Journal of Bacteriology and Parasitology

Ahmed et al., J Bacteriol Parasitol 2016, 7:1
DOI: 10.4172/2155-9597.1000257

Case Report Open Access

Cerebral *vivax* Malaria in the Postpartum Period

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Received date: January 04, 2016; **Accepted date:** January 21, 2016; **Published date:** January 25, 2016

Abstract

Cerebral malaria is severe malaria presenting with neurological symptoms, including coma that lasts longer than 30 minutes after a seizure, or it is any impairment of consciousness or convulsions in a patient of malaria with no other causes of coma. Cerebral malaria is generally the result of infection by *Plasmodium falciparum*, but rarely it is a presenting complication or occurs during the course of *P. vivax* infection. Here we report a unique case of adult cerebral malaria caused by *P. vivax* presented by seizures and other variant symptoms. Peripheral blood microscopy, parasite antigen-based assays, *plasmodium* antibodies showed the presence of *P. vivax* and absence of *P. falciparum*. The patient was diagnosed and successfully treated with parenteral quinine followed by primaquine without any sequelae. This case demonstrated that sole *Plasmodium vivax* could induce severe cerebral injury.

Keywords: Cerebral malaria; *Plasmodium vivax*; Severe malaria; Postpartum

Introduction

Cerebral malaria is severe malaria characterized by unarousable coma at least half an hour after termination of seizures or it is any impairment of consciousness or convulsions and asexual forms of the parasite seen in peripheral blood smear with no other explainable causes of coma [1]. Cerebral involvement is a frequent cause of mortality in malaria, especially in children, pregnant women and immunosuppressed adults. Usually cerebral malaria is caused by *P. falciparum* but in the past few years many cases of severe malaria are being reported due to infection with *Plasmodium vivax* [2-6]. About half of vivax severe malaria cases have occurred in children. Here we report a unique case of *P. vivax* infection complicated by severe malaria in an Indian adult female in the postpartum period.

Case Report

A 28 years old Indian female came to Saudi arabia for Hajj, two months post normal vaginal delivery. She was presented to our hospital, King Abdullah Medical City KSA, with high grade intermittent fever, associated with shortness of breath and impaired consciousness of 5 days duration. The fever was associated with chills and rigors. On the presentation to our hospital, she was found non conscious. On physical examination she was severely dehydrated, vital signs showed that the patient was tachycardic, hypotensive and tachypneic. The patient was febrile to 40°C and abdominal examination revealed hepatosplenomegaly. There were no focal neurological signs. Treatment started as noradrenaline infusion, Acquired Respiratory Distress Syndrome (ARSD) ventilation protocol and continuous renal replacement therapy (CRRT).

Her Laboratory examination showed normocytic, normochromic anemia (hemoglobin 8.5 g/dL; total RBCs count 3.2 million/cubic mm; hematocrit 27%; mean corpuscular volume 84 fL; mean corpuscular hemoglobin 27 pg; mean corpuscular hemoglobin concentration 31 g/dL), thrombocytopenia (platelet count=92,000/µL) and elevated white blood cell count of 17,600/µL. Coagulation profiles were within normal range (13 seconds prothrombin time, international normalized ratio of 1.14; activated partial thromboplastin time of 41 seconds). Abnormal liver function tests (total bilirubin=1.2 mg/dL; AST=2271 IU/L); ALT=632 IU/L); serum creatinine=1.4 mg/dL; alkaline phosphatase=78 IU/L; sodium=155 mmol/L; potassium=2.9 mmol/L; CK =1619 U/L; LDH=2793 U/L; Troponin I=5.4 ng/ml and BNP 4202=Pg/ml) and elevated inflammatory reactions (ESR=59 mm/hour; procalcitonin 0.6=ng/ml). Positive blood culture showed aerobic bacteria "*Staphylococcus aureus*". Parameters of cerebrospinal fluid obtained by lumbar puncture were unremarkable.

Chest X ray showed bilateral infiltrate and echocardiography showed EF 35%. Septic screen was positive for MRSA but serology for Dengue fever proved negative. She started oral meropenem, vancomycin and levofloxacin and adjusted dose with CRRT. In view of non-improvement since started treatment in previous hospital plus her country of origin from India, malaria was suspected.

