



## EXCEPTIONAL CASE

## Minimal change disease and malaria

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### ABSTRACT

Malaria is a tropical disease secondary to the *Plasmodium* parasite with clinical features ranging from febrile illness to acute renal failure and further renal sequelae. We present a case of a woman minimal change disease secondary to *Plasmodium falciparum* who developed nephrotic range proteinuria and ultimately acute renal failure requiring renal replacement therapy. With proper treatment of her malarial infection as well as long-term renal replacement therapy, she made a full recovery. This case is one of the few cases that highlight the association between severe malarial infections and renal failure necessitating long-term hemodialysis.

**Keywords:** acute kidney injury, malaria, minimal change disease, *Plasmodium falciparum*, proteinuria

### BACKGROUND

Renal involvement has been well described in infections caused by *Plasmodium falciparum* as well as *Plasmodium malariae*. Acute kidney injury (AKI) and acute renal failure due to immune complex deposition or sequestration of red blood cells in renal vasculature are commonly reported in *P. falciparum* [1]. In malaria-endemic areas, up to 40% of adult inhabitants with severe *P. falciparum* malaria can develop AKI [2]. Moreover, it has been found that mortality increases to 75% when renal replacement therapy (RRT) is not swiftly initiated [3]. We present a patient with nephrotic syndrome secondary to a *P. falciparum* infection.

### CASE SUMMARY

A 53-year-old woman presented with dizziness, nausea, fatigue and progressive swelling in the lower extremities associated with increased thirst and decreased urine output. Physical

examination findings and laboratory results are listed in Table 1. Given her recent history of travel to Sierra Leone and noncompliance with malaria prophylaxis, a stat malarial smear was sent, which was positive for significant *P. falciparum* parasitemia. Oral atovaquone-proguanil was started (four tabs once a day for 3 days) due to the inability to receive parental antimalarial therapy in a timely fashion. Intravenous fluid resuscitation was initiated without improvement of her renal function. On Day 2, her renal function worsened; she developed an altered mental status and became encephalopathic. A chest X-ray demonstrated pulmonary edema. Repeated laboratory results are listed in Table 1. Repeated malaria smear after treatment revealed decreasing parasitemia.

She was started on conventional hemodialysis using an F-180 dialyzer 4 h a day with a first day urea reduction ratio (URR) of 40%, followed for 3 days with subsequent URR of 50–60%. Her volume and solutes were well controlled on regular hemodialysis with no need of extracorporeal anticoagulation;

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Table 1. Physical exam findings and laboratory results

Physical exam findings	
Edema of lower extremities	
Generalized jaundice, pallor and scleral icterus	
Mildly distended abdomen with right upper quadrant tenderness	
Mild impairment of consciousness with a Glasgow score of 9	
Initial laboratory results	
Hemoglobin—8 g/dL	
Mean corpuscular volume—83 fL	
Aspartate aminotransferase—204 IU/L	
Alanine aminotransferase—103 IU/L	
Total bilirubin—52 µmol/L	
Direct bilirubin—88 µmol/L	
Serum albumin—1.6 g/dL	
Total protein—4.2 g/dL	
Random blood glucose—100 mg/L	
Serum creatinine—4.5 mg/dL	
Blood urea nitrogen—95 mg/dL	
Total cholesterol—283 mg/dL	
Low-density lipoprotein—91 mg/dL	
Triglycerides—178 mg/dL	
Cerebrospinal fluid tests were negative	
Urine protein to creatinine ratio—4 with 80% of the protein as albumin	
Urinary analysis—sediments consistent with muddy brown casts without red or white blood cells	
Repeat laboratory results on Day 2	
Serum creatinine—7 mg/dL,	
Blood urea nitrogen—99 mg/L	
Serum potassium—4.2 mEq/L	
Bicarbonate—12 mEq/L	
White blood count—12 000 cells/µL	
Platelet count— $120 \times 10^3/\mu\text{L}$	
Serum sodium—137 mEq/L	
Six weeks after hemodialysis initiation	
Serum creatinine of 1.4 mg/dL	
24-h creatinine clearance of 52 mL/min	
Marked improvement in proteinuria from 3 g to 800 mg	
Four months follow-up	
Serum creatinine—1.12 mg/dL	
24-h urine protein—400 mg	

however, initially three treatments of prefilter 1 L normal saline were used to avoid circuit clotting. A renal biopsy demonstrated glomerular podocytopeny consistent with minimal change disease (MCD) and evidence of acute tubular necrosis (ATN) and arteriosclerosis (Figure 1). Initial intermittent hemodialysis failed to improve renal function so the patient was discharged with outpatient hemodialysis. Her urine output increased from 800 mL to 1500 mL in 2 weeks; however, nephrotic-range proteinuria was noted 4 weeks after the initiation of hemodialysis. After 6 weeks of hemodialysis initiation, she regained her renal function (Table 1) and hemodialysis was discontinued eventually. Informed consent was obtained from the patient for this publication.

## DISCUSSION

Type of renal disease is largely correlated to the species of *Plasmodium* infecting the patient. Malarial acute renal failure (MARF) is largely associated with *P. falciparum*. In MARF, patients present with oliguria, electrolyte imbalance, increased urinary protein excretion and abnormal urinary sediments [4].

