Case reports

Renal Complications in Severe Malaria

ABSTRACT

Acute kidney injury (AKI) is a rare but serious complication of malaria. Its occurrence is rapidly life-threatening. The aim of this study is to shed light on the mechanism of AKI and the particularities of its clinical presentation and management.

We report three cases of patients admitted to the medical intensive care unit at the Ibn Rochd University Hospital in Casablanca with malaria complicated by acute renal failure, who had travelled to sub-Saharan Africa and neglected chemoprophylaxis. AKI was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) classification criteria. The patients were three men, aged 34, 35 and 48 respectively, with no notable medical history. The clinical presentation was severe haemoglobinuric malaria associated with AKI in all three patients. The onset of AKI was 2, 3 and 5 days respectively after the beginning of the malaria attack. Oligoanuria was present in all three patients, and the AKI was severe, requiring haemodialysis in all cases. Anemia, thrombocytopenia, hepatic cytolysis and hyperbilirubinemia were present, and thick blood cell count was positive. All three patients were treated with artesunate. Renal biopsy was deferred because of thrombocytopenia in one patient and profound anaemia in the second. In the third patient, biopsy revealed acute tubular necrosis with typical lesions of pinkish, granular or string-shaped cylinders, suggesting either myoglobin or haemoglobin cylinders. The outcome was fatal in all cases.

AKI in malaria can be either functional or organic, related to acute tubular necrosis (ATN). ATN remains the principal renal manifestation caused by P. falciparum and may be the dominant clinical presentation of a severe malaria attack. Its prognosis depends on early diagnosis and management, but remains severe, with a high mortality rate despite extrarenal replacement therapy. On the basis of this study, renal function tests should be performed routinely in patients with severe malaria.

Keywords : Acute kidney injury, Malaria, Acute tubular necrosis

INTRODUCTION

Malaria is a major public health problem in tropical countries. It is associated with a high mortality rate. In 2018, global prevalence was estimated at 228 million cases, with particularly high prevalence in African regions. [1]

Acute kidney injury (AKI) is a critical complication of severe malaria, primarily caused by acute tubular necrosis (ATN) related to Plasmodium falciparum infection. Despite intensive treatment like hemodialysis and artesunate, the prognosis remains poor, with high mortality rates observed in severe cases.

The aim of this study is to shed light on the mechanism of AKI and the particularities of its clinical presentation and management

PATIENTS AND METHODS

Study design

We present three cases of patients admitted to the medical intensive care unit at the Ibn Rochd University Hospital in Casablanca with malaria complicated by acute renal failure. All patients had travelled to sub-Saharan Africa and had neglected chemoprophylaxis. Acute renal failure was diagnosed according to the Kidney Disease Improving Global Outcomes (KDIGO) classification criteria.

Data collection

Demographic, clinical, biological and histological data were collected from patient's medical records.

1. Definitions

1.1. Severe malaria was defined as any fever with a positive thick blood cell count associated with at least one of the severity criteria defined by the World Health Organization (WHO) [2]. The severity criteria are presented in table 1 :

Troubled consciousness	Renal failure
Prostration	Jaundice
Convulsions	Pulmonary oedema
Metabolic acidosis	Haemorrhage
Hypoglycaemia	Hyperparasitemia
Severe anaemia	Shock

Table 1 : Severity criteria of malaria

1.2. Acute renal failure (ARF)

We used the Kidney Disease Improving Global Outcomes (KDIGO) group definition, which defines AKI as an increase in serum creatinine of 26.5 mmol/L in the last 48 hours, or a recent increase in serum creatinine to 1.5 times baseline creatinine in the last 7 days, or diuresis of less than 0.5 mL/kg/h for at least 6 hours [3]. ARF was then classified into 3 stages of increasing severity according to the KDIGO classification.

2. Variables studied

We collected the demographic characteristics of the patients, their clinical and biological presentations on admission, the therapeutic methods used and the progress made during hospitalisation.

