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Co-infection of COVID-19 and Plasmodium Vivax Cerebral Malaria in a Child: A Case Report

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ABSTRACT

Background and Objective: Malaria remains a critical global health challenge, exacerbated by co-infections such as COVID-19. This report aims to enhance understanding of co-infection management and inform clinical practices in similar cases.

Case Report: This case report presents an 11-year-old boy from Saravan, Iran, who developed fever, chills, anorexia, and lethargy, leading to a diagnosis of Plasmodium vivax malaria. His condition deteriorated, resulting in seizures and a Glasgow Coma Scale (GCS) score of 5, prompting transfer to a pediatric ICU for advanced care. Initial evaluations revealed a positive PCR test for SARS-CoV-2, alongside indications of cerebral malaria. Treatment included intravenous artesunate for malaria, remdesivir, and dexamethasone for COVID-19, with supportive care for neurological symptoms. Notably, laboratory parameters gradually normalized, and subsequent malaria smears were negative. By day four, the patient was successfully weaned off mechanical ventilation, and he showed steady improvement, ultimately being discharged in good condition on day fourteen. This case emphasizes the necessity for heightened clinical awareness regarding co-infections in endemic regions, particularly among pediatric patients.

Conclusion: It highlights the complexities in management, necessitating comprehensive diagnostic and therapeutic strategies to address the overlapping challenges posed by simultaneous infections.

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Introduction

Malaria remains the most significant protozoan disease globally, with its transmission and prevalence increasingly influenced by climate change [1]. Affecting approximately 5% of the world's population at any given time, malaria causes between 0.5 to 2.5 million deaths annually, primarily in low-income countries, making it a persistent global health challenge [2]. In Iran, the incidence of malaria had dramatically declined, with no indigenous cases reported in 2018 and 2019, reflecting the success of public health interventions in the country's southern regions [3]. However, a significant resurgence occurred in 2022, particularly in Sistan and Baluchestan Province, where nearly 3,000 malaria-positive cases were reported by early November, a nearly tenfold increase from the previous year. This surge has been attributed to factors such as cross-border transmission from neighboring Pakistan, increased rainfall, the arrival of foreign nationals, and insufficient case detection [4].

Among malaria's clinical forms, cerebral malaria is the most severe and life-threatening, especially in children, with a mortality rate of 15–25%. It is typically associated with Plasmodium falciparum, but other species like P. vivax can rarely cause cerebral complications. Symptoms include seizures, altered mental status, and coma, necessitating urgent diagnosis and treatment.

Simultaneously, the COVID-19 pandemic has emerged as a major global health crisis, causing extensive morbidity and mortality and overwhelming healthcare systems worldwide [5]. In malaria-endemic regions, the dual burden of malaria and COVID-19 presents serious challenges. Co-infection with these two diseases can increase diagnostic uncertainty due to overlapping clinical symptoms such as fever, fatigue, and respiratory distress. This may delay appropriate treatment and increase the risk of adverse outcomes. Individuals suffering from malaria may also have weakened immune responses, making them more vulnerable to severe manifestations of COVID-19. Therefore, prompt recognition of co-infection is essential for guiding effective treatment strategies [6].

In this report, we present a rare case of co-infection in an 11-year-old child diagnosed with cerebral malaria caused by Plasmodium vivax and COVID-19. This case underscores the clinical and diagnostic complexities of managing co-infection in pediatric patients and highlights the need for heightened vigilance in malaria-endemic settings during the ongoing pandemic. By examining this case, we aim to enhance understanding of how co-infection affects clinical decision-making and to inform best practices for future similar scenarios.

Case Presentation

An 11-year-old boy from Saravan, a city in the southern part of Sistan and Baluchestan province, Iran, presented with fever and chills that began two weeks prior to admission. The fever was intermittent, with episodes of subsidence lasting up to one day before recurring. He also experienced anorexia and lethargy during this period. The patient initially visited a local clinic, where a peripheral blood smear confirmed the diagnosis of Plasmodium vivax malaria. However, as his condition worsened, including the onset of delirium and two seizures, he was admitted to Saravan Hospital. Upon admission, his level of consciousness deteriorated, necessitating intubation. Due to the absence of a pediatric infectious disease unit at Saravan Hospital, he was transferred to Zahedan, the provincial capital, for advanced management at Ali ibn Abi Talib Hospital's pediatric intensive care unit (ICU) on March 7, 2024.