Endothelial damage, immune complex deposition and local inflammatory mediators play a role in its pathophysiology. Microvascular changes cause endothelial damage, resulting in intravascular hemolysis, cytoadherence and inflammatory mediators. Immune complex depositions may be due to polyclonal B-cells as not all depositions consist of malarial antigen [5].

There have been limited reports of MCD due to malarial infections, but to the best of our knowledge, no adult case of MCD associated with *P. falciparum* has been reported. In our patient, 4 weeks after initiating antimalarial treatment, the podocytopeny improved and completely resolved after 6–8 weeks. The patient described above had traveled to an area of chloroquine-resistant malaria and therefore treatment options were limited. Treatment for severe malaria includes a quinine-based regimen (with doxycycline, tetracycline or clindamycin) or artesunate, which is investigational. Neither of these regimens is readily available, and therefore atovaquone-proguanil was administered but with a good response. Immediate antimalarial therapy is imperative in such cases. Two randomized controlled trials examined the usage of steroids in MCD adult patients and found that there was no difference in overall remission rates between steroid and control groups [6, 7]. Steroid treatment was not initiated in our patient due to concerns raised by infectious diseases experts because of severe *P. falciparum* parasitemia. No steroid was needed for complete remission in our case. We also reviewed eight patients with MARF-related AKI-ATN and required RRT, which was indicated for acidosis (4/8 patients), uremia (2/8 patients) and fluid overload (2/8 patients); however, two patients progressed to end-stage renal disease [8]. Our patient needed hemodialysis secondary to fluid and solute overload with metabolic encephalopathy, and recovered in 6 weeks. Our patient had a more prolonged need of RRT because of nonimmune status, high parasitemia, concomitant podocytopeny and higher mean creatinine and glomerular filtration rate at admission ( $< 15 \text{ mL/min/1.73 m}^2$ ).

## CONCLUSION

Our case emphasizes the importance of quickly diagnosing *P. falciparum* malaria. Early detection of AKI, initiation of antimalarial treatment, fluid replacement, avoidance of nephrotoxic drugs and, if indicated, RRT are important components in the management of MARF.

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## CONFLICT OF INTEREST STATEMENT

None declared.

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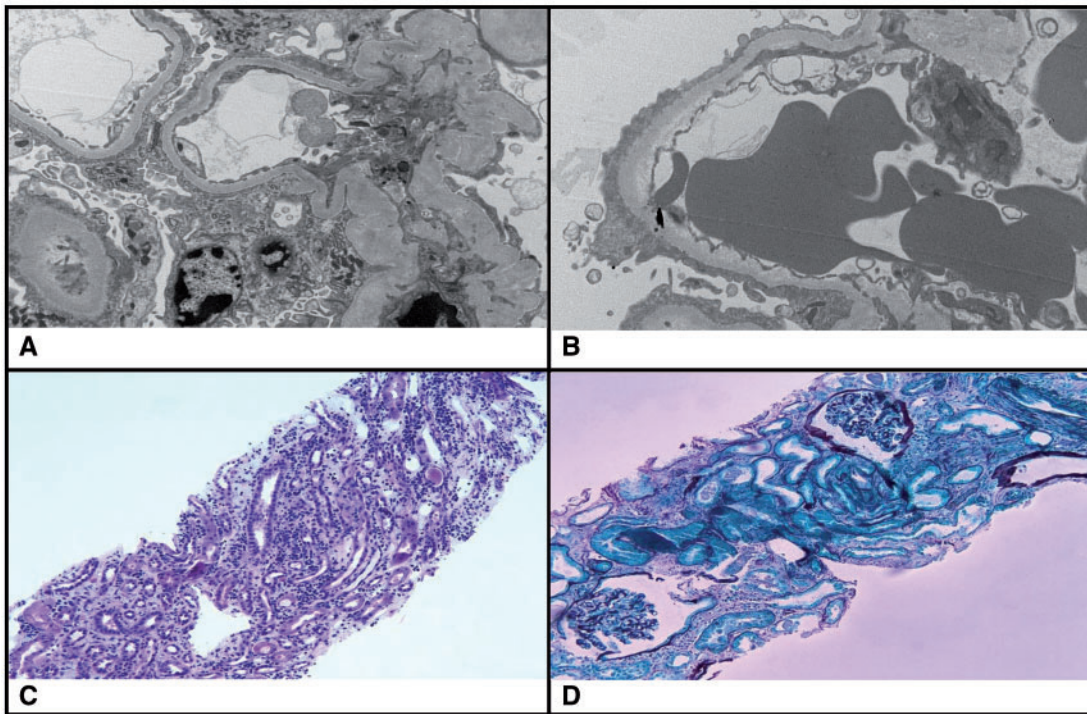


FIGURE 1: (A) Central right of the image is a glomerulus with solid lighter gray areas extending to bottom right showing glomerulosclerosis. The central clear space is Bowman's space. Peripherally surrounding the lighter gray strip are darker gray strips showing fused podocytes. (B) This is a closer-up view of the podocytopathy. Normally, slits should be seen, but fusion (darker gray periphery) of the podocytes is seen in this image. (C) Changes of acute tubular injury are seen with relatively normal tubule surrounded by thinner atrophic tubules and lymphocytic inflammation. (D) Jones' stain highlighting thickened glomerular basement membrane. Bottom left of this image is normal glomerular basement membrane for comparison. These changes support membranous nephropathy.

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