The biological tests studied were :

- Thick drop
- Plasma creatinine
- Plasma urea
- Thick blood drop
- Bilirubinemia
- Transaminases
- Haemoglobin
- Platelet count

Case presentation

The patients were three men aged 34, 35 and 48 years respectively, with no notable medical history. All had spent a period of time in an endemic area prior to infection. The clinical presentation was severe haemoglobinuric malaria associated with ARF in all three patients. The initial symptom was fever in two patients and febrile headache in the third. The duration of symptoms prior to admission was 5 days. Clinical examination revealed jaundice in all three patients. The urine dipstick was positive, with two crosses for protein and two crosses for blood.

The onset of ARF was 2, 3 and 5 days respectively after the onset of the malaria attack. Oligoanuria was present in all three patients, and the ARF was severe (classified as stage III in the KDIGO classification) requiring haemodialysis in all cases. Mean plasma creatinine was 97mg/l and urea mean was 1.7g/l. Anemia, thrombocytopenia, hepatic cytolysis and hyperbilirubinemia were present, and thick blood cell count was positive.

The signs of severity associated with acute renal failure are shown in the following graph:

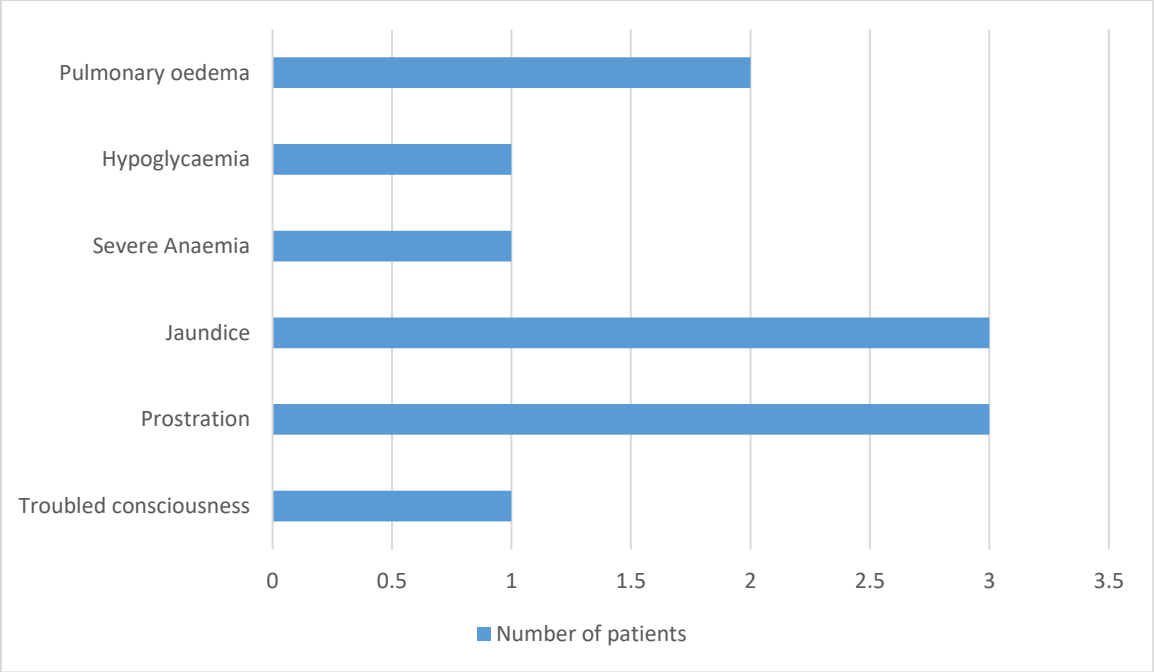

Figure 1 : Severe signs of malaria

Therapeutic management was initially symptomatic, based on rehydration or diuretics, depending on the patient's volume status. Transfusion of red blood cells was necessary in patients with severe, poorly tolerated anemia. Extrarenal replacement therapy such as intermittent hemodialysis was indicated in all patients with severe anuric renal failure.

