

Fatal Imported *Plasmodium falciparum* Malaria Despite Early Intravenous Artesunate: A Comprehensive Case-Based Review

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Abstract

Review Article

Imported *Plasmodium falciparum* malaria represents a life-threatening condition in non-endemic settings, particularly among non-immune individuals. Despite advances in early diagnosis and the use of intravenous artesunate, mortality remains significant in severe forms requiring intensive care. We report a fatal case of severe imported malaria in Morocco and provide a comprehensive, evidence-based review integrating international (WHO), European, French (SFAR), and Moroccan management protocols. This article aims to serve as a practical and scientific reference for intensivists and resident physicians managing severe malaria.

Keywords: Severe malaria, *Plasmodium falciparum*, Imported malaria, Intensive care, Artesunate, Morocco.

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1. INTRODUCTION

Malaria remains one of the most important infectious diseases worldwide, with *Plasmodium falciparum* responsible for the majority of severe and fatal cases. According to the World Health Organization, there were approximately 249 million malaria cases and over 600,000 deaths globally in 2022, predominantly in sub-Saharan Africa [1].

In non-endemic countries such as Morocco, malaria is almost exclusively imported, occurring in travelers returning from endemic regions. Imported malaria is characterized by infection acquired in an endemic area but diagnosed in a non-endemic setting. This epidemiological context is associated with increased severity due to the absence of acquired immunity [2].

Severe malaria constitutes a medical emergency requiring immediate ICU admission, with mortality rates ranging from 10% to 30% despite optimal management [3].

2. Definition and Epidemiology of Imported Malaria

Imported malaria is defined as any malaria infection contracted in an endemic area and diagnosed in a region where malaria transmission is absent or interrupted [2]. In Morocco, malaria was eliminated in

2010, but imported cases continue to be reported, primarily linked to travel to sub-Saharan Africa [10].

Non-immune individuals, such as tourists, expatriates, and migrants, are at particularly high risk of severe disease due to the lack of partial immunity that typically develops in endemic populations [4].

The absence or poor adherence to chemoprophylaxis remains the most significant risk factor for severe imported malaria [7].

3. Overview of *Plasmodium* Species Infecting Humans

Although *Plasmodium falciparum* is responsible for the most severe forms of malaria, several other species can infect humans and must be recognized for a comprehensive understanding of the disease.

The main human pathogenic species include *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, and *Plasmodium knowlesi*, a zoonotic species transmitted from primates [1].

Plasmodium falciparum is characterized by high parasitemia, cytoadherence, and a high risk of severe complications. In contrast, *Plasmodium vivax* and *Plasmodium ovale* are notable for their ability to form

dormant hepatic stages (hypnozoites), leading to relapses weeks to months after the initial infection [2].

Plasmodium malariae typically causes chronic low-grade infections but can be associated with nephrotic syndrome. *Plasmodium knowlesi*, increasingly reported in Southeast Asia, may cause rapidly progressive disease resembling severe *P. falciparum* malaria [1].

Understanding these species differences is essential for diagnosis, treatment, and prevention strategies, even when managing a confirmed *P. falciparum* infection.

4. Pathophysiology of Severe *Plasmodium falciparum* Malaria

The pathophysiology of severe malaria is complex and involves both parasite-related and host-related mechanisms. A key feature is the sequestration of parasitized erythrocytes within the microvasculature, mediated by the expression of *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1), which binds to endothelial receptors such as ICAM-1 and CD36 [3].

This process leads to microvascular obstruction, impaired tissue perfusion, and local hypoxia. Additionally, infected erythrocytes adhere to uninfected red blood cells (rosetting), further worsening microcirculatory flow [3].

A systemic inflammatory response is triggered, characterized by elevated levels of cytokines such as TNF- α , IL-1, and IL-6. This contributes to endothelial activation, increased vascular permeability, and metabolic disturbances, including lactic acidosis [6].

