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Research Article

A Chinese Patient with Imported *Plasmodium Falciparum* Malaria and Acute Renal Failure: A Case Report and Pathological Features of Kidney

Lei Shi[1#], Fang Wang[2#], Enqiang Qin[1], Lei Huang[1], Dan Wu[1], Peng Zhao[1], Bo Tu[1], Xiaojuan Yu[2], Guang Yang[1], Yumin Zhang[1], Fude Zhou[2], Minghui Zhao[2] and Fu Sheng Wang[1*]

[1]Treatment and Research Center for Infectious Diseases, The Fifth Medical Center, PLA General Hospital, Beijing 100039, China

[2]Renal Division, Department of Medicine, Peking University First Hospital; Renal Pathology Center, Institute of Nephrology, Peking University, Key Laboratory of CKD Prevention and Treatment, Ministry of Education of China, Beijing 100034, China

[#]Lei Shi and Fang Wang contributed equally to this work

*Address for Correspondence: Fu-Sheng Wang, Renal Division, Treatment and Research Center for Infectious Diseases, The Fifth Medical Center, PLA General Hospital, Beijing 100039, China, E-mail: fswang302@163.com

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Abstract

Background: There have been few local malaria cases reported in China, however imported malaria cases increased rapidly during the last several years. Most cases have been due to *Plasmodium falciparum*, but *Plasmodium vivax* and *Plasmodium knowlesi* infections have also been reported. Acute kidney injury is the most important complication of severe malaria.

Case Presentation The case presented severe *P. falciparum* malaria with acute renal failure. We described pathological features of the kidney, analyzed the etiology and reviewed the pathogenesis of malaria associated of acute renal failure.

Conclusion a patient with *P. falciparum* malaria and acute renal failure was successfully managed in our unit. Many factors may contribute to acute renal failure in patients with serious malaria; however, it can be reversed with prompt treatment.

Keywords: Malaria, Acute kidney failure, Kidney pathology

Introduction

Malaria is a potentially lethal parasitic disease that is widely prevalent in tropical and subtropical regions. More than a century of worldwide efforts have brought about significant decrease in malaria incidence and mortality, but it remains a major public health problem. In 2018 alone, it affected an estimated 228 million people globally and caused 405,000 deaths [1]. Approximately 92% of these cases were reported from Africa and 5% from South-East Asia. During this same period, 2518 cases of imported malaria

were reported in China [2].

Severe malaria is mainly caused by *Plamodium falciparum*, but also sometimes by *Plasmodium vivax* and *Plasmodium knowlesi* [3]. Patients with severe malaria may develop complications such as cerebral malaria, pulmonary edema, acute renal failure, severe anemia, and/or systemic bleeding, and die within hours or days. Even with prompt antimalarial treatment and intensive care support, the mortality rate is 10%-20% [3,4]. Without proper care, mortality is 100%. Acute kidney injury (AKI) is one of the main causes of death, but renal pathological changes in severe malaria have not been thoroughly investigated.

There has been a spike in the number of imported malaria cases in China in recent times because of the increase in international travel. Most patients have history of travel to Southeast Asia (mainly vivax malaria, with a high incidence in May/June) or Africa (*falciparum* malaria, with a year-round incidence) [4,5]. We report a patient with severe *falciparum* malaria and acute renal failure, who was successfully managed.

Case Presentation

A 56-year-old Chinese man with long-term hypertension and diabetes who had been working in Sierra Leone since January 2018 developed fever on September 2, 2018. The fever was intermittent, occurring once a day, with the temperature rising to 40°C. He took ibuprofen orally to lower body temperature. There were accompanying chills and shivering and passage of dark yellow urine. He consulted a doctor at a clinic in Freetown, Sierra Leone, on September 5, 2018. His blood smear was found to be positive for *P. falciparum*, and he was advised a course of dihydroartemisinin–piperaquine phosphate combination therapy (40/320 mg tablets; 2 tablets as first dose, followed by 1 tablet at 8 hours, 1 tablet 24 hours, and 1 tablet at 32 h). On September 6, the patient developed hiccups and vomiting, and passed soy sauce–colored urine. His urine output was only about 150-200 mL. On September 7, there was no urine output at all. On September 8, icterus and hepatosplenomegaly had subsided and the blood smear was negative for *P. falciparum*, but the patient became comatose. He was airlifted to Beijing on September 9. On September 11, he was admitted to our unit (Figure 1).

