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Case Report

Malaria with Immune-Mediated Hemolytic Anemia: A Case Report

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Abstract

This case report describes the clinical presentation, diagnosis, and management of a 34-year-old male patient with malaria caused by Plasmodium falciparum, complicated by immune hemolytic anemia. The patient initially presented with a one-day history of fever and feeling unwell, but the diagnosis of malaria was initially missed. Four days later, during the second follow-up visit, the patient was administered Artemisinin and Piperaquine tablets. Despite this treatment, persistent symptoms and hemolytic anemia necessitated multiple treatment modifications. Subsequent evaluation confirmed the presence of immune hemolytic anemia associated with malaria. The patient was then treated with intravenous methylprednisolone and received a blood transfusion. This case underscores the challenges in diagnosing and managing severe malaria and its immune-related complications.

Keyword: Malaria; Plasmodium falciparum; Immune Hemolytic Anemia

Introduction

Malaria is a widespread parasitic disease that poses a significant public health challenge in many regions, particularly in western Africa, such as Sierra Leone [1]. Plasmodium falciparum, the most virulent species, is responsible for the majority of severe malaria cases. Although malaria is typically associated with fever and other constitutional symptoms, complications such as hemolytic anemia can occur, and occasionally, immune-mediated mechanisms may contribute to the anemia [2].

Case Presentation

A 34-year-old male presented at Sierra Leone-China Friendship Hospital on August 19, 2022 (Day 1), complaining of fever and unwell for one day. He had no significant medical history but had recently traveled from China to Sierra Leone, where he resided in the outskirts of Freetown for the past two weeks. Physical examination on Day 1 was unremarkable, with no signs of fever or other abnormalities. Tests for malaria antibodies, COVID-19, and influenza were negative. The patient was advised to consider antimalarial treatment or undergo follow-up observation. The Patient refused antimalarial treatment.

On Day 5, the patient returned with persistent fever and weakness. His temperature was recorded at 36.8°C, blood pressure at 96/65 mmHg, and heart rate at 126 BPM. Lung sounds were clear, and heart rhythm was regular. Subsequent rapid antigen testing suggested severe P. falciparum infection, prompting treatment with Artemisinin and Piperaquine Tablets for six days.

Despite antimalarial therapy, the patient's symptoms persisted, and on Day 15, he reported loose stools. Suspecting a possible typhoid infection, the patient was prescribed Levofloxacin for three days.

On Day 18, the patient exhibited weakness and bloody urine. Blood tests showed low hemoglobin levels (HBG 75g/L) and elevated blood bilirubin, indicative of hemolytic anemia associated with malaria. The patient was readministered Artemisinin and Piperaquine Tablets. Further complicating the case, on Day 20, the patient reported blood-colored urine, which started on Day 7. Physical examination revealed a temperature of 36.5°C, blood pressure of 125/85 mmHg, and a heart rate of 114 BPM. Hemoglobin levels further decreased (HBG 53g/L), and the patient appeared anemic. Urine test of dry chemical method: Occult blood^{+++}, Protein^{+}, Bilirubin^{+++}, Urobilinogen $^{+}$. But red blood

cell is not seen under microscopy.

Artemisinin and Piperaquine Tablets were discontinued, and intravenous Methylprednisolone was initiated. After approximately 6 hours, the urine color returned to normal.

The patient demanded a discharge and was transferred to Princeton Medical Center in the US on Day 23. Further investigations (Direct antiglobulin positive, Poly, C3) confirmed immune-mediated hemolytic anemia. Blood smear showed rare ring forms are identified both on the thin and thick smears (0.2%). Binax Now antigen test shows strong P.falciparum band supporting persistent Falciparum malarial infection. The patient received red blood cell transfusion and was treated with Atovaquone-Proguanil and a tapering dose of oral Prednisone over a period of three months. The combination of antimalarial drugs and immunosuppressive therapy led to a successful recovery, and the patient's symptoms resolved gradually.

Time	Antigen Test	Blood Smear
Day 1	-	
Day 5	+	
Day 18	+	0%
Day 23	+	0.2%

Table 1: Malaria Test.

