Role of non-invasive ventilation in management of *Plasmodium vivax* malaria presenting as acute respiratory distress syndrome: A case report

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ABSTRACT

Plasmodium vivax malaria has been rarely found to be associated with acute respiratory distress syndrome (ARDS), and very few cases have been reported with ARDS as the presenting complication. In majority of the reported cases, invasive mechanical ventilation has been used for the management of respiratory failure in *P. vivax*-associated ARDS. We report a case of vivax malaria presenting as ARDS which was managed successfully with antimalarial drugs and non-invasive ventilation.

Key words: *Acute respiratory distress syndrome, Non-invasive ventilation, Plasmodium vivax*

Plasmodium vivax is a common cause of malaria in endemic regions and responsible for illness and mortality in these regions [1]. *Plasmodium falciparum* has been known to cause severe malaria manifested by multiple organ dysfunctions including acute respiratory failure. On the contrary, *P. vivax* malaria usually presents as a benign acute febrile disease. Although the occurrence of acute respiratory distress syndrome (ARDS) is generally associated with severe falciparum malaria, rarely *P. vivax* malaria has also been reported to cause ARDS [2]. With the advent of non-invasive ventilation (NIV), its use as the first-line ventilatory support has been suggested, particularly in patients with mild to moderate ARDS [3,4]. Herein, we report a case of *P. vivax* malaria presenting as ARDS which was managed successfully with antimalarial drugs and NIV.

CASE REPORT

A 22-year-old female was admitted in an emergency with a 4-day history of fever and progressively increasing shortness of breath. On admission, her temperature was 100°F, heart rate was 120 beats/min, respiratory rate was 42 breaths/min, and blood pressure was 114/76 mmHg. Pallor was present. The rest of the physical examination was unremarkable. Oxygen saturation was 82% while breathing oxygen at FiO_2 of 0.5. Arterial blood gas analysis showed hypoxemia with respiratory alkalosis (Table 1) with a PaO_2/FiO_2 score of 96. Investigations showed a hemoglobin of 7.8 g/dl, total leukocyte count of 9200/μL, and platelet count of 100,000/μL. Peripheral smear showed the presence of *P. vivax*. Liver and renal function tests were normal. Prothrombin and activated partial thromboplastin time were within normal limits. A chest radiograph was done which showed bilateral alveolar opacities (Fig. 1). There was no evidence of coinfection with falciparum malaria as investigated by repeated peripheral smear examination and histidine-rich protein 2 kit assay. Baseline blood, urine, and sputum cultures were collected, and the patient was started on artesunate, sulfadoxine, and pyrimethamine combination along with antibiotics.

Echocardiography was performed which showed no evidence of global hypokinesia, the left ventricular ejection fraction was 65%. All chambers were normal and there was no tricuspid regurgitation. The patient was diagnosed with ARDS and started on NIV with an inspiratory/expiratory positive airway pressure of 10/4 cm of H_2O with a FiO_2 of 0.5. Over the next 24 h, the FiO_2 requirement came down to 28% and she became afebrile. The patient's oxygen saturation, respiratory rate, and arterial blood gas parameters further improved gradually over a period of 2 days. Repeat chest radiograph showed improvement (Fig. 2). All cultures were sterile and there was no parasitemia on repeat peripheral blood smear examination. The patient was gradually weaned off the ventilatory support and discharged.

DISCUSSION

Malaria is an important treatable cause of ARDS. Although ARDS is being increasingly reported in falciparum malaria, rarely *P. vivax* malaria has also been reported to cause ARDS. Over the last few years, multiple case reports have shown the occurrence of ARDS during the course of *P. vivax* malaria [5-17]. However, few cases have been reported with ARDS as the presenting complication [18-20].

The role of NIV is now well established in patients with acute exacerbation of chronic obstructive pulmonary disease.

