Severe Plasmodium Vivax Malaria Presenting with Acute Kidney Injury and Sepsis

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ABSTRACT

Plasmodium vivax malaria is generally considered milder than P. falciparum, but in rare cases can result in severe, life-threatening complications such as acute kidney injury (AKI), severe electrolyte disturbances, hematologic abnormalities, and secondary infections, which increase morbidity and complicate management. A 31-year-old man presented with persistent cough, fever, and generalized weakness. He had a history of malaria and tested positive for IgM Plasmodium vivax, while peripheral smear and PCR were negative. On admission, he was moderately ill, showing pale conjunctiva and mild epigastric tenderness. Laboratory tests revealed severe normochromic normocytic anemia (Hb 5 g/dL), persistent thrombocytopenia (23 x10^3/µL), marked elevation of urea (328 mg/dL) and creatinine (36.8 mg/dL), severe hyperkalemia (8.8 mmol/L), hyponatremia (124 mmol/L), mild hypocalcemia, and metabolic acidosis. Imaging revealed bilateral pneumonia and parenchymal renal disease with hepatomegaly, cholecystitis, and left pleural effusion. He was also diagnosed with community-acquired pneumonia (PSI 142) and sepsis. Management included urgent serial hemodialysis, multiple transfusions, intravenous artesunate followed by dihydroartemisinin-piperaquine and primaquine, and broad-spectrum antibiotics. The patient improved clinically and biochemically, with normalization of electrolytes, improved renal function, and resolution of symptoms. Severe P. vivax malaria can present with multi-organ dysfunction, and early, comprehensive, multidisciplinary management is essential, especially when laboratory confirmation is inconclusive.

Keywords: Acute Kidney Injury; Electrolyte Imbalance; Hemodialysis; Plasmodium Vivax; Sepsis; Severe Malaria

INTRODUCTION

Plasmodium vivax was historically considered a cause of benign, uncomplicated malaria, in stark contrast to the often-fatal course of Plasmodium falciparum infection. However, a growing body of evidence over the last decade has fundamentally challenged this view, establishing that P. vivax is also a significant cause of severe and life-threatening disease [1]. Although it accounts for a smaller proportion of malaria-related deaths than P. falciparum, P. vivax is geographically the most widespread human malaria parasite and is responsible for substantial global morbidity [2].

The clinical spectrum of severe P. vivax malaria is broad and mimics that of severe falciparum malaria, including complications such as severe anemia, profound thrombocytopenia, acute respiratory distress syndrome (ARDS), shock, and multi-organ dysfunction [3, 4]. Acute kidney injury (AKI) is an increasingly recognized and serious complication, driven by a complex pathophysiology involving extensive intravascular hemolysis, renal microcirculation obstruction by parasitized erythrocytes, and a robust immune-mediated inflammatory response leading to acute tubular necrosis or interstitial nephritis [5, 6].

Diagnosing severe P. vivax malaria presents unique challenges. Infections are often characterized by low-density parasitemia, which can fall below the detection threshold of both conventional microscopy and some rapid diagnostic tests [7]. This can lead to diagnostic delays and a reliance on a high index of clinical suspicion, particularly in patients presenting with severe, unexplained sepsis-like syndromes in endemic or potentially exposed regions.

This report aims to present a complex case of severe P. vivax malaria in a young adult, characterized by an unusually extreme degree of acute kidney injury (AKI AKIN 3), life-threatening hyperkalemia, and concurrent community-acquired pneumonia with sepsis. We highlight the diagnostic challenges encountered and describe the successful multidisciplinary management that led to the patient's recovery, despite inconclusive initial parasitological findings.

CASE PRESENTATION

Patient Information and Presentation

A 31-year-old man with a recent history of a positive malaria serology was referred to our hospital from a regional facility due to worsening shortness of breath over the preceding five days. The patient’s primary complaint was persistent dyspnea, which began one week prior and had become progressively severe over the five days leading up to admission. The shortness of breath was constant, exacerbated by activity, and accompanied by a non-productive cough. For about one month before admission, he had experienced intermittent fevers, which were more prominent at night. In the three days prior to admission, he developed red spots on his arms, along with nausea and vomiting. He also reported a significant decrease in appetite and profound generalized weakness for the past month. His urinary output had decreased to approximately 50 cc per void, and the urine was dark, described as tea-colored. Notably, about an hour after arrival at our facility, he experienced a transient episode of unresponsiveness to verbal and painful stimuli. While he had not traveled to a known malaria-endemic region, he reported interacting with an individual from Papua in last year.

