Severe Malaria with Multiple Complications

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ABSTRACT

Background: Malaria is still a major global health concern with a high mortality rate. The clinical spectrums of malaria range from mild to life-threatening. **Case:** A 25-year-old male with weakness, fever, and anuria. Physical examination showed febris, jaundice, and abdominal tenderness at the right upper quadrant. Laboratory findings revealed *Plasmodium falciparum* hyperparasitemia with increased total bilirubin and creatinine levels. Diagnosis of severe falciparum malaria with multiple complications (cholecystitis, acute kidney injury, and anemia) was established. Intravenous antimalarial and antibiotics were administered along with hemodialysis. The patient was discharged after 11 days of treatment with the improvement of clinical status and laboratory parameters. **Conclusion:** A comprehensive approach to the diagnosis of malaria is necessary to detect complications and appropriate management.

Kata Kunci: Acute kidney injury, anemia, cholecystitis, malaria.

ABSTRAK

Latar belakang: Malaria masih menjadi masalah kesehatan global utama dengan tingkat kematian tinggi. Spektrum klinis malaria bervariasi dari ringan hingga mengancam nyawa. **Kasus:** Laki-laki usia 25 tahun datang dengan keluhan demam disertai badan lemah dan tidak buang air kecil lebih dari 12 jam. Pada pemeriksaan fisik didapatkan febris, ikterus, nyeri tekan kuadran kanan atas abdomen. Hasil laboratorium menunjukkan hiperparasitemia *Plasmodium falciparum* disertai anemia, peningkatan kadar total bilirubin dan kreatinin. Diagnosis malaria *falciparum* berat dengan komplikasi (kholesistitis, *acute kidney injury,* anemia). Terapi antimalaria dan antibiotik intravena serta hemodialisis. Pasien diizinkan pulang setelah 11 hari perawatan. **Simpulan:** Pendekatan diagnosis malaria yang komprehensif diperlukan untuk deteksi komplikasi dan tata laksana yang tepat. **Andrio Palayukan, Nisan Soeheri. Malaria Berat dengan Komplikasi Multipel.**

Keywords: *Acute kidney injury*, anemia, kholesistitis, malaria.

INTRODUCTION

Malaria is one of the most common infectious diseases in the world and one of the most significant challenges encountered by the public health system in many developing countries. A 229 million malaria cases and 409,000 malaria deaths were registered worldwide in 2019.[1] COVID-19 pandemic has established a perturbing threat to already delicate malaria control programs, by further encumbering the healthcare systems of malaria-endemic countries.[2]

Malaria is spread by *Plasmodium spp.* – infected female *Anopheles* mosquito. The clinical spectrum can range from asymptomatic, uncomplicated malaria, to severe malaria, characterized by life-threatening symptoms.[3,4] We report a severe malaria case with multiple complications: hyperparasitemia, cholecystitis, acute kidney injury (AKI), and anemia.

CASE

A 25-year-old male came to the emergency room with the chief complaint of fluctuating fever and body aches 5 days before admission. His eyes and skin became yellowish within 24 hours. The patient also complained of nausea, vomiting, and less urination. On examination, body temperature showed fever (38°C), icteric sclera, and right upper quadrant abdominal tenderness with hepatomegaly (approximately 2 cm below the right rib arch).

Laboratory examinations showed leucocytosis, thrombocytopenia, positive malaria smear, increased bilirubin levels along with liver enzymes, hypoalbuminemia, and abnormal renal function parameters (BUN and creatinine) **(Table 1).** Chest x-ray on admission showed no significant abnormality.

The patient was given intravenous artesunate 2.4 mg/kg every 12 hours for the first 24 hours, continued every 24 hours until clinical improvement was achieved, and ceftriaxone iv 1 gram every 12 hours. On second day of treatment, anuria developed. Fine crackles on both lung bases, and abdominal distension were on physical examination and a fluid balance of +10.170 mL in 24 hours. BUN and creatinine levels were increased. Abdominal ultrasound revealed ascites, hepatomegaly, and cholecystitis. Chest x-ray shows the impression of pulmonary congestion.

AKI stage III was diagnosed; and managed with renal replacement therapy (RRT) by intermittent hemodialysis. The first hemodialysis was performed within 2 hours.

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Table 1. Laboratorium parameters on admission.

Parameters	Result	Reference Range
Hemoglobin (Hb)	12.5 g/dL	13.3 – 16.6 g/dL
White blood cell (WBC) count	30.71 x 10^3/µL	3.37 – 10 x 10^3/µL
Platelet (PLT)	65 x 10^3/µL	150 – 400 x 10^3/µL
Malaria smear	PFRF 7112/200 (parasitemia 19%)	negative
Total bilirubin	12.94 mg/dL	0.3 – 1.9 mg/dL
Direct bilirubin Indirect bilirubin	10.9 mg/dL 1.94 mg/dL	0 – 2 mg/dL
Albumin	2.9 g/dL	3.4 – 4.8 g/dL
Aspartate amino transferase (AST)	168 U/L	5 – 50 U/L
Alanine amino transferase (ALT)	115 U/L	5 – 50 U/L
Gamma GT Alkaline Phosphatase	116 U/L 112 U/L	10 – 71 U/L 40 – 129 U/L
Creatinine	3.99 mg/dL	0.7 – 1.4 mg/dL
Blood urea nitrogen (BUN)	152 mg/dL	13 – 43 mg/dL
Na^+	132 mmol/L	135 – 147 mmol/L
K^+	4.7 mmol/L	3.5 – 5.5 mmol/L
Cl^-	91 mmol/L	95 – 103 mmol/L

