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Case Report

Acute Kidney Failure Confused with Thrombocytopenic Thrombocytic Purpura in Malaria: A Case Report

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Abstract

Malaria has become widespread, especially in sub-Saharan Africa, owing to disruptions experienced during the Covid-19 pandemic. Both cerebral malaria and acute kidney injury are important indicators of severe malaria. Depending on the degree of acute renal failure, hemodialysis/hemofiltration treatment is required. Our patient was a 22-year-old male from the Republic of Chad. The patient with confusion came to our country 15 days prior and was admitted to the internal medicine intensive care unit. Initially, Thrombocytopenic Thrombocytic Purpura (TTP) was considered because of clinical and laboratory similarities. As the patient had a history of coming from an endemic area, anemia, thrombocytopenia, and splenomegaly, malaria was considered. The patient was diagnosed with *falciparum* malaria due to the presence of multiple ring-shaped trophozoites and banana gametocytes. The patient with cerebral malaria, hyperparasitemia (parasite load 15%), hyperbilirubinemia and acute kidney injury was considered to have severe malaria. Intravenous artesunate was planned, but since it could not be obtained immediately, oral artemether+lumefantrine was started, and the patient became conscious at the 24th hour of treatment. During the follow-up, the patient's creatinine levels increased to 6.9, and the patient was subjected to hemodialysis several times. After effective hemodialysis and antimalarial treatment, the patient was discharged without sequelae on the 20th day of hospitalization. This case report is thought to be important in that it emphasizes that the diagnosis of malaria may be delayed due to its confusion with microangiopathic hemolytic anemias, and that it emphasizes the importance of correct management of complications.

Introduction

Malaria is on the rise again in many African and South American countries, worsened by COVID-19-related healthcare disruptions (1). The WHO reported 249 million malaria cases and 608,000 deaths worldwide in 2022, with most cases (95%) and deaths (96%) occurring in Africa (2,3). Malaria is endemic to the Republic of Chad, and *Plasmodium falciparum* malaria is the most common disease. Severe malaria is caused by *P. falciparum*, which can progress to complications such as cerebral malaria, severe anemia, acidosis, hypoglycemia, jaundice, hyperparasitemia, pulmonary edema, and acute renal failure (4). Despite effective treatment, the mortality rates are between 15% and 25%. Immediate treatment with appropriate antimalarial agents is required, but the prognosis often depends on the treatment of other complications, such as renal failure, hyperbilirubinemia, and acidosis. Deterioration in kidney function is a key symptom in young children, but acute kidney injury (AKI) requiring kidney replacement therapy is virtually confined to older children and adults (5).

A case of severe malaria that was confused with Thrombocytopenic Thrombocytic Purpura (TTP), presented with a cerebral malaria clinic, had a high parasite load, which was monitored in intensive care and responded to oral treatment by starting oral artemether lumefantrine until intravenous artesunate treatment was provided; the patient was successfully treated with hemodialysis several times during the development of severe renal failure during follow-up.

Case Report

A 22-year-old male patient of Chad nationality, without any chronic disease, was brought to the Karabük University Training and Research Hospital with confusion. It was learned that he came from the Republic of Chad for university education two weeks ago and complained of weakness, cold, and shivering for 4-5 days, but his temperature was never measured. The unconscious patient was agitated and his Glasgow Coma Scale was eight. Body temperature was 37.4 °C, pulse 94/min, oxygen saturation was 96% on room air, and blood pressure was 100/60 mm Hg. On physical examination, the patient appeared pale and the spleen could be palpated under the ribs. Other examination findings were normal. There was no neck stiffness, and Kerning and Bruzinski signs were negative. Written informed consent was obtained from the patient.

Blood tests revealed white blood cells: $2.7x10^3$ µl/L, hemoglobulin: 8.9 g/dL, platelets: $36x10^3$ µl/L. In other blood tests, glucose: 80 mg/dL, AST: 58 U/L, ALT: 34 U/L, LDH: 572 U/L, total bilirubin: 5.6 mg/dL, direct bilirubin: 3.5 mg/dL, INR: 1.1, urea: 58 mg/dL, creatine: 1.5 mg/dL, Crp: 271 mg/L, sediment: 99 mm/h, direct and indirect Coomb's were negative (Table 1). Hepatıtıs markers and TORCH group test results did not contain any values indicating acute infection. Brucella were negative. There was no growth in blood cultures. No pathology was detected on brain and thorax tomography, but splenomegaly (spleen, 14 cm) was detected on abdominal imaging. No pathology was detected on the brain MRI. Plasma exchange treatment was planned for the patient, who was admitted to the internal medicine intensive care unit with a preliminary diagnosis of TTP due to anemia, thrombocytopenia, neurological findings, and renal failure; however, due to technical delay, supportive treatment was provided with fresh frozen plasma. We were consulted with unconscious and agitated patient. The patient, who was unconscious and agitated, was consulted to us.

