Vivax-induced ARDS: Report of Two Cases

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Abstract

Plasmodium vivax is known for its benign nature but now recognition of life threatening complications related to this infection is on rise. We report two cases of Plasmodium vivax malaria complicated by ARDS. Patients were treated with Artesunate, followed by Sulfadoxin Pyerimethamin combination. Rarely, ARDS is a presenting complication or occurs during the course of Plasmodium vivax.

Introduction

India is high endemic area for malaria and symptoms associated with the infection due to malaria parasite are extremely variable. Plasmodium vivax accounts for more than half of all malaria cases in Asia1. Severe malaria is typically caused by Plasmodium falciparum and it is manifested by various organ involvement for example kidney, lung or CNS. Plasmodium vivax malaria usually presents as a benign acute febrile disease and pulmonary complications are exceedingly rare in Plasmodium vivax malaria1. We report two patients who presented with acute respiratory distress syndrome (ARDS) caused by P. vivax and successfully treated by Artesunate followed by Sulfadoxin Pyrimethamine combination.

Case Report: 1

A 52 year old man presented with seven days history of fever, myalgia and cough. He also developed breathlessness one day before admission. He was admitted in a local hospital with diagnosis of malaria, where he had received chloroquine. In view of his worsening general condition, patient was referred to our hospital. On admission his temperature was 38°C, pulse 102/min, respiratory rate 48/min and blood pressure 100/70 mm of Hg. He was conscious and oriented. On examination purpura was present on legs. Systemic examination revealed bilateral crackles in infraaxillary and infrascapular area. Liver was palpable 4 cm below subcostal margin. Oxygen saturation was 78% while breathing on room air. Arterial blood gas analysis showed hypoxemia PaO2/FiO2 ratio was 100. Investigations revealed hemoglobin 10.7 gm/dl, total leukocyte count 11,000/ mm³, platelets 30000/ mm³. Blood urea was 102mg/dl, serum creatinine 1.9 mg/dl, total bilirubin 4.1mg/dl, direct 2.8mg/dl, ALT 67 U/l, AST 47 U/l, total protein 4.8 gm/dl, and albumin was 2.3gm/dl. Peripheral film examination showed Plasmodium vivax (< 0.1%). Falciparum infection was ruled out by peripheral film examination and histidine-rich protein 2 kit assay (optimal). Dengue serology and leptospira were negative. Urine culture and blood culture were negative. X ray chest showed bilateral nonhomogenous opacities (Figure 1). Echocardiography was normal. Patient was shifted to intensive care unit and started on artesunate and amoxicillin clavulanic acid combination. He was kept on non invasive ventilation. But in view of persistent hypoxia he was intubated and ventilated. Patient’s oxygenation improved but PO2/FiO2 ratio was showing fluctuations. On 9th admission day patient received Sulfadoxin Pyerimethamin combination and PO2 improved markedly after that. Patient extubated successfully and discharged from hospital. On follow up after 4 weeks of discharge patient was healthy.

Case Report 2

A 30 years old female presented with 5 days history of fever and 3 days history of breathlessness and pain in abdomen. On admission her temperature was 38.5°C, pulse 86/min, respiratory rate 36/min and blood pressure 110/70 mm of Hg.
Patient was conscious and oriented. On examination, pallor was present. Respiratory system examination revealed bilateral basal crackles. Abdominal examination showed hepatomegaly and splenomegaly. Oxygen saturation was 97% while breathing on room air. Blood investigations revealed hemoglobin 7.7 gm/dl, total leukocyte count 4200/mm³, platelets 65000/mm³. Blood urea was 53 mg/dl, serum creatinine 0.7 mg/dl, total bilirubin 2.73 mg/dl, direct 1.76 mg/dl, ALT 77 U/l, AST 46 U/l, total protein 4.8 gm/dl, and albumin was 1.8 gm/dl. Blood urea was 53 mg/dl, serum creatinine 0.7 mg/dl, total bilirubin 2.73 mg/dl, direct 1.76 mg/dl, ALT 77 U/l, AST 46 U/l, total protein 4.8 gm/dl, and albumin was 1.8 gm/dl. Peripheral film examination showed plasmodium vivax (1%). Falciparum infection was ruled out by peripheral film examination and histidine-rich protein 2 kit assay (optimal). Dengue serology was negative. X ray chest showed bilateral infiltrates in bilateral lung fields (Figure 2). Urine culture and blood cultures were negative. Echocardiography was normal. Patient was started on Artesunate and Doxycycline combination. Fever subsided but her tachypnoea was persisting. On third day of hospitalization arterial blood gas analysis showed hypoxemia PaO²/FiO² ratio was 110. Patient received high flow oxygen and two blood transfusions. On 5th day patient received Sulfadoxin Pyerimethamin combination and her breathlessness disappeared rapidly. Her oxygenation improved markedly after administration of Sulfadoxin Pyerimethamin.

**Discussion**

Our both patients had presented with history of fever and breathlessness, which is not a usual presentation of malaria. In first case patient was diagnosed malaria outside, while in second case it was an incidental finding on routine blood investigations. Any patient infected with P. vivax who exhibits severe malaria is presumed to be suffering from mixed infection but this is not true always. Pulmonary involvement is rarely noted and to our knowledge, acute respiratory distress syndrome (ARDS) as a complication of vivax malaria has previously been described only in twenty two cases 3. The pathophysiologic mechanism of this complication is unclear but may be similar to ARDS observed in P falciparum malaria. The mechanism of pulmonary damage caused by Plasmodia is not fully explained. In falciparum malaria, it has been suggested that sequestration of the RBCs occurs as several adhesion molecules present on parasitized RBCs membrane which facilitate its adherence to the endothelial cells 4. This mechanism thought to be absent in Plasmodium vivax infection but recent data suggest that plasmodium vivax infected red cell may also cytoadhere to endothelial cell ligand chondroitin sulfate A 4 but this theory is also questionable, as most of the similar previous cases showed low parasitemia as in our cases and usually patient develops symptoms of respiratory failure after starting treatment when clinical improvement is taking place and the parasitemia is falling 4. In contrast to ARDS caused by Plasmodium falciparum, reported mortality is very less in case of plasmodium vivax malaria 3. Together, sequestration of P vivax in the lungs, followed by a post-treatment inflammatory response, might explain the lung injury in P vivax Malaria. Chloroquines, Artesunate, Primaquine, invasive and noninvasive ventilation were treatment modalities in previously reported cases. Sulfadoxin Pyerimethamine is often assumed as non effective against Plasmodium vivax but our both patients showed rapid clinical improvement with this drug. This was one new observation with Plasmodium vivax induced lung injury. An open-label randomized controlled trial showed that antifolates are effective against P vivax malaria in South Asia 1. Further studies are required to explore mechanism and to improve management strategies of this complication of malaria.

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**References**