At admission, his vital signs were as follows: heart rate, 109/min; respiratory rate, 29/min; rectal temperature, 36.2°C; and blood pressure, 136/87 mm Hg. On examination he was unconscious (Glasgow Coma Scale: 7) with intermittent agitation. Physical examination revealed pitting edema of both lower limbs, conjunctival edema, scattered moist rales in the lung bases, and suspected positive mobile murmurs. Serum creatinine was 930μmol/L and blood urea nitrogen 40.6 mmol/L. Abdominal ultrasound showed bilateral kidney enlargement and renal pelvis separation. Our diagnosis was: 1) *falciparum* malaria with stage 3 AKI; 2) grade II hypertension; and 3) type 2 diabetes mellitus [6].

Treatment was started with furosemide, ceftriaxone sodium, human serum albumin, and omeprazole. He remained anuric, and so continuous renal replacement therapy(CRRT) was started immediately after admission. Consciousness gradually returned to normal on September 13. Low-grade fever and occasional cough was present, but blood routine examination was normal

Figure 1: Timeline of disease progression.

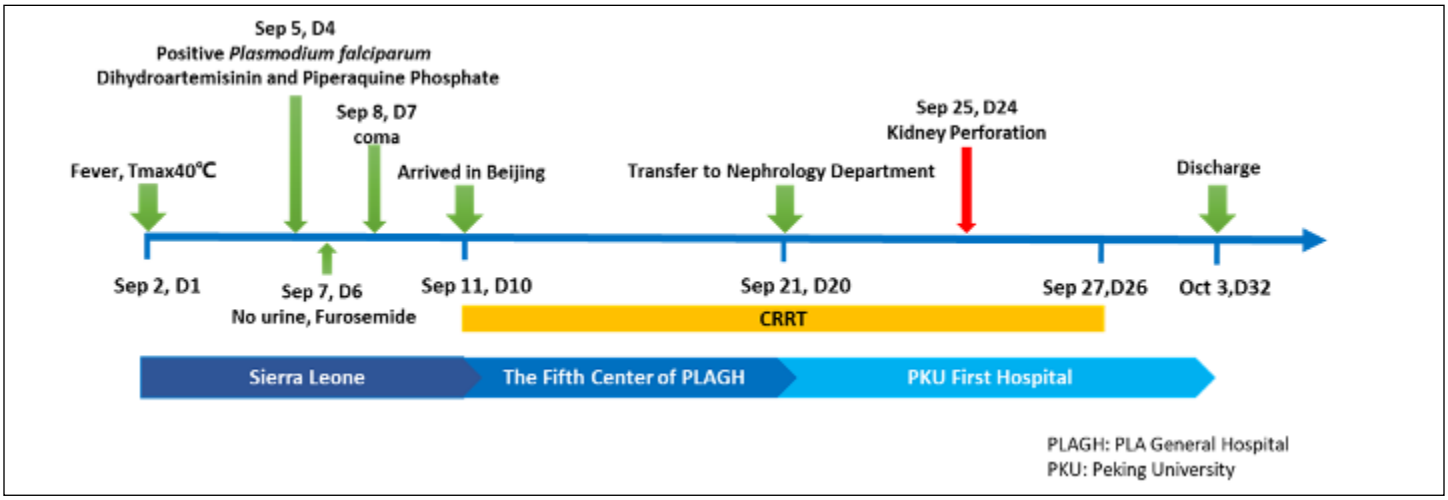
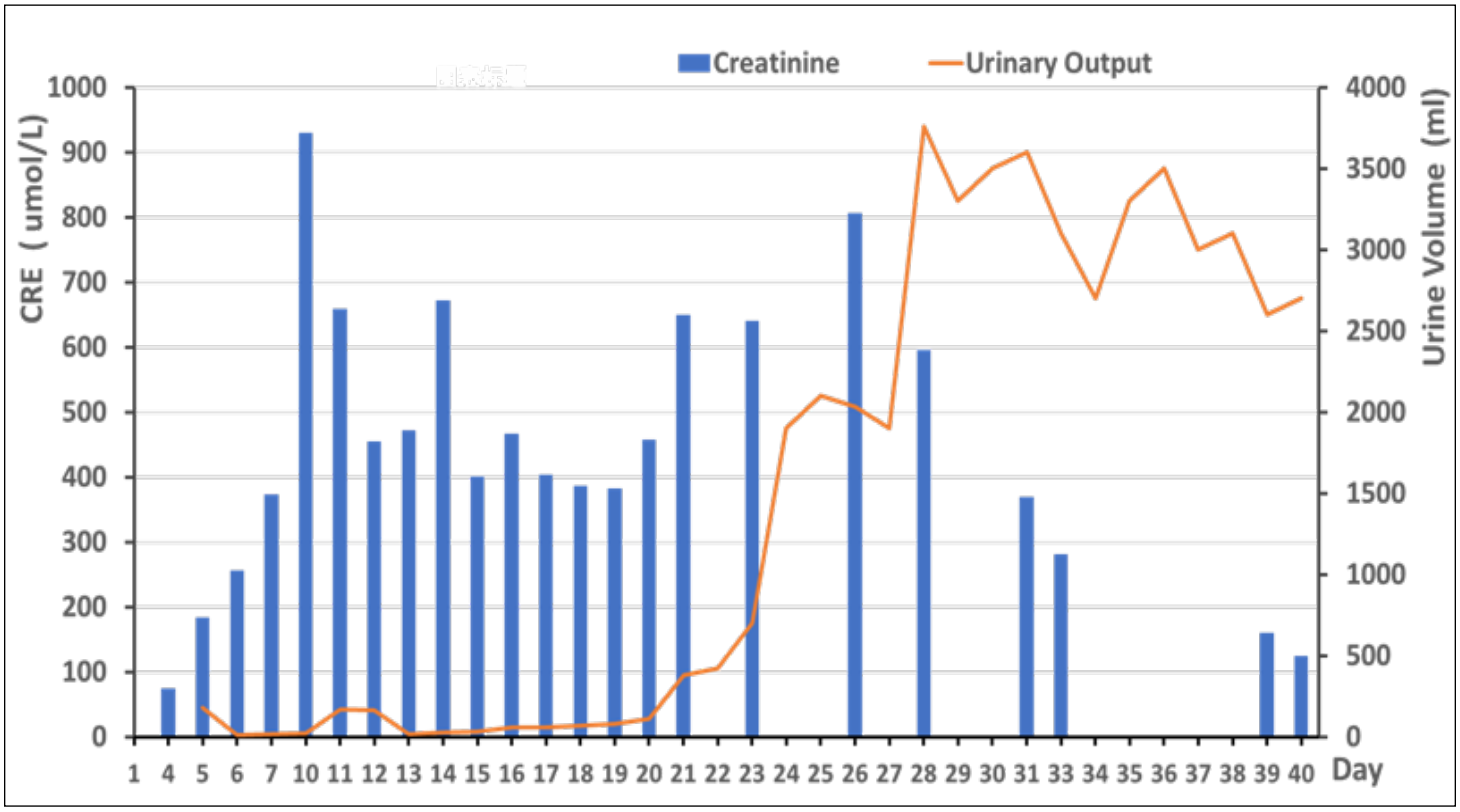


Figure 2: Changes in urine output and serum creatinine level over time. Oliguria/anuria lasted from September 6 (D5) to September 22 (D21), after which urine output gradually increased. Dihydroartemisinin–piperaquine phosphate (40/320mg) treatment was started on September 5 (D4). Continuous renal replacement therapy was from September 11 (D10) to September 28 (D27). Kidney biopsy was performed on September 25 (D24).



and peripheral smears were persistently negative for *P. falciparum*. Urine output gradually increased, and was 700 mL on September 24 (Figure 2).