Upon arrival at the ICU, the patient was intubated and on a ventilator. His Glasgow Coma Scale (GCS) score was 5, indicating a severely reduced level of consciousness. Vital signs were notable for a temperature of 38.5°C, heart rate of 110 bpm, and blood pressure of 60/95 mmHg. Cardiovascular and pulmonary examinations were normal, and no organomegaly was observed.

Given the patient's neurological symptoms, including seizures and a decreased level of consciousness, the differential diagnoses included cerebral malaria, viral encephalitis, and possible COVID-19 co-infection. Empiric treatment was initiated with anticonvulsants (phenytoin), broad-spectrum antibiotics (ceftriaxone and vancomycin),

antiviral therapy (acyclovir), and intravenous artesunate as the antimalarial agent.

To further investigate the etiology of his symptoms, nasopharyngeal swabs were obtained for PCR testing for SARS-CoV-2 and influenza viruses. A chest X-ray was performed, showing mild peribronchial markings without infiltrates. Brain CT scan revealed no evidence of intracranial hemorrhage or mass effect (Fig. 1). Routine laboratory workup showed mild anemia, thrombocytopenia, and elevated liver enzymes. A repeat peripheral blood smear was positive for P. vivax trophozoites.

CSF Analysis

Lumbar puncture was performed after stabilization. The cerebrospinal fluid (CSF) was clear and colorless. CSF analysis revealed:

- White blood cell count: 2 cells/μL (lymphocyte predominant)
- Red blood cell count: 0 cells/μL
- Protein: 28 mg/dL
- Glucose: 62 mg/dL (with corresponding blood glucose of 96 mg/dL)
- Gram stain and bacterial culture: negative
- PCR panel for common viral pathogens (HSV, VZV, enteroviruses): negative

These findings were not consistent with bacterial or viral meningitis, supporting the diagnosis of cerebral malaria.

Hospital Course

Over the first 48 hours of ICU admission, the patient remained intubated with minimal neurological response. Antimalarial therapy with artesunate was continued for 5 days, followed by oral primaquine after G6PD deficiency was ruled out. By the third day of hospitalization, the patient showed gradual neurological improvement; GCS increased to 9, and he began to respond to painful stimuli. On the fifth day, he was successfully extubated, and spontaneous breathing resumed without respiratory distress.

COVID-19 PCR returned positive, confirming co-infection. The child remained in isolation, and supportive care for COVID-19 was provided. No signs of respiratory failure or severe pneumonia developed during the hospital stay. By day 10 of admission, the patient had fully regained consciousness and was transferred to the pediatric infectious diseases ward for continued monitoring. Neurological examination was normal at discharge. He was discharged home in stable condition on day 14, with a follow-up plan including neurological evaluation and malaria prophylaxis education.

Laboratory and Imaging Findings

Upon admission, the patient underwent comprehensive laboratory testing. The Complete Blood Count (CBC) revealed the following abnormalities: an elevated white blood cell count ($18.7 \times 10^3/\mu L$), a decreased lymphocyte count ($0.5 \times 10^3/\mu L$), and a reduced hemoglobin level (9.1 g/dL), while the platelet count remained normal ($459 \times 10^3/\mu L$). Liver function tests showed mildly elevated liver enzymes: ALT (52 U/L) and AST (79 U/L), along with slightly elevated total bilirubin (1.5 mg/dL), but normal direct bilirubin (0.4 mg/dL). Kidney function tests, including blood urea nitrogen (BUN) and creatinine, were within normal limits, suggesting that renal function was intact. Inflammatory markers were significantly elevated, with C-reactive protein (CRP) at 96 mg/L, consistent with an ongoing inflammatory response. The electrolyte panel revealed normal blood glucose (87 mg/dL), sodium (138 mmol/L), potassium (4.8 mmol/L), calcium (8.1 mg/dL), phosphorus (3.1 mg/dL), and magnesium (2.3 mg/dL, with no significant electrolyte disturbances).