Time	Medication
Day 5-10	Artemisinin (62.5 mg) and Piperaquine (375 mg) Tablets,2 tablets / day
Day 15-17	Levofloxacin Hydrochloride tablet 0.4g/day
Day 18-19	Artemisinin (62.5 mg) and Piperaquine(375mg) Tablets, 2 tablets / day
Day 20-22	Methyl prednisone 160mg intravenous
Day 23-108	Tapering dose of oral Prednisone, start form 100mg
Day 22-24	Atovaquone (250 mg)-Proguanil (100 mg) Tablets, 4 tablets / day

Table 2: Medication.

Discussion

Challenges in Early Diagnosis

The early diagnosis of malaria, especially caused by Plasmodium falciparum, can be difficult due to its nonspecific initial symptoms, which resemble common cold or flu. These symptoms may include fever, fatigue, and sweating. Throughout the entire course of this case, there was no recorded instance of elevated body temperature. Microscopy remains the gold standard for the diagnosis of malaria. It is recommended to perform two smears of each thick and thin smears to increase diagnostic yield. If the initial set of smears is negative, they should be repeated 12 to 24 h apart until at least 3 sets are negative [3]. Nevertheless, this microscopy method relies on the expertise of the interpreter [4,5]. Consequently, two significant limitations emerge: the requirement for skilled laboratory personnel and the need for an adequate parasite density for accurate results. Malarial antigens are wide used rapid diagnostic test in practice, and results are available within minutes [5]. Microscopy and antigens test might not detect the presence of the malaria parasite at earlier stage of malaria [3]. In regions like Sierra Leone, where malaria is endemic and cases of severe malaria are not uncommon, local healthcare providers rely on their experience to initiate treatment promptly. If a patient presents with flu-like symptoms and is in an area with high malaria prevalence, they may administer antimalarial drugs without waiting for further test results to prevent potentially severe outcomes.

Challenges of Antimalarial Drug Resistance

Artemisinin-based combination therapies remain the first line choice [6]. Antimalarial drug resistance is a growing concern worldwide [7]. The case report mentioned a prolonged treatment course of nine days, indicating a possible decline in treatment effectiveness. This prolonged duration suggests that the malaria parasites in this patient showed reduced susceptibility to the medication. Drug resistance poses a significant challenge in the management of malaria, as it limits the effectiveness of available treatments, requiring the development of alternative therapies to combat resistant strains.

Immune Hemolytic Anemia

Immune hemolytic anemia is a rare but known complication of malaria infection [2,8]. Severe malaria caused by P. falciparum can lead to the destruction of red blood cells and subsequent anemia. In this case, the patient developed immune hemolytic anemia after malaria infection, resulting in significantly decreased hemoglobin levels. While drug-induced hemolysis cannot be completely ruled out as a potential contributing factor, there have been no reported cases of immune hemolytic anemia associated with Artemisinin and Piperaquine tablets or levofloxacin. The prevailing belief is that immune hemolytic anemia is primarily caused by malaria itself. Local healthcare providers' experiences suggest that malaria-induced hemolysis might not be as uncommon as reported due to underreporting or lack of awareness. Given the limited medical resources and conditions, further diagnostic investigations usually will not be pursued.

Conclusion

The presented case report highlights several challenges in managing severe malaria, including early diagnosis difficulties, emerging drug resistance, and rare immune-related complications. Healthcare providers in malaria-endemic regions, like Sierra Leone, often rely on their clinical experience to promptly initiate antimalarial treatment when confronted with flu-like symptoms in patients at risk for malaria. Continuous surveillance and monitoring of drug resistance patterns are essential in the fight against malaria. Additionally, raising awareness about rare complications like immune hemolytic anemia following malaria infection can lead to better recognition, diagnosis, and management of these conditions, potentially improving patient outcomes in regions with high malaria prevalence. Collaborative efforts between healthcare professionals and researchers are crucial in addressing the challenges posed by malaria and enhancing the effectiveness of malaria control and treatment strategies.

Disclosure

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