Acute Respiratory Distress Syndrome due to Vivax Malaria

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Introduction

Severe pulmonary involvement in malaria has been frequently reported in cases of *Plasmodium falciparum* infection, but rarely in vivax malaria. Of the 11 reported cases of vivax-related severe respiratory involvement, all except one occurred after beginning of anti-malarial treatment. Respiratory involvement appears to correspond to an exacerbation of the inflammatory response. We report a case of 38 year old male, who presented with acute respiratory distress syndrome (ARDS) caused by *P. vivax* before initiation of anti-malarial treatment.

Case Report

A 38 year old male was admitted with fever, myalgia, headache and fatigue of one week duration. On the day of admission, the patient complained of worsening of symptoms with dry cough, tachypnea and dyspnoea. He was fully oriented, alert and coherent. The patient had no previous history of malaria and had never received anti-malarial prophylaxis. The temperature was 102°F, blood pressure 100/64 mm Hg, pulse 115 beats per minute and respiratory rate 50/minute. The liver was palpable at the costal margin. The spleen was enlarged two centimeters under the costal margin. Pallor and icterus were present. There was no cyanosis, clubbing or lymphadenopathy. On auscultation there was scattered bronchial breath sounds on right side of chest with crepitations on both sides of the chest. The rest of the examination was unremarkable. Relevant laboratory investigations included haemoglobin level of 7.4 g/dL, hematocrit of 37.2%, white blood cell count of 7800/cumm, with 64% neutrophils, 31% lymphocytes, 03% monocytes and 02% eosinophils. The platelet count was 1,45,000/mm³, serum creatinine level 1.0 mg/dL, serum bilirubin 4.8 mg/dl direct positive, aspartate aminotransferase 156 U/l and alanine aminotransferase 99 U/l. Prothrombin and activated partial tissue thromboplastin times were normal, as were the results of tests for serum electrolytes. Hypoxemia (82%), was assessed by oxygen desaturation on pulse oximetry. He had

not received intravenous infusion and there were no clinical manifestations of fluid overload. Oxygen (Venturi mask 40%) was given at the rate of six litres per minute and a chest radiograph was taken, which showed patchy air space consolidation in mid and lower zones. The patient was sent to the Intensive Care Unit. His $\text{FiO}_2/\text{PaO}_2$ ratio was < 200, consistent with a diagnosis of ARDS. A thin blood smear was obtained that revealed vivax malaria. The Malaria Reference Laboratory subsequently confirmed the diagnosis and there was no microscopic evidence for coinfection with *P. falciparum*. A rapid immuno chromatographic test (Acon Laboratories, Inc), based on the detection of Histidine Rich Protein-2 (HRP-2) of *P. falciparum* was negative. Due to the severe respiratory complications, he was treated on the lines for falciparum malaria with artesunate 120 mg intravenous (IV) once on first day followed by 60 mg IV for four days, monocef 2 gm IV once a day, levofloxacin 500 mg IV once a day, amikacin 500 mg IV 12 hourly and hydrocortisone 100 mg IV stat. The antibiotics were continued for five days. Parasitemia of the patient became undetectable after 48 hours of treatment. The patient showed progressive improvement, with progressive reduction of the positive end-expiratory pressure (PEEP) level. On fourth day tablet primaquine 15 mg OD was added to the therapy and was continued for 14 days. Tracheal aspirates were taken for culture. The bacterial culture was negative. Four samples from blood cultures were also negative. Cytomegalovirus antigenemia, antibodies against mycoplasma pneumoniae (IgM), and legionella spp (IgM) were negative. Antibodies against dengue virus were negative in two samples obtained during admission and seven days later. HBsAg and anti HCV were negative. The patient was also prescribed capsule autrin and multivitamin for 15 days. Patient improved gradually and was discharged on Day 19.

Discussion

We reviewed 11 cases of vivax malaria with severe pulmonary involvement [6-10]. There are several clinical manifestations of malaria, and clinical evolution depends on factors of the parasite, the host, and on geographic characteristics [10]. The main clinical manifestation of

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severe malaria caused by *P falciparum* includes severe anaemia, jaundice, renal failure, cerebral malaria, and ARDS. Sporadically, all of these complications have been reported in vivax malaria [6-10].

A recent study demonstrated that clinically uncomplicated cases of both falciparum and vivax malaria presented compromised pulmonary function (small airway obstruction, gas exchange alterations, and increased pulmonary phagocytic activity) [2]. Researchers suggest that an accumulation of pulmonary monocytes occurs leading to an intravascular inflammatory response, which contributes to pulmonary manifestations in malaria [3]. The greater severity and frequency of cases due to falciparum malaria could be explained by a synergy of immune and physical responses, as the parasitized erythrocytes sequester in the pulmonary microcirculation. People living in endemic areas seem to develop some immunity to the parasites, which would partially explain the low frequency of these complications in endemic areas. It is known that non-immune subjects can present severe clinical manifestations of malarial infection. Severe pulmonary complications of vivax malaria usually appear from six hours to eight days after the initiation of anti-malarial treatment. These findings are consistent with what is observed in cases of falciparum malaria and corresponds to an exacerbation of the post-treatment inflammatory response [5]. Nevertheless, our patient presented with severe pulmonary symptoms before the initiation of anti-malarial treatment, suggesting that severe pulmonary involvement is not necessarily a consequence of an inflammatory response produced after anti-malarial treatment. The level of parasitemia is variable in cases of severe pulmonary involvement. Two patients presented parasitemia counts higher than 2% [8,10], and another case was defined as "heavy" [7]. On the other hand, four patients had levels of parasitemia that were considered low; three had < 2% [13,15], and one case had 1,784 trophozoites/mm³ [10]. In some cases, worsening of the clinical picture was seen after reduction of parasite counts, reinforcing the possibility of a mediated inflammatory response [7]. Immunochromatographic assays allow rapid diagnosis of *P falciparum* malaria. Preferred targeted antigens are HRP-2 from *P falciparum* and parasite-specific lactate dehydrogenase. Since HRP-2 is expressed only by *P falciparum*, its usefulness for malaria diagnosis is limited, because many cases of non-falciparum malaria may be misdiagnosed as malaria negative [2]. However, in cases of severe malaria due to *P vivax*, a rapid immunochromatographic test could be useful to reduce the possibility of falciparum malaria or mixed malaria. Due to the clinical possibility of bacterial pneumonia,

most of the patients received antibiotics [6,7]. Researchers have suggested the hypothesis that the widespread use of chloroquine and doxycycline in malaria-endemic areas could be attenuating or diminishing the number of severe cases of vivax malaria because of the anti-inflammatory properties of these drugs [9]. The possible role of an inflammatory mechanism in pulmonary damage by vivax malaria suggests a potential benefit with the use of corticosteroid therapy. However, there is no evidence that supports this therapeutic approach. The use of corticosteroids was reported in only one case diagnosed as bronchiolitis obliterans organizing pneumonia (BOOP), secondary to malaria [6]. The use of antimalarial treatment with respiratory support is associated with a good outcome in most cases of severe pulmonary involvement due to vivax malaria.

In conclusion, vivax malaria should be considered in the differential diagnosis of patients with consistent epidemiological history, acute febrile syndrome and respiratory symptoms before anti-malarial treatment.

Conflicts of Interest

None identified

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