The malaria smear confirmed Plasmodium vivax infection, with a parasitic load of infected red blood cells observed under the microscope. A PCR test for SARS-CoV-2 was positive, indicating concurrent COVID-19 infection. The chest X-ray showed bilateral infiltrates suggestive of pneumonia, while the brain CT scan did not show any evidence of brain edema, mass lesions, or other structural abnormalities that could explain the patient's neurological symptoms.

Treatment and Management

The patient was treated with intravenous artesunate for the treatment of Plasmodium vivax malaria, followed by oral primaquine after four days. A neurology consultation recommended continuing

anticonvulsant therapy with phenytoin to prevent further seizures, and a brain MRI was performed, which was normal, ruling out other potential structural causes for the altered consciousness and seizures. Given the positive PCR result for COVID-19, antiviral therapy was initiated with remdesivir and dexamethasone for five days, starting on the second day of hospitalization.

On the first day, the patient developed mild hyponatremia, for which he was treated with half-normal saline. By day four of hospitalization, the patient was successfully weaned off the ventilator and began oral feeding. Due to normal cerebrospinal fluid (CSF) analysis and negative CSF culture, the empirical treatment with acyclovir and vancomycin was discontinued. As his condition stabilized, he was transferred to the pediatric infectious disease ward on day six for continued monitoring and treatment.

Throughout his hospitalization, laboratory values gradually improved, and subsequent malaria smears were negative for Plasmodium vivax, confirming effective treatment. By day fourteen, the patient's clinical condition had significantly improved, and he was discharged in good general condition, demonstrating a full recovery.

Follow-Up and Outcome

During his hospital stay, the patient's laboratory parameters normalized, with no further evidence of Plasmodium on follow-up smears. He remained afebrile and was stable with no requirement for supplemental oxygen by the time of discharge. His recovery highlights the importance of prompt diagnosis and treatment in cases of co-infection, particularly in malaria-endemic regions where both Plasmodium vivax and SARS-CoV-2 may be present simultaneously.

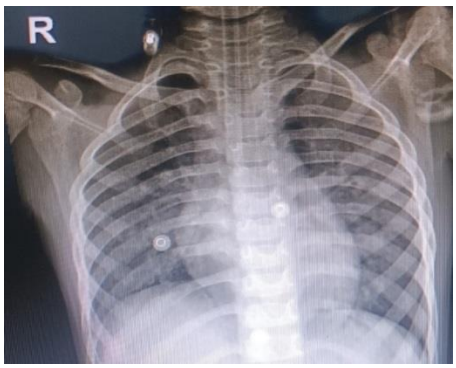

Figure 1. The chest X-ray shows bilateral infiltrates of pneumonia

Discussion

The most significant finding of this case study is the co-infection of Plasmodium vivax cerebral malaria and COVID-19 in an 11-year-old child—an exceptionally rare and clinically complex presentation. While P. vivax typically leads to milder malaria, it can, in rare instances, cause severe complications such as cerebral involvement. In our case, the simultaneous presence of SARS-CoV-2 infection may have triggered an exaggerated inflammatory response, potentially worsening the clinical course and contributing to the severity of neurological symptoms. This highlights the need for greater clinical awareness regarding co-infections in pediatric patients, especially in endemic regions.

Throughout the COVID-19 pandemic, healthcare systems globally have been under unprecedented stress, with clinicians at the forefront of diagnosing and managing overlapping infectious diseases. Many symptoms of COVID-19-such as fever, headache, and myalgia-are non-specific and overlap with a wide range of tropical infections, including malaria [7-8]. This symptom similarity demands heightened vigilance and rapid diagnostic capabilities, particularly in regions with high burdens of both diseases.

Although co-infections in COVID-19 patients are relatively underexplored, emerging reports have identified concurrent infections with influenza [9], varicella-zoster virus [10], respiratory syncytial virus (RSV), Pseudomonas aeruginosa, Haemophilus influenzae, Klebsiella pneumoniae, and Plasmodium vivax malaria [11]. These findings suggest that SARS-CoV-2 infection may not only coexist with but potentially aggravate other infections through immune modulation or inflammatory synergy. Notably, both malaria and COVID-19 have been linked to heightened pro-inflammatory responses, which may explain the severe manifestations observed in some co-infected individuals.