Table 1: Times series of laboratory values of the patient

Variable	*Day*					*Reference Range*
	1st	5th	10th	14th	20th	
Hemoglobin	8.7	7.6(ES)	8.6	8.0	8.0	11-16 g/dL
White blood cell	2.7	7.6	8.6	8.1	5.1	4-10x10³
Platelet	36	160	390	384	209	130-400x10³
Urea	63	124	114	43	22	10-49 mg/dL
Creatine	1.5	5.0	6.8	2.3	0.9	0.5-1.3 mg/dL
AST	58	38	21	26	26	5-34 IU
ALT	34	37	51	28	36	10-49 IU
Total bilirubin	5.6	2.6	1.2	1.6	-	0.3-1.2 mg/dL
Direct bilirubin	3.5	1.9	0.8	0.8	-	0-0.3 mg/dL
LDH	-	618	320	404	273	225-450 IU
Meditation		-				
Parasitemia	%15					-

ES: Erythrocyte Suspension, LDH: Lactate dehydration, AST: Aspartate transferase, ALT: Alanine transferase, A+L: Artemether+lumefantrine, AS: Artesunate

Malaria was suspected due to his history of coming from Africa, subfebrile fever, pancytopenia and splenomegaly. In the screening performed using the Malaria Ag P.f/ P.v/ Pan Rapid Diagnostic Kit (Microcult®), positivity for *P. falciparum* was detected. Multiple ring-shaped trophozoites and banana-shaped gametocytes were observed in the Giemsa-stained thick drops and thin smear preparations (Figs. 1-3). The parasitic load was determined as 15%. Patients with cerebral malaria, hyperparasitemia (>10%), hyperbilirubinemia (bilirubin level> 3 mg/dL), and acute kidney injury were considered to have severe malaria. Intravenöz (IV) artesunate treatment was planned, but was not immediately available. Treatment was initiated by administering oral artemether lumefantrine via a nasogastric feeding tube.

