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Acute respiratory distress syndrome in plasmodium vivax malaria

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Abstract
Background: Malaria is endemic and represents an important public health issue in India. Knowledge of risk factors for disease progression represents an important step in preventing and controlling malaria-related complications. Reports of severe forms of Plasmodium vivax malaria are now becoming a common place, but respiratory complications are described in less than 3% of global literature on severe vivax malaria.
Case presentation: A 59 years old female presented the chief complaints of shortness of breath, fever with chills, generalized weakness, Nausea and vomiting for 4 days. Patient had positive history of diabetes mellitus, hypertension and was on regular medication since 6 years. Investigations showed raised TLC (12,300), Rapid Malarial Antigen test was positive, Smear for malarial parasite was positive for plasmodium vivax schizonts. Pt was kept on NIV, was started on Antibiotics, Artesunate therapy and was managed symptomatically. Patient general condition was improved at the time of discharge.
Conclusions: To conclude it may be suggested that vivax malaria can cause ARDS, This point should be kept in mind while treating such patients. However, it is imperative to exclude associated mixed infections (P. falciparum or bacterial) or treat them simultaneously. The use of NIV in P. vivax related ARDS is associated with a good outcome.

Keywords: Plasmodium vivax malaria, important public health, hypertension

Introduction

The increasing recognition of Plasmodium vivax as a cause of severe malaria forms, traditionally associated with Plasmodium falciparum, marks a significant shift in the understanding of malaria's clinical landscape, particularly in regions like India where P. vivax predominates [1]. This shift underscores the complexity of P. vivax infections, which, despite their historical classification as "benign," can lead to severe and potentially fatal complications, including kidney injury, acute respiratory distress syndrome (ARDS), splenic rupture, and cerebral malaria [2]. The mechanisms driving these severe manifestations remain poorly understood, challenging the global health community to re-evaluate strategies for diagnosis, treatment, and prevention.

Several factors may contribute to the observed increase in P. vivax-associated morbidity and potential shifts in virulence, including [3]

1. Genetic Diversity of P. vivax: The genetic variability of P. vivax may contribute to its ability to cause severe disease. Different strains might possess unique virulence factors that predispose to severe outcomes.
2. Immune Response: The host's immune response to P. vivax infection is complex and can sometimes exacerbate the disease's severity. Inflammatory responses, while crucial for fighting the infection, can also lead to tissue damage and severe disease manifestations.
3. Challenges in Diagnosis and Treatment: P. vivax malaria is often underdiagnosed or misdiagnosed due to the similarity of its symptoms to those caused by other pathogens and the reliance on diagnostic tools that may not be sensitive enough to detect low parasitemia levels. Additionally, the species' ability to form hypnozoites (latent liver stages) complicates treatment, as these stages are resistant to most antimalarial drugs, leading to relapses that can exacerbate the disease's severity.
4. Drug Resistance: The emergence of drug-resistant P. vivax strains poses a significant challenge to controlling the disease. Resistance to chloroquine, the traditional treatment for P. vivax malaria, has been reported in several regions, necessitating the use of alternative, potentially less effective, or more toxic treatments.
5. Socioeconomic and Environmental Factors: Factors such as inadequate healthcare infrastructure, lack of access to prompt and effective treatment, and environmental changes affecting vector distribution and behavior may also contribute to the increased severity of P. vivax infections.

The evolving understanding of P. vivax's role in severe malaria necessitates a reassessment of global malaria control strategies. This includes enhanced surveillance for severe cases, research into the pathogenesis of severe P. vivax malaria, development of new diagnostic tools capable of identifying low-level infections and latent stages, and the advancement of more effective treatments, including drugs targeting hypnozoites [4]. Additionally, public health efforts must address the socioeconomic and environmental determinants of malaria to reduce the overall burden of the disease [5].

Given these challenges, the global health community must prioritize P. vivax not only as a cause of malaria but as a potentially serious public health threat capable of causing severe disease and death. This will require concerted efforts in research, healthcare delivery, and policy to adequately address the unique challenges posed by this species and to mitigate the impact of severe vivax malaria on affected populations.

