


Acute Kidney Injury and Bloody Diarrhea in Falciparum Malaria

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ABSTRACT

Malaria remains one of the deadliest infectious disease in worldwide. In adults, one of the commonest complication of falciparum malaria is acute kidney injury. Bloody diarrhea is rarely documented. This is a case report of a 24 year-old male with falciparum malaria presenting to the emergency department with fever, vomiting, bloody diarrhea, and decreased urine output. The patient was given rehydration therapy and antiemetics before administration of artesunate and primaquine. After three days, the patient had recovered. Acute kidney injury was primarily caused by dehydration, which explained the rapid recovery of the serum marker after proper fluid resuscitation. Exclusion of other potential pathogens must be done in a case of falciparum malaria with bloody diarrhea.

Keywords: Acute kidney injury, bloody diarrhea, falciparum malaria

ABSTRAK

Malaria masih merupakan salah satu penyakit infeksius paling mematikan di dunia. Pada dewasa, komplikasi paling sering malaria falsiparum adalah gagal ginjal akut. Diare berdarah jarang dilaporkan. Laporan ini membahas kasus pasien laki-laki usia 24 tahun dengan malaria falsiparum dengan keluhan demam, muntah, diare berdarah, dan penurunan jumlah urin. Pada pasien dilakukan rehidrasi dan pemberian antiemetik sebelum diberi artesunat dan primakuin. Setelah tiga hari pengobatan, pasien kembali normal. Gagal ginjal akut disebabkan terutama oleh dehidrasi, yang menjelaskan cepatnya pemulihan kadar ureum dan kreatinin setelah resusitasi cairan yang tepat. Eksklusi penyebab kuman patogen potensial harus dilakukan pada kasus diare berdarah pada malaria falsiparum. **Widdy Winarta, Gevanski Maturbongs. Gagal Ginjal Akut dan Diare Berdarah pada Malaria Falciparum: laporan kasus**

Kata Kunci: Diare berdarah, gagal ginjal akut, malaria falsiparum

INTRODUCTION

Malaria remains one of the deadliest infectious disease in worldwide, especially in developing countries such as Indonesia. Despite widespread malaria elimination program that almost successfully eradicate malaria from the western part of the archipelago, east Indonesia remains plagued by the disease, particularly Papua. The annual parasite incidence of malaria in Papua and West Papua were 31.93 and 31.29 respectively, far outnumbered other provinces.[1,2]

Severe malaria is described as a case with systemic complications. Two of the most common complications in adult are acute kidney injury (AKI) and jaundice.[3] Bloody diarrhea is rarely documented but could possibly occur in malaria. The occurrence of bloody diarrhea may be misdiagnosed as dysentery and inappropriate treatment may be given.[4-6]

The first line treatment of uncomplicated malaria includes dihydroartemisinin piperaquine and primaquine.[3] These drugs have been associated with vomiting, which can further aggravate the pre-existing nauseous feeling experienced by malaria patients.[3,7,8] Vomiting and diarrhea have been known to cause dehydration due to excessive water loss. Subsequently, the occurrence of dehydration can lead to acute kidney injury.[9-11]

Theoretically, acute kidney injury in malaria can be caused by both acute tubular necrosis or glomerulonephritis associated directly with malaria and or dehydration occurring in malaria. We described a case of concurrent bloody diarrhea and acute kidney injury in a falciparum malaria patient.

CASE

A 24 year-old male patient came to the emergency department, with high fever since 4 days, accompanied with chills, headache, epigastric pain and vomiting everything he eat and or drink. The patient also experienced bloody diarrhea and dark tea-colored urine with a decreased output since 4 days. The frequency of bloody diarrhea were 5 to 6 times per day, accompanied with abdominal cramp. No other spontaneous bleeding such as epistaxis or bleeding gum were reported.

Rapid diagnostic test (RDT) at the first day of fever was positive for falciparum malaria. He was treated with standard antimalarial drugs regiment containing dihydroartemisinin–piperaquine in combination with primaquine for 3 days, however he vomited after each dose of drugs. One day before presented to the emergency department, the patient was

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retested with the RDTs and still positive for falciparum malaria. He was given the same drug regiment, and had taken the first dose before coming to the emergency department.

Upon presentation, the patient appeared weak with a pale conjunctivae, icteric sclerae and sunken eyes. There were also sign of abdominal tenderness and increased bowel sounds. Blood pressure was normal with palpable and strong radial pulse, thus no sign of inadequate tissue perfusion.

Initial laboratory results showed signs of acute kidney injury, with elevated ureum (103 mg/dL) and creatinine (4.8 mg/dL) level. Other significant results include anemia (hemoglobin 7.6 g/dL), and elevated bilirubin level (total bilirubin 4.6 mg/dL) (**Table**). Interestingly, microscopic examination of thick blood films showed no malaria infection. The patient was assessed of having a post malaria infection and suspected to have severe malaria infection with acute kidney injury, jaundice and bloody diarrhea. The patient was then initially treated with symptomatic treatment and rehydration therapy with ringer lactate intravenous solution, antiemetics (ranitidine and ondansentron), and paracetamol.

Twelve hours after admission, ureum and creatinine levels returned to normal; total, direct and indirect bilirubin decreased significantly. Artesunate and primaquine therapy for severe malaria infection was started on the second day.

On the third day, the patient showed significant recovery. He was no longer suffering from diarrhea and the colour and quantity of urine had recovered to normal. Physical examination also showed no scleral icterus, no signs of abdominal tenderness and normal bowel sounds. The patient was discharged the following day, fully recovered.