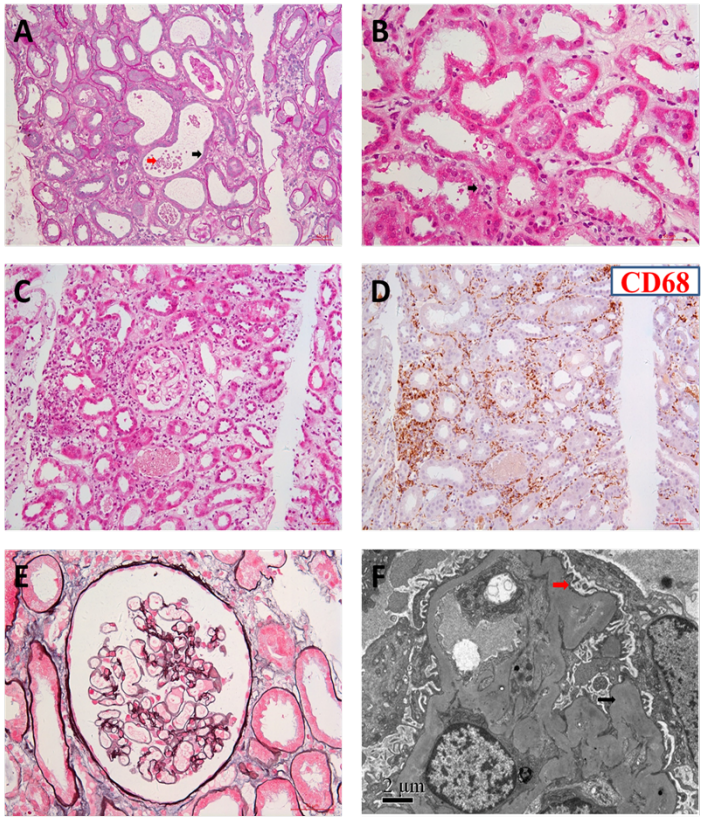
Kidney biopsy was performed on September 25. Pathological diagnosis was subacute tubulointerstitial nephropathy (mainly renal tubular injury; Figure 3). Urine output had increased and was 1500-2000 mL per day. On October 3, the patient was discharged from hospital. At follow-up 2 weeks after discharge, the patient was asymptomatic, serum creatinine was 124μmol/L, and daily urine output was around 2500-3500 mL.

Discussion and Conclusion

Currently, the World Health Organization recommends artesunate-based combination therapy as first-line treatment for malaria [3]. In the case of relapse, artesunate may be repeated. Primaquine is the most effective drug for clearing intrahepatic plasmodium stages and is therefore the first choice for preventing recurrence [7]. In our patient, parasite clearance was achieved with one course of dihydroartemisinin–piperaquine phosphate. However, he developed acute renal failure.

Several factors, including malaria-associated kidney injury (MAKI), hemosiderosis of kidney, drug-induced damage, and hypertensive and diabetic nephropathy, may have contributed to the AKI in our patient. Dehydration, release of inflammatory mediators and vasoactive substances, and parasite-induced hemolysis can lead to multiple organ damage, including MAKI [8]. The incidence of MAKI is 13%-17.8% in severe malaria, and the mortality rate is 11.9%-29% [9]. The typical presentation is with the triad of anemia, jaundice, and renal failure. The mechanism of MAKI has not been fully clarified. Mechanical blockage by parasitized erythrocytes, a direct toxic effect of hyperbilirubinemia, insufficient effective circulating blood volume, cytokines release, deposition of immune complexes in the glomeruli, and damage to renal microcirculatory capillary network, have all been implicated [12] [10]. Malaria may also cause thrombotic microangiopathy, possibly due to the damage of endothelial cells by plasmodium [11]. In such cases, renal biopsy shows necrosis of renal cortex, mesangial proliferative glomerulonephritis with