The resulting pathophysiological cascade leads to multiorgan dysfunction, including cerebral malaria, acute respiratory distress syndrome (ARDS), acute kidney injury, and circulatory shock [5].

High parasite biomass, reflected by parasitemia levels exceeding 5–10%, is strongly associated with poor prognosis [3].

5. WHO and International Criteria for Severe Malaria

According to WHO guidelines, severe malaria is defined by the presence of *P. falciparum* parasitemia associated with one or more clinical or laboratory criteria of severity [2].

These include impaired consciousness (Glasgow Coma Scale <11), prostration, multiple convulsions, shock, respiratory distress or ARDS, acute kidney injury (creatinine >265 $\mu\text{mol/L}$), severe anemia, hypoglycemia, metabolic acidosis (lactate >5 mmol/L), jaundice, and hyperparasitemia ($\geq 10\%$) [2].

European and French guidelines, including those from SFAR, emphasize similar criteria but highlight the importance of ICU admission in any patient presenting with organ dysfunction or high parasitemia, even in the absence of classical signs [8].

Moroccan protocols align closely with WHO recommendations, stressing early identification and immediate referral to intensive care units [10].

6. Diagnostic Approach

The diagnosis of malaria relies primarily on parasitological confirmation. Microscopic examination of thick and thin blood smears remains the gold standard, allowing both detection and quantification of parasitemia [4].

Rapid diagnostic tests (RDTs), particularly those detecting HRP2 antigens, are useful for rapid screening but should not replace microscopy [4].

Polymerase chain reaction (PCR) techniques provide high sensitivity and specificity but are generally reserved for reference laboratories [4].

In non-endemic settings, any febrile patient with a history of travel to endemic areas should be tested urgently for malaria, as delayed diagnosis is a major contributor to mortality [7].

7. Case Presentation

We report the case of a 55-year-old male with no significant past medical history who was admitted to the intensive care unit in Morocco for altered mental status in the context of febrile illness.

The patient had recently returned from sub-Saharan Africa and had not received any malaria chemoprophylaxis. The interval between return and symptom onset was approximately 11 days.

On admission, clinical examination revealed high-grade fever, a Glasgow Coma Scale score of 10/15, tachypnea with hypoxemia (SpO₂ 88% on room air), and signs of hemodynamic instability.

Laboratory investigations showed severe thrombocytopenia (35,000/mm³), acute kidney injury, mild hepatic cytolysis, and metabolic acidosis.

Malaria diagnosis was confirmed by thick and thin blood smears, revealing *Plasmodium falciparum* infection with an initial parasitemia of 7%. Intravenous artesunate was initiated within one hour of diagnosis, in accordance with international guidelines [2].

Despite early and appropriate management, the clinical course was marked by rapid deterioration, including the development of cerebral malaria, acute

respiratory distress syndrome requiring mechanical ventilation, refractory shock, and acute kidney injury.

Parasitemia increased to 20% by day 3, reflecting a high parasite burden and poor prognosis.

The patient ultimately died due to refractory multiorgan failure.

8. ICU Management of Severe Imported Malaria

Management of severe malaria in ICU settings requires a combination of specific antimalarial therapy and aggressive supportive care.

Intravenous artesunate is the first-line treatment recommended by WHO. It is administered at a dose of 2.4 mg/kg at 0, 12, and 24 hours, followed by daily dosing until oral therapy can be initiated [2].

Randomized controlled trials have demonstrated that artesunate reduces mortality by approximately 35% compared to quinine, particularly in adults [5].

Supportive care is essential and follows principles similar to those used in sepsis management. Mechanical ventilation is required in cases of ARDS, using lung-protective strategies. Hemodynamic instability should be managed with cautious fluid resuscitation and early vasopressor support, typically norepinephrine [8].

Renal replacement therapy should be initiated early in cases of acute kidney injury. Metabolic complications, including hypoglycemia and acidosis, must be corrected promptly [8].

Close monitoring of parasitemia is critical, with daily or twice-daily measurements recommended. Failure of parasitemia to decrease within 48 hours is associated with poor outcomes [2].