Physical Examination and Initial Investigations

On initial examination, the patient appeared moderately ill but was conscious and alert (GCS E4V5M6). Vital signs were significant for hypertension (157/82 mmHg), tachycardia (94 bpm), and tachypnea (28 breaths/minute) with a temperature of 37.8°C. He required supplemental oxygen via a nasal cannula at 4-5 L/min to maintain an SpO_2 of 97%. Key physical findings included pale conjunctivae , mild epigastric tenderness on abdominal palpation , and bilateral fine crackles on lung auscultation.

Table 1. Hematology and Clinical Chemistry Laboratory Results

Parameter	Result	Normal Range	Unit

Parameter	Result	Normal Range	Unit
Hematology			
Hemoglobin	5	g/dL	12.0 - 15.6
Hematocrit	15	%	35 - 45
Leukocytes	8.7	$10^3/\mu L$	4.5 - 11.0
Platelets	39	$10^3/\mu L$	150 - 450
Erythrocytes	1.82	$10^6/\mu L$	4.5 - 5.9
Neutrophils	90.50	%	55.0 - 80.0
Lymphocytes	7.10	%	22.0 - 44.0
Blood Chemistry			
Random Blood Sugar	97	mg/dL	60 - 140
SGOT	36	U/L	< 35.00
SGPT	41	U/L	< 41.00
Albumin	3.8	g/dL	3.5 - 5.2
Creatinine	36.9	mg/dL	0.9 - 1.3
Urea	328	mg/dL	< 50.00
Sodium	124	mmol/L	136 - 145
Potassium	8.8	mmol/L	3.3 - 5.1
Ionized Calcium	1.16	mmol/L	1.17 - 1.29
Arterial Blood Gas			
pH	7.190		
pCO_2	21.5		mmHg
pO_2	123.7		mmHg
HCO_3^-	8.0	mmol/L	21.0 - 28.0
Base Excess	-20.17		-2 to +3
O_2 Saturation	98.6	%	94.0 - 98.0
Urinalysis			
Protein	+++ / Positive 3	mg/dL	Negative
Erythrocytes	+++ / Positive 3	mg/dL	Negative
Color	Orange		
Clarity	Cloudy		
Serology (from clinic, June 25, 2025)			
IgM *Plasmodium vivax*	Positive		Negative

Diagnostic Assessment

Initial laboratory investigations revealed a complex multi-organ dysfunction. He had severe normocytic normochromic anemia (Hemoglobin 5.0 g/dL) (Table 1.), severe thrombocytopenia (platelet count 39,000/µL), and neutrophilia (90.50%). Biochemical analysis showed an extreme degree of acute kidney injury (Creatinine 36.9 mg/dL, Urea 328 mg/dL), life-threatening hyperkalemia (K^+ 8.8 mmol/L), severe hyponatremia (Na^+ 124 mmol/L), and mild hypocalcemia (ionized Ca^{2+} 1.16 mmol/L). Arterial blood gas analysis confirmed severe uncompensated metabolic acidosis (pH 7.190, HCO_3 8.0 mmol/L, Base Excess -20.17 mmol/L). Urinalysis was remarkable for +3 proteinuria and +3 hematuria. A serology report from a prior clinic visit on June 25, 2025, was positive for IgM to Plasmodium vivax. However, a peripheral blood smear for malaria parasites performed on admission was negative.

A chest X-ray on admission showed bilateral infiltrates consistent with pneumonia and cardiomegaly (CTR 65%). An electrocardiogram (ECG) showed a sinus rhythm with prominent tall T-waves, consistent with severe

hyperkalemia. The patient's Pneumonia Severity Index (PSI) score was 141, placing him in Class V (high risk), and his Sequential Organ Failure Assessment (SOFA) score was 10, indicating a high risk of mortality.

DISCUSSION

This case presents a complex and severe manifestation of Plasmodium vivax malaria in a young adult, complicated by multiple organ dysfunction syndrome (MODS), including an extreme degree of acute kidney injury (AKI), severe electrolyte derangements, concurrent pneumonia, and sepsis. The case is notable for the severity of its complications, the diagnostic challenges posed by negative initial parasitology, and the successful outcome following aggressive, multidisciplinary intensive care.