Table 1: Arterial blood gas parameters of the patient before and after application of NIV

Parameter	Value (before NIV)	Value (after 48 h of NIV)
pH	7.5	7.41
PCO_2 (mmHg)	22.5	36
PO_2 (mmHg)	48	84
HCO_3 (mEq/L)	21.6	26
FiO_2	0.5	0.28

NIV: Non-invasive ventilation

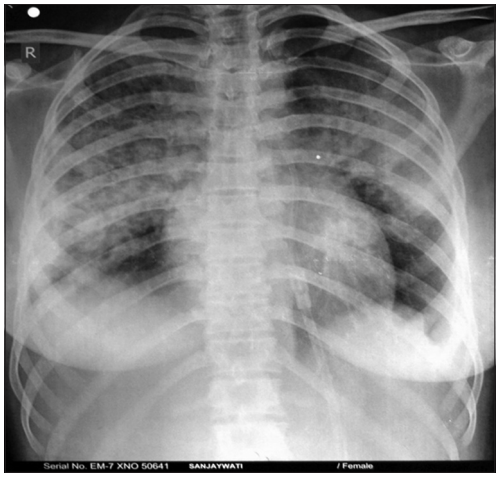

Figure 1: Chest radiograph showing bilateral alveolar opacities

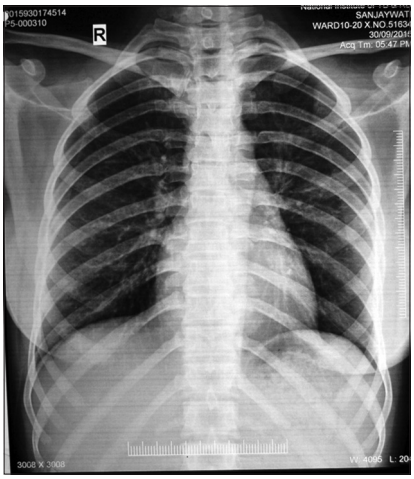

Figure 2: Repeat chest radiograph after 48 h of antimalarial treatment and non-invasive ventilation support

However, the beneficial effects of NIV remain unclear in patients with acute hypoxemic respiratory failure [3]. In the majority of reported cases, invasive mechanical ventilation has been used for the management of respiratory failure *in P. vivax*-associated ARDS [9]. Very few cases have reported the use of NIV [6,9,15].

As in the case of ARDS due to other causes, increased alveolar permeability is considered to be the key functional abnormality in ARDS due to severe falciparum malaria [2]. The release of the adhesion molecules results in peripheral sequestration of parasite, which facilitates in cytoadherence to the endothelial cells, thus causing a blockade of microcirculation. These events result in release and activation of proinflammatory cytokines and upregulate the endothelial expression of vascular ligands, thus explaining the development of systemic complications including ARDS in falciparum malaria [9]. However, the mechanism of ARDS in *P. vivax* malaria has not been explained as *P. vivax* is widely believed to be incapable of cytoadherence and microvascular sequestration. However, recent *in vitro* data have suggested that *P. vivax*-infected red cells do cytoadhere to the endothelial cell ligand chondroitin sulfate A (CSA). Lung and brain also express CSA, thus explaining the occurrence of ARDS in vivax malaria. Lung injury in vivax malaria usually occurs following initiation of antimalarial treatment [21]. This post-treatment exacerbation of inflammation triggers a hyperimmune response which results in lung injury [20]. Pulmonary complications may occur before initiation of antimalarial treatment [18-20]. In our case also, ARDS developed before starting antimalarial treatment.

The mainstay of treatment for patients with ARDS is intubation and mechanical ventilation. The use of NIV has also been suggested in ARDS though it is not as well established as in hypercapnic respiratory failure [3]. NIV is an effective technique for improving gas exchange and avoiding endotracheal intubation in selected patients with acute respiratory failure. As per a prospective investigation of NIV focused on patients with ARDS, NIV applied by experienced clinicians as a first-line intervention to treat early ARDS avoided intubation in about 50% of the eligible patients [22]. However, as per another meta-analysis, NIV should be used cautiously in patients with ARDS because of high failure rates [23]. In our case, the patient was managed with NIV support.

CONCLUSION

P. vivax malaria can cause ARDS even before initiation of antimalarial treatment; hence, a high index of suspicion should be kept while treating such patients. NIV, when used cautiously, can be used to avoid intubation and related complications, thus decreasing mortality.

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