DISCUSSION

The most common complication of severe malaria in adult is acute kidney injury. Acute kidney injury is almost always associated with *P.falciparum* malaria; while renal involvement has also been reported in *P.malariae*, and recently in *P.vivax* infection.[12] The pathogenesis of acute kidney injury in malaria is still not clearly understood. Blockage of renal microcirculation due to sequestration of infected erythrocytes, immune-mediated glomerular injury and volume depletion are some of the proposed hypotheses.[13] Kidney injury may occur in case of circulatory insufficiency, but it may also be due to the precipitation of hemoglobin crystals in renal tubules during intravascular hemolysis. In case of high parasitemia, anoxic-ischemic lesions may be observed in connection with the phenomenon of adhesion of *P. falciparum* trophozoite- and schizont-infected erythrocytes to the endothelium of renal capillaries.[14]

Initially, the patient was assessed as having a post malarial infection with acute kidney injury, jaundice, and bloody diarrhea. The assessment was based on the result of initial microscopic examination which showed no malarial infection. However, at the second day of hospitalization, the artesunate and primaquine therapy was given. The consideration was that a negative thick blood films could mean a false negative result or a true negative result caused by the effect of antimalarial drugs taken before. The chance of false negative result increases with decreasing parasite densities. Greater microscopist experience and more examination done/number of microscopic fields examined should reduce such error.[15]

This patient was dehydrated, evidenced by the sunken eyes. Both vomiting and diarrhea contributed to the dehydration. Ibadin, et al, also found a significant association between dehydration and malaria parasitemiain pediatric patients; 83.1% had some and severe dehydration.[6] This study supported our findings that dehydration may occur in falciparum malaria, which could subsequently cause acute kidney injury. More study are needed to determine the extent and prevalence or incidence of dehydration in adult falciparum malaria patients. Clinicians should be aware of the possibility of dehydration especially in patients with diarrhea and vomiting.

Most AKI patients do not require renal replacement therapy and a return to baseline kidney function level is achieved in the vast majority of patients with anti-malarial therapy and fluid resuscitation alone.[16] The creatinine level in acute kidney injury associated with severe malaria returns to baseline after 17 ± 6 days.[17] Creatinine and blood ureum level in this patient decreased significantly after twelve hours with only rehydration therapy. The rapid recovery of renal function suggests that the main underlying mechanism of acute kidney injury was due to dehydration, although the involvement of renal microcirculation blockage and immune mediated glomerular

Table. Laboratory examination results

Laboratory Examinations	Day 1 (20.05 WIT)	Day 2 (07.00 WIT)	Day 3 (07.00 WIT)
Hemoglobin (g/dL)	7.6	-	-
Leukocytes (/uL)	9300	-	-
Basophils (%)	0.3	-	-
Eosinophils (%)	1.0	-	-
Neutrophils (%)	61.1	-	-
Lymphocytes (%)	26.8	-	-
Monocytes (%)	10.8	-	-
Hematocrit (%)	22	-	-
Thrombocytes (/uL)	333000	-	-
Malaria	Negative	Negative	-
Total Bilirubin (mg/dL)	4.6	2.2	-
Direct Bilirubin (mg/dL)	0.5	0.3	-
Indirect Bilirubin (mg/dL)	4.1	1.9	-
SGOT (U/L)	32	18	-
SGPT (U/L)	15	10	-
Alkali Phosphatase (U/L)	-	164	-
Gamma GT (U/L)	-	37	-
Ureum (mg/dL)	103	45	49
Creatinine (mg/dL)	4.8	1.1	1.0
Random Blood Glucose (mg/dL)	167	100	-
Total Protein (mg/dL)	-	6.7	-
Albumin (mg/dL)	-	4.1	-
Globulin (mg/dL)	-	2.6	-


injury cannot be ruled out.

Bloody diarrhea in this patient was resolved at the third day without antibiotics or antiparasitic. It was concluded that the bloody diarrhea was supposedly caused by Plasmodium falciparum.

Bloody diarrhea has been described in patient with falciparum malaria. Ibadin et al reported bloody diarrhea in 3.5% children with malaria parasitemia, while the reported incidence of diarrhea during malaria ranges from 5 to 38%.[5,6] Patients with malaria can pass stools containing blood, pus, mucous, and epithelial cell debris which would be undistinguishable from acute dysentery caused by bacteria or parasite.[4] Due to the fact that falciparum malaria may also manifest as bloody diarrhea, albeit uncommonly, clinicians were recommended to perform a stool analysis for other bacteria or parasite before starting any additional treatment. In this case, stool analysis was not done because the sample cannot be collected.

The mechanism of bloody diarrhea in malaria remains uncertain and multifactorial. Rosetting and sequestration of red blood cells leading to capillary occlusion and ischemia was thought to be the main mechanism behind diarrhea in malaria.[4] In addition, the adherence of erythrocytes infected with parasite to endothelial cells may cause the activation of cytokine, apoptosis of the endothelium and intestinal inflammatory response. These resulted in capillary leakage and increased intestinal permeability.[4] Malabsorption of nutrients such as sugars, amino acids, and fats may also occur and had been documented.[4] Gastrointestinal bleeding may be due to rupture of villi or mucosal lining[4], with multiple foci of mucosal hemorrhage observed.[5] Bloody diarrhea is also associated with increased concentration of tumor necrosis factor and free oxygen radicals which can cause tissue injury.[5]

CONCLUSION

Dehydration is one of an important cause of acute kidney injury in falciparum malaria infection. An appropriate fluid resuscitation was needed to restore kidney function. Proper antimalarial drugs remains an important element of therapy, considering the significance of infected erythrocytes sequestration and glomerular injury caused by malaria parasite.

Bloody diarrhea can rarely occur in falciparum malaria. A stool analysis and microscopic examination is recommended to rule out any coinfection. Conversely, in bloody diarrhea accompanied with high fever, the presence of malaria must be explored, especially in endemic areas or in patients with travelling history to endemic region.

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