The long-held notion of P. vivax as a "benign" malaria has been definitively refuted over the last decade [4]. A comprehensive meta-analysis has shown that a significant portion of hospitalized P. vivax patients develop severe disease, with an associated mortality rate, challenging the historical perspective [1]. The clinical spectrum of severe disease is broad and can mimic that of P. falciparum, encompassing complications such as severe anemia, profound thrombocytopenia, acute respiratory distress syndrome (ARDS), and multi-organ dysfunction [3]. This case exemplifies the most critical end of this spectrum. The diagnostic pathway was complicated by the initial negative peripheral blood smear. This is a recognized challenge in P. vivax infections, which are often characterized by low-density parasitemia that can fall below the detection threshold of conventional microscopy [7]. This underscores the importance of maintaining a high index of clinical suspicion based on epidemiological links and clinical presentation, especially in patients presenting with severe, unexplained sepsis-like syndromes [7]. The positive IgM serology provided the first clue, leading to the initiation of targeted therapy despite the negative smear.

The patient's presentation with a creatinine level of 36.8 mg/dL represents an extreme degree of uremia. Acute kidney injury is an increasingly recognized and serious complication of P. vivax malaria [5]. A systematic review found that AKI is a significant contributor to morbidity in this context [5], with another meta-analysis confirming its prevalence across different malaria species [6]. The pathophysiology of malaria-associated AKI is multifactorial, involving extensive intravascular hemolysis, renal microcirculation obstruction, and a robust immune-mediated inflammatory response leading to acute tubular necrosis or interstitial nephritis [5]. This patient's condition fits the profile of AKI in the critically ill, a demographic where the condition is common and associated with poor outcomes [8]. Given the extreme uremia, the initiation of urgent hemodialysis was critical to prevent life-threatening uremic complications [9]. While a landmark trial on the timing of renal replacement therapy (RRT) did not find a mortality benefit for accelerated versus standard initiation in a general population of critically ill patients [10], that study did not specifically address patients with such profound uremia, where delayed therapy could lead to irreversible complications. The patient's underlying renal status was unknown, but the development of AKI in the context of potential pre-existing chronic kidney disease (acute-on-chronic kidney disease, ACKD) carries a significantly worse prognosis than de novo AKI, with a nearly three-fold higher risk of all-cause mortality and a ten-fold increased risk of progression to end-stage renal disease within 12 months, as defined by consensus reports [11].

The life-threatening hyperkalemia (8.8 mEq/L) was a direct consequence of both massive hemolysis and acute renal failure. Lysis of red blood cells releases large amounts of intracellular potassium into the circulation, overwhelming the compromised kidney's ability to excrete it. This constitutes a cardiac emergency, and management aligns with evidence-based protocols for hyperkalemia in the emergency setting, prioritizing cardiac membrane stabilization with intravenous calcium, followed by therapies to shift potassium intracellularly [12]. The concurrent severe hyponatremia is also a common finding in severe malaria [3].

The patient was also diagnosed with severe community-acquired pneumonia (CAP), with a Pneumonia Severity Index (PSI) score of 141, placing him in the highest risk class (Class V). This category carries a high 30-day mortality risk and typically warrants ICU admission. The bilateral pneumonia seen on imaging could represent

a primary malarial lung injury or a secondary bacterial infection. In a critically ill, immunocompromised host, broad-spectrum antibiotic coverage is mandatory [13]. The 2019 ATS/IDSA guidelines for severe CAP recommend combination therapy with a β-lactam plus either a macrolide or a respiratory fluoroquinolone, which should be initiated within the first hour of recognition [13].

The overall clinical picture was that of sepsis and MODS, as indicated by a SOFA score of 10. The management approach was guided by the Surviving Sepsis Campaign 2021 guidelines, which emphasize the "Hour-1 bundle" of lactate measurement, blood cultures, broad-spectrum antibiotics, and fluid resuscitation/vasopressors [14]. However, fluid management in severe malaria must be approached with extreme caution. Unlike typical bacterial sepsis, the perfusion defect in malaria is largely due to microcirculatory obstruction from parasite sequestration. Aggressive fluid resuscitation is associated with an increased risk of pulmonary edema and higher mortality. Therefore, a conservative fluid strategy is now advocated [14]. Norepinephrine remains the first-line vasopressor to maintain a mean arterial pressure (MAP) ≥65 mmHg [14].