Giemsa stained thick and thin blood smears showed trophozoites and gametocytes of *P. vivax* infected RBCs are slightly enlarged. Macrogametocytes appeared rounded in shape with homogeneous cytoplasm; diffuse delicate light brown pigment throughout the parasite; eccentric pink compact chromatin and it filled the red blood cell (Figure 1). Microgametocytes appeared rounded in shape with large central pink to purple chromatin mass surrounded by pale or colorless halo and evenly distributed pigment and it filled the red blood cell (Figure 2). Trophozite appeared as irregular ameboid parasite; streamers of cytoplasm close to large chromatin dot; vacuole retained until close to maturity. Thick blood film showed the malaria

trophozoite as large amoeboid cytoplasm with large chromatin dots and fine, yellowish-brown pigment. *P. vivax* gametocytes appeared in the thick film: round to oval with scattered brown pigment chromatin compact, eccentric (macrogametocyte) or diffuse (microgametocyte) (Figure 3).

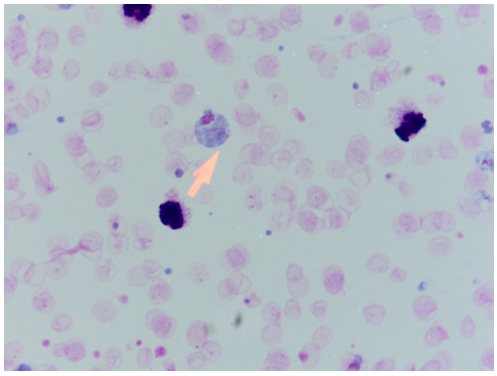

Figure 1: Thin film showed that infected RBCs are slightly enlarged, macrogametocytes appeared rounded in shape with homogeneous cytoplasm; diffuse delicate light brown pigment throughout the parasite; eccentric pink compact chromatin and it fill the red blood cell.

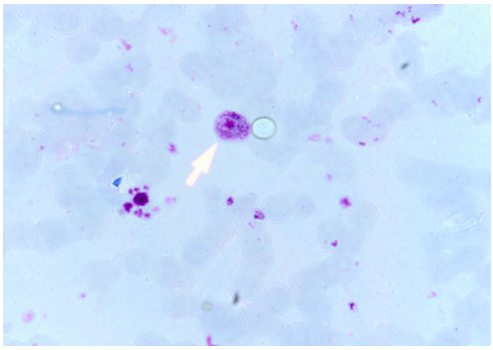

Figure 2: Thin film showed that infected RBCs are slightly enlarged, Microgametocytes appeared rounded in shape with large central pink to purple chromatin mass surrounded by pale or colorless halo and evenly distributed pigment and it fill the red blood cell.

Parasitaemia quantitatively reported as >10%. Rapid Antigen detection test (Optimal) was negative for *P. falciparum*, while positive for *P. vivax*. Antifalciparum antibodies were negative.

Treatment started as Quinine in a dose of 600 mg I.V. TID, plus other medical support. There was a good response; however during her stay in the hospital, the patient had tonic clonic seizures treated with midazolam and phenytoin. Urgent CT and MRI brain were done revealed signs suggestive of extensive vasculitis related to malaria. Peripheral blood films were repeatedly reviewed to document the patient's parasitaemia. Her Kidney function improved, she passed urine with improved creatinine and urea, followed by discontinuation of CRRT. Patient became fully conscious, extubated and transferred from ICU to medical ward. Repeated blood smear showed clearance of the parasite. Then the patient discharged in a clinically stable condition and started primaquine for 14 days, in order to destroy the hypnozoites.

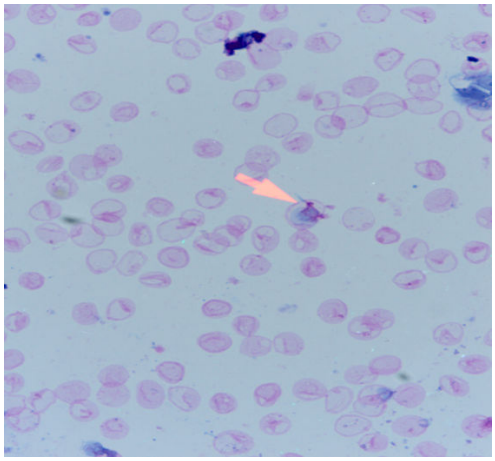

Figure 3: Thin film showed that infected RBCs are slightly enlarged, multishaped irregular ameboid parasite; streamers of cytoplasm close to large chromatin dot; vacuole retained until close to maturity.