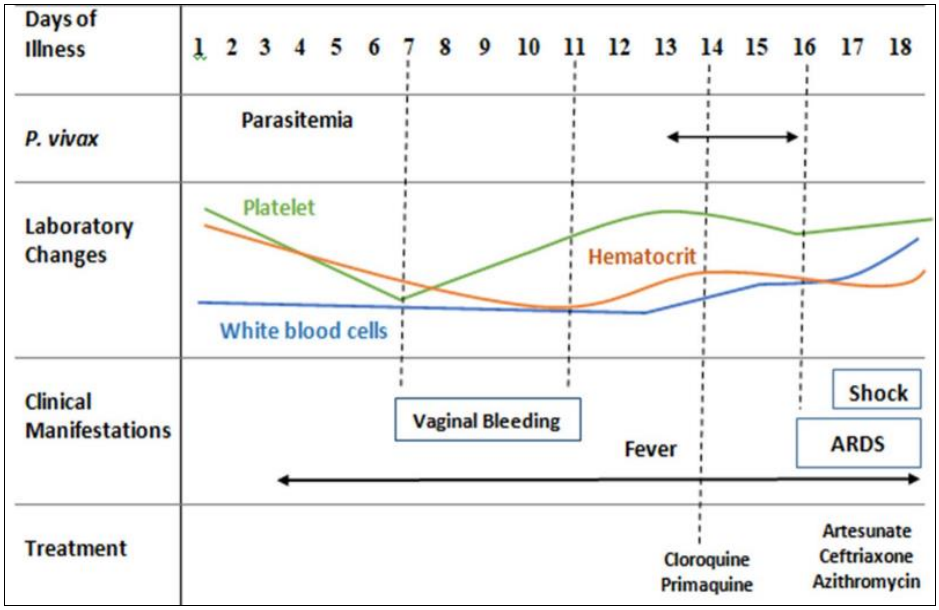

Fig 1: Clinical Progression and Management of Plasmodium vivax Malaria [6]

The image displays a clinical timeline for a patient with Plasmodium vivax malaria over 18 days. It shows parasitemia detected from day 3 to day 14, indicating active malaria infection. Laboratory data indicates initial thrombocytopenia with platelet count recovery by day 9, stable hematocrit suggesting mild anemia, and fluctuating white blood cell count reflecting immune response changes. Clinically, the patient experiences vaginal bleeding, persistent fever, and later develops shock and ARDS. Treatment includes the antimalarials chloroquine and primaquine, with artesunate for severe symptoms, and antibiotics ceftriaxone and azithromycin, likely for concurrent bacterial infection or as prophylaxis (Fig 1).

Case Overview

A 59-year-old female presented to the Medicine Intensive Care Unit (MICU) with a 4-day history of intermittent fever, chills, and significant breathlessness classified as MMRC Grade 4. Initial evaluation at GIMSR Hospital in Visakhapatnam identified Plasmodium vivax schizonts in a peripheral blood smear. Upon admission, clinical parameters were as follows: temperature of 39°C, heart rate of 120 beats/min, respiratory rate of 44 cycles/min, and blood pressure of 120/80 mmHg. The patient was conscious but exhibited drowsiness, with orientation intact to time, place, and person. Physical examination revealed pallor and hepatosplenomegaly, while the remainder of the examination was unremarkable. Oxygen saturation was 84% on 50% fraction of inspired oxygen (FiO2). Arterial blood gas analysis indicated hypoxia and respiratory alkalosis, with a PaO2/FiO2 ratio of 100.

Laboratory and Diagnostic Findings

- Hemoglobin: 9.9 gm%
- Total Leukocyte Count: 5200/cumm
- Platelet Count: 65,000/cumm
- Peripheral smear: Positive for Plasmodium vivax
- Liver and Renal Function Tests: Within normal ranges
- Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT): Normal
- Chest Radiograph: Bilateral alveolar opacities
- No evidence of Plasmodium falciparum co-infection
- Blood, sputum, and urine cultures were initiated

Table 1: Arterial blood gas parameters of the patient at baseline and after application of niv

	Baseline	1 hr	2 hr	4 hr	12 hr	24 hr	48 hr	72 hr
pH	7.45	7.4	7.40	7.4	7.24	7.41	7.43	7.40
PaO_2	55	85	74	70	88	104	88	99
$PaCO_2$	35	45	36	38	36	42	34	36
HCO_3	20	26	24	24	24	26	24	24
FiO_2	0.5	0.5	0.5	0.45	0.45	0.45	0.35	0.35
IPAP/EPAP (H_2O)	-	10/4	15/5	15/5	15/5	15/5	9/5	-
Ventilatory Support	spontaneous	NIV	NIV	NIV	NIV	NIV	NIV	spontaneous