The cornerstone of treatment for severe malaria is intravenous artesunate, which is the WHO-recommended first-line therapy [15]. Its superiority over quinine in reducing mortality has been firmly established. Following at least 24 hours of parenteral therapy, and once the patient can tolerate oral intake, treatment is completed with a full 3-day course of an oral artemisinin-based combination therapy (ACT), such as dihydroartemisinin-piperaquine (DHP) [15]. For P. vivax, this must be followed by a "radical cure" with primaquine to eradicate the dormant liver-stage hypnozoites and prevent relapse [15]. This requires prior G6PD testing to avoid inducing severe hemolysis. The patient's severe anemia necessitated multiple blood transfusions. Current WHO guidelines recommend transfusion for a hemoglobin threshold of <6 g/dL in patients with complications like acidosis or shock [15]. Prophylactic platelet transfusion, however, is not recommended even in cases of severe thrombocytopenia, unless there is active, significant bleeding [15]. The patient’s successful recovery from such a severe, multi-faceted illness is a testament to the importance of early, aggressive, and evidence-based multidisciplinary care that addressed each organ system failure while targeting the underlying infection.

CONCLUSION

Severe Plasmodium vivax malaria can present with life-threatening, multi-organ complications, including extreme acute kidney injury, severe hematological abnormalities, and sepsis, even when initial parasitological examinations like peripheral blood smears are negative. This case highlights the critical importance of maintaining a high index of suspicion based on clinical and epidemiological factors. Early, aggressive, and comprehensive multidisciplinary management—including prompt renal replacement therapy for severe uremia, targeted anti-malarial and broad-spectrum antibiotic treatment, transfusion support, and meticulous correction of fluid and electrolyte imbalances—is essential for a favorable outcome in such complex presentations

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Informed Consent Statement

Written informed consent has been obtained from the patients to publish this paper.

Conflicts of Interest

The authors declare no conflict of interest

References

1. Kotepui, M., Kotepui, K. U., Milanez, G. D., & Masangkay, F. R. (2020). Global prevalence and mortality of severe Plasmodium vivax malaria: a systematic review and meta-analysis. Malaria Journal, 19(1), 1-13.
2. World Health Organization. (2023). World malaria report 2023. Geneva: World Health Organization.
3. Rahimi, M., & Shokri, A. (2023). The clinical spectrum and complications of Plasmodium vivax malaria: A systematic review and meta-analysis. Pathogens and Global Health, 117(3), 195-209.
4. Baird, J. K. (2017). Evidence and implications of mortality associated with acute Plasmodium vivax malaria. Clinical Microbiology Reviews, 30(1), 67-101.
5. Karunajeewa, H. A., Mueller, I., & Davis, T. M. (2019). Acute kidney injury in Plasmodium vivax malaria: a systematic review. Transactions of the Royal Society of Tropical Medicine and Hygiene, 113(12), 773-780.
6. Naing, C., Whittaker, M. A., Nyunt, W. T., & Mak, J. W. (2019). Acute kidney injury in patients with malaria: an updated systematic review and meta-analysis. Wellcome Open Research, 4, 193.
7. Baird, J. K. (2018). The challenges of diagnosing and treating Plasmodium vivax malaria. Malaria Journal, 17(1), 1-5.
8. Hoste, E. A., Bagshaw, S. M., Bellomo, R., Cely, C. M., Colman, R., Cruz, D. N., et al. (2015). Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. Intensive Care Medicine, 41(8), 1411-1423.
9. Gaudry, S., Hajage, D., Schortgen, F., Martin-Lefevre, L., Pons, B., Boulet, E., et al. (2016). Initiation strategies for renal-replacement therapy in the intensive care unit. New England Journal of Medicine, 375(2), 122-133.
10. STARRT-AKI Investigators. (2020). Timing of initiation of renal-replacement therapy in acute kidney injury. New England Journal of Medicine, 383(3), 240-251.
11. Chawla, L. S., Bellomo, R., Bihorac, A., Goldstein, S. L., Siew, E. D., Bagshaw, S. M., et al. (2017). Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. Nature Reviews Nephrology, 13(4), 241-257.
12. Peacock, W. F., Rafique, Z., Clark, C. L., Nair, R., Singer, A. J., Birgersdotter-Green, U. M., et al. (2018). Real world evidence for treatment of hyperkalemia in the emergency department (REVEAL-ED): a multicenter, prospective, observational study. The Journal of Emergency Medicine, 55(6), 741-750.
13. Metlay, J. P., Waterer, G. W., Long, A. C., Anzueto, A., Brozek, J., Crothers, K., et al. (2019). Diagnosis and treatment of adults with community-acquired pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. American Journal of Respiratory and Critical Care Medicine, 200(7), e45-e67.
14. Evans, L., Rhodes, A., Alhazzani, W., Antonelli, M., Coopersmith, C. M., French, C., et al. (2021). Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Medicine, 47(11), 1181-1247.
15. World Health Organization. (2022). Guidelines for the treatment of malaria. Geneva: World Health Organization.