acidosis, leukocytosis, elevated SGOT and SGPT in cerebral malaria. All the above were significantly associated with ARF among CM patients [38].

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