Figure 3: Pathological examination of renal tissue. There were 25 glomeruli and 1 ischemic sclerosis in the biopsy specimen. The glomerular mesangial cells and matrix shows slight proliferation, and the basement membrane shows degenerated vacuoles. Renal tubular epithelial cells shows granular degeneration, multiple focal and flaky brush margin exfoliation, and focal atrophy. Renal interstitial edema is present, and there is a small amount of focal lymphocyte and monocyte infiltration as well as some fibrosis. There is thickening of the walls of arterioles. Congo red staining is negative. Pathological diagnosis is subacute tubulointerstitial nephropathy (mainly renal tubular injury). Particle-like deposition in the C3 mesangial area: ALB capillary wall, renal tubular basement line deposition. A. The bristle margin of renal tubular epithelial cells has exfoliated, focal cells disintegrated (black arrow). Cell fragments (red arrow) are seen in the renal tubular lumen. (periodic acid-Schiff stain, ×200). B. There is cavitation degeneration of renal tubular epithelial cells (hematoxylin and eosin stain, ×400). C. Increase of renal interstitial mononuclear cells were observed (hematoxylin and eosin stain, ×200). D. The increased renal interstitial cells are mainly mononuclear macrophages (immunohistochemistry stain, ×200). E. There are no significant glomerular lesions (periodic Schiff-methenamine silver + Masson trichrome stain, ×400). F. Electron microscopy shows segmental basement membrane shrinkage (black arrow) and segmental foot process fusion (red arrow) (×8000).



oligoimmune complex deposition, membranous nephropathy, and acute tubular necrosis [12]. Most MAKI patients have complete recovery of renal function, but about 15% have only partial recovery and need to continue hemodialysis [13].

Hemosiderosis of kidney, which may occur in patients with intravascular hemolysis or valvular heart disease, can cause AKI [14]. Our patient had intravascular hemolysis and hemoglobinuria, and so the possibility of hemosiderin deposition should be considered. Drug-induced renal damage also cannot be excluded, especially because the patient received ibuprofen at the start of his illness. In addition, our patient had history hypertension and diabetes mellitus for more than 10 years, with proteinuria since January 2017. Typical pathological manifestations of hypertensive nephropathy and diabetic nephropathy include glomerular ischemic changes, with folding and thickening of glomerular capillary loops, glomerular consolidation and sclerosis, renal tubular atrophy, renal interstitial fibrosis, renal arterioles hyalinization and wall thickening, lumen stenosis, and so on [15]. There may be segmental necrosis of the loop and cellulose-like necrosis of the arteriole wall. Diabetic nephropathy is characterized by thickening of the glomerular basement membrane and obvious hyaline degeneration of the arterioles. Typical Kimmelstiel–Wilson nodules may be present. It is not exceptional for hypertensive and diabetic nephropathy to present as acute renal failure.

To summarize, a patient with *P. falciparum* malaria and acute renal failure was successfully managed in our unit. Many factors may contribute to acute renal failure in patients with serious malaria; however, it can be reversed with prompt treatment.

Declarations Section

Ethical Approval and Consent to participate

The study was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the Ethics Committee of The Fifth Medical Center, PLA General Hospital.

Availability of Supporting Data

All data generated or analysed during this study are included in this published article.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

Lei Shi, Lei Huang, Fusheng Wang organized this cure and

study, analyzed data, wrote the manuscript. Fang Wang, Enqiang Qin, Dan Wu, Peng Zhao, Bo Tu, Guang Yang, Fude Zhou, Minghui Zhao contributed to therapy and arrangement of clinical data. Xiaojuan Yu took pathological photos of Kidney.

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