The table 1 tracks a patient's respiratory status and ventilatory support over 72 hours, highlighting arterial blood gas (ABG) values, oxygen supplementation levels (FiO_2), and non-invasive ventilation (NIV) settings. Initially, the patient exhibits hypoxemia (low PaO2) and receives 50% oxygen, necessitating NIV to assist breathing. ABG values show slight fluctuations within normal ranges, except for a temporary drop in pH indicating acidosis at 24 hours. Over time, oxygenation improves (PaO_2 increases), allowing for a reduction in FiO_2 to 35% and adjustments in NIV pressure settings. By 72 hours, the patient returns to spontaneous breathing, indicating improved respiratory function and successful treatment intervention

Treatment and Management

The patient was administered intravenous Artesunate, Doxycycline, and Ceftriaxone to address the malaria infection and potential bacterial co-infection. Bedside

echocardiography revealed no global hypokinesia, normal cardiac chamber sizes, and a left ventricular ejection fraction of 62%, with end-systolic and end-diastolic dimensions of 20 mm and 28 mm per sqm, respectively. The patient remained on these therapeutic settings with vigilant clinical and laboratory monitoring.

Outcome

After 72 hours of continuous ventilation, interspersed with short breaks for daily activities, there was a notable improvement in the lung injury score. A follow-up peripheral blood smear at 48 hours showed resolution of parasitemia. The patient was successfully weaned off mechanical ventilation and discharged after a 7-day hospital stay, continuing antimalarial and antibiotic therapy for a total of seven days. At a 1-month follow-up, the patient was asymptomatic and demonstrated full recovery.

Conclusion

This case underscores the potential for severe respiratory complications in Plasmodium vivax malaria, challenging the notion of its benign nature and highlighting the necessity for prompt recognition and comprehensive management of such cases to ensure favorable outcomes.

Discussion

Acute Respiratory Distress Syndrome (ARDS) in the context of malaria is a critical condition with complex pathogenesis. It has been hypothesized that ARDS associated with malarial fever, particularly in cases of Plasmodium vivax infection, arises from the peripheral sequestration of parasites. This process is mediated by the expression of various adhesion molecules that facilitate the cytoadherence of the parasite to endothelial cells, leading to obstruction of microcirculation [7]. This vascular blockage triggers a systemic inflammatory response, characterized by elevated levels of inflammatory cytokines, which in turn contributes to the onset of ARDS among other complications [8, 9].

The heart's function, specifically the right atrium and ventricle, was assessed and found to be normal with no evidence of tricuspid regurgitation, ruling out cardiac contributions to the respiratory distress. Given the clinical diagnosis of ARDS, the patient was initiated on Non-Invasive Ventilation (NIV) with settings of Inspiratory/Expiratory positive airway pressure (IPAP/EPAP) of 10/4 cm H2O and an oxygen fraction (FiO2) of 0.5. Remarkably, within two hours, there was an improvement in oxygen saturation, respiratory rate, and arterial blood gas measurements, demonstrating the effectiveness of NIV in managing this case [10].

Notably, the inflammatory response is more pronounced in P. vivax infections compared to P. falciparum, with higher plasma levels of cytokines observed in the former. This heightened inflammatory response, particularly after the commencement of antimalarial treatment, can exacerbate lung injury. This phenomenon suggests that the inflammatory cascade plays a significant role in the pathogenesis of lung injury in malaria, with a notable increase in severity post-treatment initiation [11].

Non-Invasive Ventilation (NIV) has emerged as a transformative approach in managing acute respiratory failure, significantly reducing the need for endotracheal intubation. The successful application of NIV in this case underscores its potential in treating ARDS related to P. vivax malaria.

In conclusion, it is critical to recognize the potential of vivax malaria to induce ARDS. This awareness is essential for the timely and effective management of patients, highlighting the importance of ruling out or concurrently treating mixed infections (P. falciparum or bacterial) to improve outcomes. The deployment of NIV in managing ARDS associated with P. vivax infections has shown promising results, advocating for its consideration as a viable therapeutic option in such clinical scenarios.

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