Discussion

Cerebral malaria is the most severe neurological complication of malaria and presents as a syndrome of decreased consciousness, repeated seizures and coma [1]. Focal neurological signs are not seen and meningeal irritation is unusual [7].

Our patient exhibited seizures, impaired consciousness, acute renal failure, circulatory collapse, severe anemia, jaundice and acute respiratory distress syndrome; together with hypoalbuminemia and hyperbilirubinemia. Focal neurological signs are not seen. Peripheral blood microscopy, parasite antigen–based assays and plasmodium antibodies showed the presence of *P. vivax* and absence of *P. falciparum* with hyperparasitaemia >10%. Early ant malarial treatment causes early restoration of cerebral blood flow and recovery of neurological function, and other organ functions.

Recent data suggest that there were an estimated 207 million cases and around 627 000 deaths from malaria worldwide in 2012. The global annual incidence of severe malaria can be estimated at approximately 2 million cases [8]. 90% of all malaria deaths occur in sub-Saharan Africa. India accounts for nearly 40% of all malaria cases outside Africa and 60-70% of cases in India are due to vivax infection [9].

Although *P. vivax* is seldom fatal, it is an important contributor to the malaria burden worldwide [10]. Even, some authors suggested that any patient infected with *P. vivax* who exhibits severe malaria is presumed to be suffering from mixed infection. However, the present report demonstrated that sole *P. vivax* could be dangerous. In agreement with our study, Sarkar and Bhattacharya in 2008 reported 3 patients of cerebral malaria caused by *P. vivax*, two had predominantly meningeal signs, while in the third patient; the features were purely of encephalitis [11]. Furthermore, in the last few years, there have been many reports regarding cerebral vivax malaria [3].

Only 45 cases of cerebral malaria caused by *P. vivax* malaria have been previously reported in the literature since 1920; about half of these cases have occurred in children [4].

The exact pathogenic mechanism however remains elusive. The presumed pathogenesis of cerebral malaria involves adherence of parasitized red blood cells to the cerebral vascular endothelium leading to the impeding of cerebral blood flow. The ischemic hypoxia may enhance cytokine-induced nitric oxide synthase, resulting in detrimental nitric oxide generation [11-12]. Kochar et al. indicated that *P. vivax* can cause both sequestration related and non-sequestration related complications of severe malaria, all of which are commonly associated with P. falciparum infections [6]. The impaired immune response of *P. vivax*-infected patients could be a compounding factor as evidenced by more incidence of *P. vivax* severe malaria in patients with low immunity [13].

High fever per say could induce mild changes in sensorium and it is mandatory to rule other systemic and central nervous system infections as an explanation for fever and neurologic presentations [10]. Only *P. vivax* could be detected in repeated blood smears in this case. However, the possibility of a mixed plasmodial infection with a chloroquine-sensitive strain of *P. falciparum* could also be entirely ruled out by using specific plasmodial species-specific antigen detection method and the absence of *Plasmodium falciparum* antibodies serologically. Hence, these findings conclusively demonstrated that *P. vivax* alone may induce severe cerebral injury.

In India, over the past two decades, the incidence of malaria has been fluctuating between 2-3 million each year. *P. vivax* infection predominates over *falciparum* malaria in India and it is the most important cause of morbidity [9]. Atypical presentation seen in the present case may be related to this unique epidemiology of malaria in India.

Moreover, our patient presented in her post-partum period and several studies have shown a prolonged or increased susceptibility to malaria in the post-partum period. Boel et al. demonstrated that in areas of low seasonal malaria transmission post-partum women were less likely to develop falciparum malaria but more likely to develop vivax malaria than controls [3]. This was explained by reduced risk of exposure and increased risk of relapse, respectively. The treatment of *vivax* malaria during and immediately after pregnancy needs to be improved. They also followed our strategy to give primaquine and stated that treatment for the *P. vivax* hypnozoites with primaquine after delivery would be beneficial. Clearly the management of vivax malaria in pregnancy must be improved.

This study highlighted the severity of *P. vivax* infection and its liability to cause cerebral malaria in addition to multi-organ damages. Early careful diagnosis and administration of antimalarial treatment could increase the survival rates with minimum sequelae.

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