

# Unrecognized Malaria and Its Consequences – A Case Report of Severe Malaria with Acute Renal Failure

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## ABSTRACT

*Severe malaria is a medical emergency that requires urgent recognition and treatment, because it may rapidly progress to serious complications and death. We report a case of imported severe malaria tropica in an adult traveller, with a parasitemia of 20%, complicated by acute renal failure. Patient was initially misdiagnosed by a physician unaware of the importance of patients travel history, as having a viral infection. Despite the treatment delay, the patient was successfully cured with parenteral artemether combined with peroral mefloquine and vigorous supportive measures including renal replacement therapy.*

**Key words:** severe malaria, misdiagnosis, renal failure

## Introduction

Malaria is one of the most common infectious diseases worldwide, causing 350–500 million illnesses and a million deaths per year<sup>1</sup>. Due to increase in global travelling incidence of imported malaria has risen, and approximately 8,000 cases of imported malaria are reported in Europe yearly<sup>2</sup>. In a large survey of travel clinics, malaria was the most frequent cause of fever without localizing signs or symptoms, and it was particularly common in febrile travellers returning from Africa<sup>3</sup>.

Severe malaria is defined by major signs of organ dysfunction or a hyperparasitemia ( $\geq 5\%$  parasitemia in low-transmission and  $\geq 10\%$  in high-transmission regions), and is almost exclusively caused by *Plasmodium falciparum*<sup>4</sup>. It usually occurs in individuals without immunity to malaria or in those with decreased immunity, such as visitors from non-endemic regions to endemic regions and young children (1 month to 5 years of age). Pregnant women are also at increased risk for severe malaria<sup>5</sup>. Travellers returning from endemic regions are at risk of progression from uncomplicated to severe malaria if the infection is not recognized and treated on

time. Severe malaria can evolve within few hours, thus enormously increasing the mortality risk (up to 20%), even in patients taken adequate antimalaric drugs<sup>4</sup>. Since the disease often starts with unspecific signs, lacking the typical fever pattern, a proper travel history and consideration of malaria in all febrile patients with a history of travel to endemic regions, as well as appropriate anti-malarial treatment initiation on time, are extremely important steps in successful treatment of these patients.

## Case Report

We present a case of a 56-year old male with a 5-day history of intermittent fever, chills, headache, vomitus and diarrhoea. His family doctor evaluated his symptoms three days before admission to our hospital and diagnosed him with a viral disease. The patient had returned from a 6-months stay in Nigeria a week before disease onset. He reported receiving recommended immunizations before his travel, but without taking any anti-malarial chemoprophylaxis. The patient had no medical his-

tory beside previous antimalaric treatment for tertian malaria (caused by *Plasmodium vivax*) acquired 12 years earlier, while working in Congo, Africa.