All three patients were treated with artesunate.

The following table summarizes therapeutic management:

Therapeutic means	Number of patients
Rehydratation	2
Diuretics	1
Red blood cell transfusion	1
EER	3
Artesunate	3

Table 2: Therapeutic means

Renal biopsy was deferred because of thrombocytopenia in one patient and profound anaemia in the second. In the third patient, biopsy revealed acute tubular necrosis with typical lesions of pinkish, granular or string-shaped cylinders, suggesting either myoglobin or haemoglobin cylinders. The outcome was fatal in all cases.

DISCUSSION

207 million cases of malaria infection worldwide were reported by WHO for the year 2012. AKI was reported in 1 to 4.8% of falciparum malaria cases. [4] This incidence is higher in some regions. A Thai study found that 44% of AKI cases were seen in malaria-infected patients. [5] The pathophysiological mechanism of renal damage is not clearly understood, many mechanisms have been implicated, including endothelial damage, inflammatory cytokines, vasoconstriction, hemolysis and disseminated intravascular coagulation. [4,6,7,8,9] Other hypotheses have been proposed such as mechanical obstruction by parasitized red blood cells and exaggeration of host immune responses [6,9] Renal vasoconstriction and ATN are thought to occur as a result of microvascular obstruction and cellular damage caused by the sequestration of *P. falciparum* and the filtration of nephrotoxins, such as free hemoglobin, myoglobin, and other cellular debris, within the kidneys. [10]

A study carried out in Madagascar has found oligo-anuria in 46 to 76% of cases. [11] It was an independent risk factor of mortality according to another study. [12]

Hyponatremia is frequently observed, affecting up to 69% of severe malaria cases [13]. This biochemical disturbance can result from various mechanisms, including the syndrome of inappropriate antidiuretic hormone (SIADH) and cerebral salt wasting (CSW). Hyponatremia is frequent, while hypernatremia is rarer and has been observed mainly in neuromalaria. The most fatal electrolyte disorder was hyperkalaemia because of its cardiac repercussions, attributed either to renal failure, metabolic acidosis, hemolysis or rhabdomyolysis. The main anatomopathological lesions encountered are acute tubular necrosis, interstitial nephritis, glomerulonephritis and vascular damage [14,15]. Treatment is usually based on a combination of antimalarial drugs, rehydration and diuretics. Anti-malarial drugs and rehydration alone have been shown to improve renal function in the majority of cases. ERA speeds up recovery of renal function, and its introduction has helped to reduce malaria mortality. For TRANG et al [16], the introduction of dialysis reduced mortality from 75% to 26%. In the same authors series, only 2 of 41 anuric patients responded to diuretic treatment. Diuresis was normalized after about two weeks. This highlights the importance of early diagnosis and appropriate, timely management in order to improve both renal and overall prognosis.

This manuscript appears to be scientifically robust and technically sound for several reasons. First, given the rarity of Moroccan studies focusing on kidney damage during malaria.

Second, in the presence of histological evidence objectively attesting to the proposed hypotheses that could explain this renal damage.
It also highlights the critical link between severe malaria and kidney failure, emphasizing the pathophysiological mechanisms, clinical manifestations, and management strategies. Its insights are crucial for the scientific community to enhance early diagnosis, optimize therapeutic interventions, and improve outcomes in affected patients, especially in endemic regions.

CONCLUSION

AKI in malaria can be either functional or organic, related to acute tubular necrosis (ATN). ATN remains the main renal manifestation caused by P. falciparum and may be the dominant clinical picture of a severe malaria attack. Its prognosis depends on early diagnosis and management, but remains severe, with a high mortality rate despite extrarenal purification. On the basis of this study, renal function tests should be performed routinely in patients with severe malaria.

Ethical Approval:

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

Consent

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

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Details of the AI usage are given below:

The author states that he used ChatGPT in the grammatical correction of certain paragraphs.

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