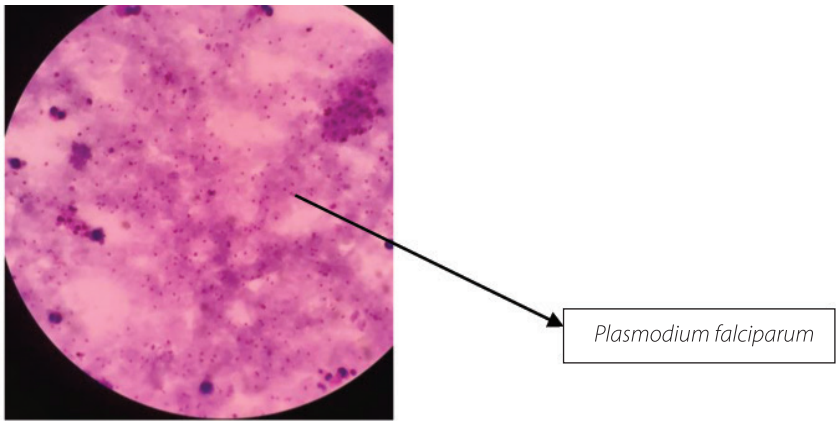

Figure 1. The thick film under one of the microscope field of view showed *Plasmodium falciparum*.

Table 2. Laboratorium parameters on the third day of treatment.

Parameters	Result	Reference Range
Hemoglobin (Hb)	7.9 g/dL	13.3 – 16.6 g/dL
White blood cell (WBC) count	22.12 x 10^3/µL	3.37 – 10 x 10^3/µL
Platelet (PLT)	64 x 10^3/µL	150 – 400 x 10^3/µL
Malaria smear	74/200	negative
Total bilirubin	16.11 mg/dL	0.3 – 1.9 mg/dL
Direct bilirubin Indirect bilirubin	13.90 mg/dL 2.21 mg/dL	0 – 2 mg/dL
Albumin	2.8 g/dL	3.4 – 4.8 g/dL
Aspartate amino transferase (AST)	159 U/L	5 – 50 U/L
Alanine amino transferase (ALT)	68 U/L	5 – 50 U/L
Gamma GT Alkali Phosphatase	59 U/L 92 U/L	10 – 71 U/L 40 – 129 U/L
Creatinine	6.35 mg/dL	0.7 – 1.4 mg/dL
Blood urea nitrogen (BUN)	229 mg/dL	13 – 43 mg/dL
Na^+	119 mmol/L	135 – 147 mmol/L
K^+	3.7 mmol/L	3.5 – 5.5 mmol/L
Cl^-	84 mmol/L	95 – 103 mmol/L

Intravenous ceftriaxone and artesunate were still given.

The patient was discharged on the 12th day of treatment with improved clinical condition and laboratory parameters (but not yet fully normal kidney function). The patient was in the normal function of mobilization, the complaints on the admission were relieved and normal urination. The patient was scheduled for hemodialysis 2 times a week and finished therapy after 6 hemodialysis.

DISCUSSION

This is a case of malaria with simultaneous hyperparasitemia, cholecystitis, acute kidney injury, and anemia. Acute acalculous cholecystitis (ACC) is only responsible for 2%-15% of the total cases of acute cholecystitis across all ages.[5] Malaria-related ACC is uncommon in both adults and children. Most cases were related to *Plasmodium falciparum*.[5] Although the pathophysiology of ACC in malarial infection has not been fully understood, three mechanisms are proposed: (1) sequestration of parasites in gallbladder microvasculature leading to gallbladder ischemia, (2) fasting state that caused biliary stasis, and (3) production of cytokines and mediators by infected erythrocytes.[5] Secondary infection by enteric flora can follow.[5] Diagnosis of cholecystitis without gallstone was established based on abdominal ultrasound findings.

Malaria is the first parasitic infection known to be associated with renal impairment in tropical areas.[6] Severe malaria can cause disturbances in the glomerulus, tubules, and interstitials.[6] Renal insufficiency in the context of severe malarial infection commonly develops 3-7 days after the onset of fever; serum creatinine typically improves in 17 ± 6 days.[6] AKI in malaria has not been fully studied, but several pathological processes have been described. Impaired renal microcirculation due to sequestration from infected erythrocytes is considered to be the main cause. Immune-mediated glomerular injury is also considered to play a role in the development of AKI in malaria. Another proposed theory is hyperbilirubinemia associated with liver damage can form kidney deposits.[7–9] Diagnosis of acute kidney injury was made because of the escalation of BUN and creatinine levels. Hemodialysis was performed because acute


lung edema had developed, assumed as the consequence of AKI.

In severe falciparum malaria, heavy parasite burden and anemia develop rapidly. The main contributor to this usually rapid decline in hematocrit is the hemolysis of unparasitized red cells. The whole red cell population becomes less deformable and this is significantly associated with the decline of hemoglobin.[10] The mechanisms responsible for reduced uninfected erythrocyte deformability have not been identified, in acute malaria there is evidence for increased oxidative damage which might concede red cell membrane function and reduced deformability.[10] In severe multisystem disease, the patient may lose 2 or more grams of hemoglobin per deciliter in the first 24 hours of treatment.[10] Due to a lack of resources, we could not perform further examination to differentiate the type of anemia.

CONCLUSION

Malaria continues to be a global threat. Early detection and treatment of severe malaria are of paramount importance. Future studies are needed to better understand the disease and to provide better treatment.

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