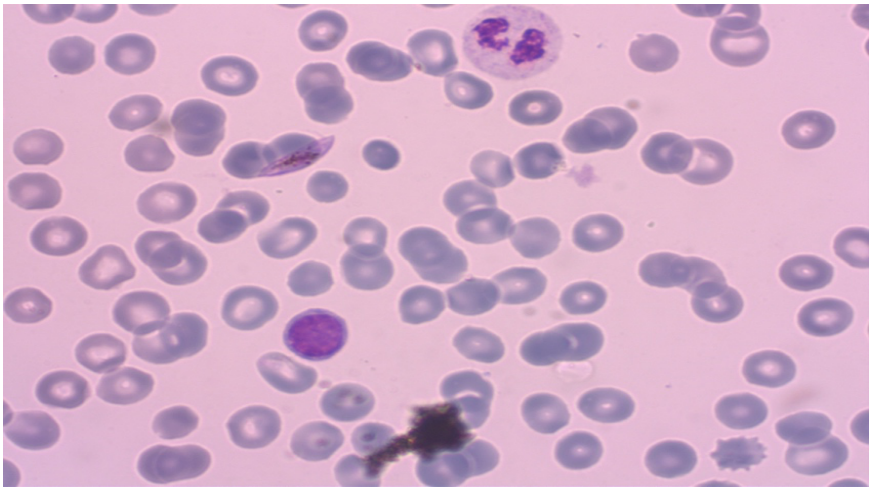

Fig. 1: Thin smear, banana gametocyte of *Plasmodium Falciparum*

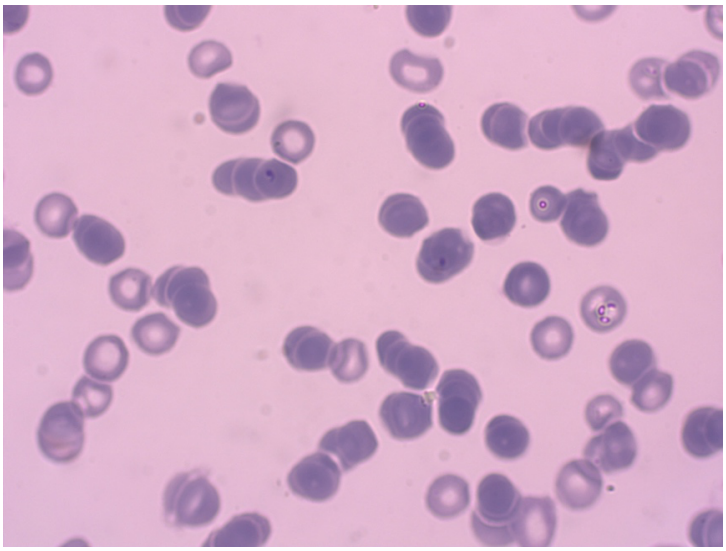

Fig. 2: Thin smear, intraerythrocytic multiple trophozoites

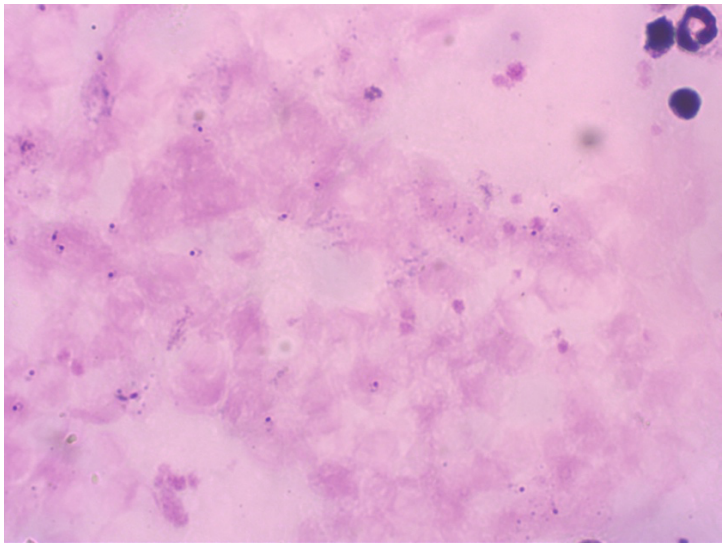

Fig. 3: Thick drop, multiple ring-shaped trophozoites

Artemether+lumefantrine was given at 0,8 and 24 hours. At the 24th hour of oral treatment, the patient regained consciousness, his cooperation and orientation were limited, and he had no fever during the follow-up. IV artesunate was administered at the 36th hour of oral administration. As the patient's oral intake was poor and the arrival parasite load was high, artemether lumefantrine was stopped, and artesunate treatment was started. Artesunate (2.4 mg/kg) was administered at 0, 12 and 24 hours. Artesunate treatment was stopped when the parasite load on the 3rd day of the total treatment was below 1% and the patient's oral intake was good. Three more doses of artemether+lumefantrine were given and a total of six doses of oral treatment were completed. When the patient's history was further examined, it was learned that he had not received malaria chemoprophylaxis. During the follow-up, the patient's creatinine levels gradually increased, reaching 6.9 on the 7th

day of hospitalization despite hydration, so the patient was placed on hemodialysis. During the follow-up of the patient, who required hemodialysis for 4 days, the creatine values decreased and reached normal levels on the 16th day. The patients' creatine values are shown in Fig. 4. The patient was discharged without any sequelae on the 20th day of hospitalization.