Initial physical examination revealed the patient with fever up to 39 °C. He was prostrated but alert, had mild jaundice and hepatomegaly. Routine laboratory tests showed thrombocytopenia ( $19 \times 10^9/L$ ) with a normal erythrocyte count ( $4.9 \times 10^{12}/L$ ), haemoglobin concentration (145 g/L) and leukocyte count ( $9.6 \times 10^9/L$ ). C-reactive protein (272 mg/L), urea (31.5 mmol/L), creatinine (478  $\mu\text{mol}/L$ ) as well as bilirubin (92  $\mu\text{mol}/L$ ), alanine aminotransferase (77 U/L), aspartate aminotransferase (84 U/L) and lactate dehydrogenase (652 U/L) concentrations were elevated. Serum sodium concentration (134 mmol/L) was low, while potassium and glucose levels were normal. Urine analysis showed proteinuria, hemoglobinuria, microscopic hematuria (8–10 red cells/ $\mu\text{L}$ ) and leukocyturia (10–15 white cells/ $\mu\text{L}$ ). Chest X-ray and abdominal ultrasound were normal, except for a mild hepatomegaly. A Giemsa-stained blood smear revealed numerous ring forms of *P. falciparum*, with a hyperparasitemia of 20%. The patient was diagnosed with severe falciparum malaria and artemether therapy was started immediately (3.2 mg/kg intra-muscular on day 1, followed by 1.6 mg/kg daily, from days 2 to 7) combined with oral mefloquine during the first two days of treatment (750 mg once, followed by 500 mg and 250 mg in intervals of 8 hours). Successful antimalaric treatment resulted in undetectable parasitemia in blood smears by the fourth day of therapy. Despite intensive parenteral rehydration, the patient became anuric with further rise in creatinine and urea levels (creatinine levels were elevated up to 789  $\mu\text{mol}/L$  and urea levels up to 43.2  $\mu\text{mol}/L$ , respectively), so haemodialysis was initiated and continued over the next 3 weeks. During the course of treatment the patient developed severe anaemia (decreased erythrocyte count to  $2.44 \times 10^{12}/L$  and haemoglobin level to 63 g/L, respectively) which required erythrocyte transfusion. He recovered gradually and was discharged after four weeks of hospitalization when clinical and laboratory examinations showed significant improvement. During two-month

follow-up, all laboratory parameters returned to normal values.

## Discussion

The vast majority of malaria cases present as non-specific febrile illnesses that are relatively easily terminated by anti-malarial treatment<sup>6</sup>. If the disease is not recognised it can progress to severe form, with numerous complications and a high mortality. Acute, life-threatening complications include severe shock, cerebral malaria, pulmonary oedema, hepatic or renal impairment<sup>7–9</sup>. Malaria – associated renal failure is a consequence of tubular renal necrosis and often requires some form of renal replacement therapy. According to the WHO guidelines, artemisinin derivatives are preferred drugs for severe malaria in adults and children in regions of low transmission<sup>10</sup> due to their superior efficacy, fewer side effects and a better safety profile as compared to intravenous quinidine. However, the poor availability of artemisinins outside Asia and the fact that they are not registered in many countries, leads to logistic and legal problems, often causing a delay in antimalaric therapy. Our patient received the only readily available parenteral artemisinins, artemether for intramuscular applications, in combination with peroral mefloquine, with a great success. Mefloquine is given to prevent recrudescence and is an adequate choice in case that no signs of cerebral malaria are present. The patient recovered completely, without any permanent sequelae. Despite the hyperparasitemia, no other adjunctive treatment modalities, like blood exchange transfusion or erythrocyte aphaeresis, were necessary.

The presented case underlines the outmost priority of rapid recognition, proper clinical assessment and administration of full dose parenteral anti-malarial treatment with any available effective anti-malarial drug<sup>6</sup>. In conclusion, it is extremely important for physicians to consider malaria in all febrile patients and patients who present with any of possible malaria-related complications, who have a history of travel in malaria-endemic regions.

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## **AKUTNO BUBREŽNO ZATAJENJE KAO POSLJEDICA ZAKAŠNJELE DIJAGNOZE TROPSKE MALARIJE**

### **S A Ž E T A K**

Teški oblik malarije predstavlja medicinsku hitnoću koja zahtijeva pravovremeno prepoznavanje i liječenje. U suprotnom slučaju dolazi do brzog razvoja ozbiljnih komplikacija s mogućim smrtnim ishodom. Prikazujemo slučaj muškarca s teškim oblikom tropske malarije obilježene parazitacijom od 20% i akutnim bubrežnim zatajenjem. Bolesnika je inicijalno pregledao obiteljski liječnik koji je dijagnosticirao blaži oblik virusne infekcije, zanemarujući epidemiološku anamnezu. Unatoč odgođenom početku terapije, bolesnik je izliječen bez trajnih posljedica, parenteralnom primjenom artemetra u kombinaciji s peroralnim meflokinom, uz suportivne mjere, uključujući i hemodijalizu.