9. Moroccan and International Management Algorithms

Moroccan guidelines, developed by the Ministry of Health, are based on WHO recommendations but adapted to local healthcare infrastructure [10]. They emphasize rapid diagnosis, immediate initiation of intravenous artesunate, and early transfer to specialized centers.

The SFAR guidelines further detail ICU-specific management, including ventilation strategies, fluid management, and organ support [8].

European (ESCMID) recommendations align with these approaches and stress the importance of multidisciplinary care involving infectious disease specialists and intensivists [9].

These converging guidelines highlight a universal principle: time to treatment is the most critical determinant of survival, yet it does not fully eliminate mortality risk.

10. DISCUSSION

The present case illustrates the fulminant progression of severe imported malaria despite early diagnosis and prompt initiation of artesunate therapy.

The rapid increase in parasitemia from 7% to 20% reflects a high parasite biomass and suggests extensive sequestration, a phenomenon well described in severe *P. falciparum* infections where circulating parasitemia underestimates total parasite burden [3].

The occurrence of cerebral malaria, ARDS, shock, and acute kidney injury corresponds to the classical spectrum of severe disease described in WHO and SFAR guidelines [2-8]. These complications are driven by endothelial dysfunction, inflammatory response, and impaired microcirculation [6].

This case underscores that early treatment, although essential, does not fully reverse the pathophysiological cascade once multiorgan failure is established. Similar observations have been reported in international cohorts, where mortality remains significant despite optimal management [5].

In the Moroccan context, this case highlights the importance of maintaining a high index of suspicion for malaria in any febrile patient returning from endemic areas and the necessity of rapid referral to ICU structures [10].

11. Prevention of Imported Malaria

Preventive strategies remain the most effective approach to reducing mortality. Chemoprophylaxis using agents such as atovaquone-proguanil, doxycycline, or mefloquine is highly effective when taken correctly [7].

Vector control measures, including insecticide-treated bed nets and repellents, further reduce transmission risk [1]. Education of travelers is essential, as poor adherence to prophylaxis is a major contributing factor to severe imported malaria.

12. CONCLUSION

Severe imported *Plasmodium falciparum* malaria remains a major challenge in intensive care medicine. Despite adherence to international guidelines and early initiation of artesunate, mortality remains significant due to complex pathophysiological mechanisms and rapid progression to multiorgan failure.

This article provides a comprehensive, evidence-based framework integrating WHO, SFAR,

and Moroccan guidelines, aiming to support clinicians in the optimal management of this life-threatening condition.

REFERENCES

1. World Health Organization. *World Malaria Report 2023*. Geneva: WHO; 2023.
2. World Health Organization. *Guidelines for the treatment of malaria*. 3rd ed. Geneva: WHO; 2015.
3. White NJ, Turner GDH, Medana IM, Dondorp AM, Day NPJ. The pathology of malaria. *Malar J*. 2013; 12:1–14.
4. Moody A. Rapid diagnostic tests for malaria parasites. *Clin Microbiol Rev*. 2002;15(1):66–78.
5. Dondorp AM, Nosten F, Stepniewska K, et al. Artesunate versus quinine for treatment of severe falciparum malaria. *N Engl J Med*. 2005; 353:455–467.
6. Idro R, Jenkins NE, Newton CRJC. Pathogenesis, clinical features, and neurological outcome of cerebral malaria. *Lancet Neurol*. 2005; 4:827–840.
7. Schlagenhauf P, Petersen E. Malaria chemoprophylaxis: strategies for risk groups. *Clin Microbiol Rev*. 2008;21(3):466–472.
8. Société Française d'Anesthésie et de Réanimation (SFAR). *Prise en charge du paludisme grave en réanimation*. 2019.
9. European Society of Clinical Microbiology and Infectious Diseases (ESCMID). *Guidelines for malaria*. 2018.
10. Ministère de la Santé Maroc. *Guide de prise en charge du paludisme importé*. Rabat; 2020.