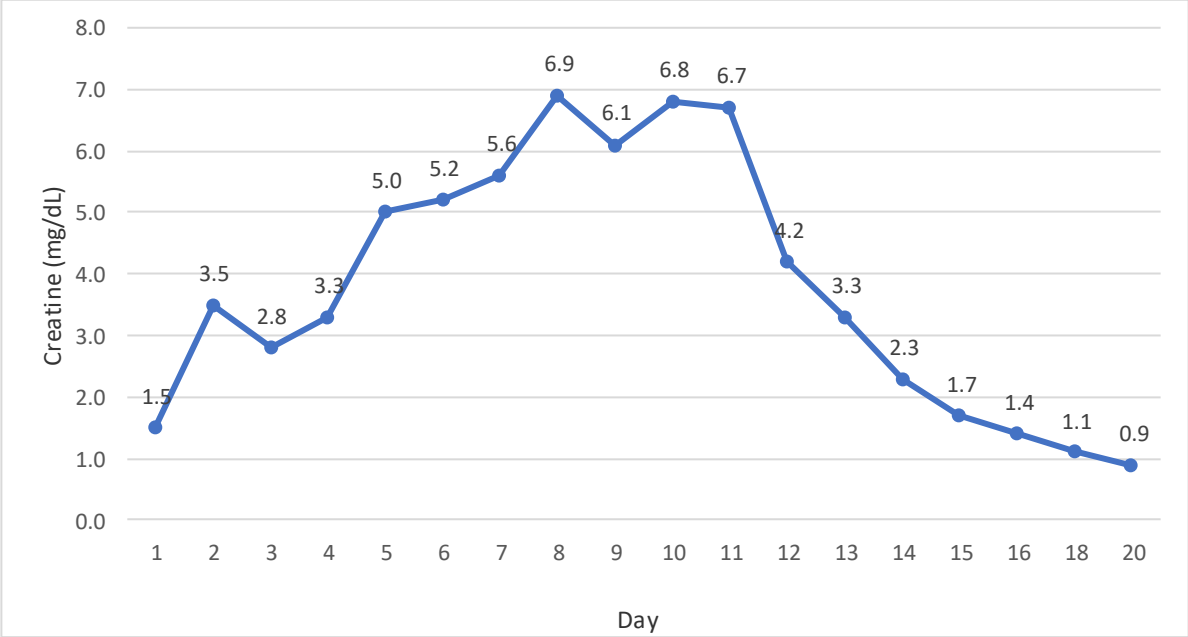

Fig. 4: Creatine values monitored in the follow-up

Discussion

Malaria, endemic to the Republic of China, is prevalent in 40.9% of the general population. *P. falciparum* (85.1%) was the dominant species. Interventions such as Chemoprevention of Seasonal Malaria are available in some parts of the Republic of Chad, but our patient did not receive chemoprophylaxis (6).

Cerebral malaria and acute kidney injury are leading causes of severe malaria. Cerebral malaria is a cause of high mortality. Altered consciousness has been linked to various pathophysiologies, such as mechanical microvascular occlusion by infected erythrocytes, activation of immune cells, release of pro-inflammatory cytokines, endothelial dysfunction, altered permeability of the blood-brain barrier, and brain edema (7–9). Cerebral malaria is often accompanied by multiple organ dysfunctions. Concomitant renal failure, severe jaundice, or metabolic acidosis significantly worsens the prognosis (10). AKI is one of the most feared complications of severe malaria and commonly occurs in *P. falciparum* malaria. The overall prevalence of AKI in *P. falciparum* malaria varies between 1% and 60%, with a mortality rate of up to 45%. Its pathogenesis remains unclear. Acute tubular necrosis due to sequestration of infected erythrocytes, immune-mediated glomerular damage, and obstruction of renal microcirculation due to extracellular fluid loss are some of the proposed hypotheses. Factors that increase erythrocyte hemolysis, such as a high parasite load and late admission to a healthcare institution for treatment, may also increase the risk of AKI (11). Due to the hypercatabolic state of

AKI caused by falciparum malaria, hemodialysis should be performed immediately when there is a rapid increase in creatinine concentration (12). The fulminant form of AKI, which is often associated with multiple vital organ dysfunction, is associated with poor prognosis. In contrast, there is a good prognosis in the subacute presentation, where the plasma or serum creatinine level rises steadily as the patient recovers. Renal replacement therapy (preferably hemofiltration or hemodialysis) may be required for a period of time, but survivors always achieve full recovery of kidney function. Renal replacement therapy has been shown to improve prognosis in patients with severe malaria and advanced renal failure (13). The reason for the need for hemodialysis in our patient might be the development of acute tubular damage secondary to intense erythrocyte destruction due to the high parasite load. However, because there was no urine output during the dialysis period, hemoglobinuria could not be demonstrated.

For the treatment of severe malaria, the WHO recommends the use of intravenous and intramuscular antimalarial drugs, and the most effective drug for this purpose is artesunate, which should be administered for at least 24 hours and until patients can tolerate oral medication (14). However, cases of severe malaria that responded to oral treatment have been reported in the literature (4). We started oral treatment in our case until parenteral treatment was obtained, and we observed that the patient responded to treatment on the second day of treatment.

Microangiopathic hemolytic anemia describes anemias that occur due to non-immune erythrocyte destruction within the vessels and in which schistocytes and fragmented erythrocyte fragments are seen in the peripheral blood smear. Hemolysis may cause acute anemia, jaundice, hematuria, dyspnea, tiredness, tachycardia, and possibly hypotension in those diseases (15). Diagnosis of malaria can be difficult because of its clinical similarity to other microangiopathic hemolytic anemias.

As a result, malaria is an important health problem that is seen worldwide with the increase in international travel, and where mortality increases due to the development of complications if rapid treatment is not initiated. Acute renal failure may develop in patients with severe malaria, especially those with a high parasite burden. Acute renal failure requiring hemodialysis is a rare complication. Even if intravenous treatment is not available, initiating oral treatment as soon as possible is important for prognosis. Diagnosis may be difficult due to the similarity of clinical findings and laboratory values to other microangiopathic hemolytic anemias. This case report is thought to be important in that it emphasizes that the diagnosis of malaria may be delayed due to its confusion with microangiopathic hemolytic anemias, and that it emphasizes the importance of correct management of complications.

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Conflict of Interest

Non-declared.

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