In our patient, the administration of artesunate, an artemisinin derivative, was part of the malaria treatment regimen. Interestingly, this compound has shown potential in experimental studies for its antiviral and anti-inflammatory effects, including inhibition of the NF-κB signaling pathway implicated in viral replication and cytokine release in

COVID-19 [12]. Although artesunate was administered primarily to treat malaria, it is worth exploring whether it also had a moderating effect on the COVID-19 disease course in this patient, who notably did not develop severe respiratory involvement.

Relapses of malaria, especially with P. vivax, are often due to the activation of hypnozoites, dormant liver-stage parasites that can be reactivated by systemic illnesses or co-existing infections. Prior studies have reported relapse episodes triggered by typhoid fever and other febrile conditions [13]. In this context, SARS-CoV-2 may have served as the precipitating factor for malaria reactivation in our patient, indicating a potential pathogenic interplay between viral and parasitic infections.

In endemic regions, the occurrence of simultaneous infections is a realistic and concerning clinical scenario. Symptoms such as fever, fatigue, and altered mental status may mask the presence of a second infection if not actively investigated. Therefore, routine screening for both COVID-19 and malaria in patients with overlapping symptoms is crucial to avoid missed or delayed diagnoses [14].

Management of patients with co-infections like cerebral malaria and COVID-19 necessitates a comprehensive, multidisciplinary approach. Malaria treatment relies on artemisinin-based combination therapies (ACTs), with intravenous therapy preferred for severe cases. At the same time, COVID-19 care requires close monitoring for respiratory compromise, supportive interventions such as oxygen therapy, and infection control measures. Simultaneous treatment requires careful attention to potential drug interactions and cumulative effects on organ systems.

Monitoring vital signs-including temperature, oxygen saturation, respiratory rate, and neurological status-is essential during the hospitalization of co-infected patients. Nutritional support and hydration are also critical in strengthening the immune response and facilitating recovery. The overlap in clinical manifestations between the two diseases complicates diagnosis and underscores the importance of combining molecular diagnostic tests and rapid antigen detection in frontline clinical settings.

This case underscores the need for integrated protocols and heightened clinical suspicion in malaria-endemic settings during the ongoing COVID-19 pandemic. Long-term sequelae, including potential cognitive and neurological impairments from cerebral malaria and post-COVID complications, necessitate coordinated follow-up care. Understanding the interaction between endemic infections like malaria and pandemic threats like COVID-19 is essential for optimizing patient outcomes and informing resource allocation in low- and middle-income countries.

Ultimately, this report reinforces the importance of further research into the mechanisms, outcomes, and management strategies of co-infections in pediatric populations, particularly in areas where multiple infectious diseases co-circulate. As the world continues to navigate the COVID-19 pandemic, expanding our understanding of co-infections will be critical for improving clinical care and shaping future public health interventions.

Conclusion

This case report highlighted the importance of early recognition, accurate diagnosis, and prompt treatment of co-infections involving Plasmodium vivax malaria and COVID-19, especially in endemic regions. Clinicians should be vigilant in evaluating patients with febrile illnesses for multiple potential infections, even when one diagnosis, such as COVID-19, has been confirmed. The overlapping symptoms of these diseases can delay treatment and increase morbidity if co-infection is not considered.

For frontline healthcare providers, the use of standard diagnostic and treatment protocols, including malaria smears, PCR testing, and artemisinin-based therapies, remains essential to ensure timely intervention. In this case, early initiation of intravenous artesunate played a key role in recovery and may have offered additional benefits in mitigating COVID-19 severity, underscoring the need to further investigate the therapeutic potential of artemisinins in viral infections like SARS-CoV-2.

For policymakers, this report reinforces the need to strengthen integrated surveillance systems in endemic regions to detect co-infections early and

allocate resources accordingly. Training programs should also equip healthcare workers to manage such complex presentations using multidisciplinary approaches.

In addition, future research should focus on identifying specific risk factors, understanding the immunopathological mechanisms of co-infection, and optimizing treatment strategies through controlled clinical trials. These efforts will be essential for improving outcomes in vulnerable populations and ensuring resilient health systems capable of responding to overlapping infectious disease threats.

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Ethical Considerations

This case report has been approved by the Ethics Committee of Zahedan University of Medical Sciences under the code IR.ZAUMS.REC.1403.162, and all necessary ethical guidelines were followed in the preparation of this report.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this case report.

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