How benign is benign tertian malaria?

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Abstract

Objective: This retrospective study was conducted to determine the incidence of various complications of Plasmodium vivax malaria based on review of case records.

Methods: The case records of all confirmed cases of malaria over the period of one year (September 2005–August 2006) were studied. Complete blood count, peripheral blood findings, liver and kidney functions were reviewed. The results of rapid diagnostic test for malaria (OptiMAL test, Diamed AG, Switzerland) were correlated with the peripheral blood smear findings in the patients in whom it was requested. All abnormal results like a positive direct Coomb’s test were noted. Findings were clinically correlated.

Results: There were 265 confirmed cases by peripheral blood examination. Of these 221 were due to Plasmodium vivax and 41 due to P. falciparum. Two cases had mixed infection and in one case the species could not be identified as it showed only malarial pigment. The peak incidence of malaria was seen in September 2005 and August 2006. The complications in P. vivax were thrombocytopenia, biochemical evidence of hepatic dysfunction, renal damage, positive DCT and death due to ARDS. Thrombocytopenia was seen in 213 patients with counts < 20 × 10^3/μl in 13 patients. Nine (4%) patients had serum bilirubin >3 mg/dl with normal liver enzymes. Liver enzymes were elevated in 60 patients with seven patients showing liver enzymes level, three times the normal. Renal dysfunction was seen in 17 patients with serum creatinine ranging from 1.3–10.65 mg/dl. One patient went into acute renal failure following quinine therapy and showed red cell fragments in the peripheral blood. In two children DCT was positive with the peripheral smear showing RBC agglutinates around the parasitised RBC. There were three maternal deaths at about 32 weeks gestation due to ARDS. The peripheral blood smear in these patients showed WBC agglutinates.

Conclusion: This paper is presented to highlight that P. vivax malaria though considered to be a benign entity can also have a severe and complicated course which is usually associated with P. falciparum malaria.

Key words Benign tertian malaria – complications of Plasmodium vivax malaria

Introduction

Malaria is a well-known cause of morbidity and mortality in India. Among the four species of Plasmodium, Plasmodium falciparum and P. vivax are commonly found in our country and only few cases of P. malariae have been reported from Orissa and Karnataka1. Benign tertian malaria is an acute febrile illness caused by P. vivax in which the paroxysm of fever comes every third-day (48 h). It usually has a benign course. Classically, severe malaria is caused by P. falciparum. Literature, however, shows isolated reports of severe P. vivax malaria associated with thrombocytopenia, cerebral malaria, disseminated intravascular coagulation, acute respiratory distress syndrome (ARDS), hepatic dysfunction and renal involvement2–14. This is a retrospective study to determine the incidence of various complications...
of *P. vivax* malaria based on review of case records.

**Material & Methods**

The case records of all the patients of *P. vivax* malaria cases admitted to St. Stephen’s Hospital, Delhi from September 2005–August 2006 were studied. Complete blood count and peripheral blood findings, liver and kidney function tests were reviewed. The results of rapid diagnostic test for malaria (OptiMAL test, Diamed AG, Switzerland) were correlated with the peripheral blood smear findings in the patients in whom it was requested. Additional abnormal results like a positive direct Coomb’s test were noted. All abnormal laboratory results were clinically correlated.

**Results**

The peak incidence of malaria was seen in the month of September 2005 followed by August 2006 (Fig. 1). There were a total of 265 cases of malaria, 221 were due to *P. vivax*, 41 caused by *P. falciparum*, two cases of mixed infection and in one case the species could not be identified as the blood smear showed only malarial pigment. Among the patients with *P. vivax* malaria, 161 were males and 60 were females with age ranging from two months to 75 years (median age 32 years). Thirty-seven patients were in the paediatric age group in the age ranging from two months to 12 years (median age 3 years). Thrombocytopenia was present in 213 (96.3%) patients and of which 13(6%) patients had a count <2 0 x 10^3/μl. Sixty (27.1%) patients showed hepatic dysfunction based on raised liver enzymes. SGOT ranged from 43–1901 U/l and SGPT ranged from 44–848 U/l. Seven patients had liver enzymes three times the normal level. Nine (4%) patients had serum bilirubin >3 mg/dl with normal liver enzymes. Seventeen (7%) patients had serum creatinine above 1.2 mg/dl. One patient went into acute renal failure with serum creatinine of 10.64 mg/dl and her peripheral blood smear showed red cell fragments and microspherocytes (Fig. 2a). Two children had positive direct Coomb’s test with the smear showing agglutination of red blood cells around the parasitized RBC (Fig. 2b). Three maternal deaths occurred due to ARDS, diagnosis based on blood gas analysis, chest radiograph and normal central venous pressure. The peripheral blood smear showed heavy parasitaemia with >5% RBCs parasitized and WBC agglutinates. Phagocytosed parasites were seen in the neutrophils (Figs. 2c and d). Rapid diagnostic test for malaria based on specific *Plasmodium* LDH antigen (OptiMAL test) was done on 21 of these patients. Sixteen patients were positive for *P. vivax* and five were positive for *P. falciparum*. There was no discrepancy in the diagnosis between peripheral blood smear examination and the rapid diagnostic test.

**Fig. 1:** Incidence of malaria in St. Stephen’s Hospital, Delhi, India

**Fig. 2:** (a) Red cell fragments and microspherocytes; (b) Agglutination of RBCs around parasitized RBC; (c) WBC agglutinates; and (d) WBC agglutinate with phagocytosed parasite
Discussion

Malaria is a common infection in most parts of the world. Benign tertian malaria generally has an uncomplicated course but sporadically, all complications usually associated with *P. falciparum* malaria have also been reported in vivax malaria. Profound thrombocytopenia is a well recognized complication of falciparum malaria but there have been conflicting reports regarding thrombocytopenia in vivax malaria. In our study, thrombocytopenia was a common finding in the patients with vivax malaria. Direct lytic effect, immunological reactions, splenic sequestration and oxidative stress are some of the suggested mechanisms for thrombocytopenia. Although 96.3% of our patients had low platelets, none of them had bleeding complications and hence did not require platelet transfusion. There is a paucity of reports of hepatic dysfunction in benign tertian malaria. Malarial hepatitis has been well-described in falciparum malaria. In our study group 4% of patients had only indirect bilirubinemia suggesting haemolysis and 27.1% patients had raised liver enzymes indicative of “malarial hepatitis” due to direct hepatic injury by the parasite. All patients with *P. vivax* malaria were screened for G6PD enzyme deficiency before starting primaquine therapy and showed normal activity of the enzyme. This rules out a possibility of oxidant haemolysis in these patients as cause of indirect bilirubinemia. Renal manifestations of malaria have a wide spectrum. Though renal involvement is more common in falciparum malaria, there have been reports of acute renal failure, electrolyte abnormality, abnormal urinary sediment, and increased urinary protein excretion in vivax malaria. Seven percent of patients had raised serum creatinine and one patient went into acute renal failure in our study. This patient had received quinine hydrochloride and the peripheral blood smear showed red cell fragments and microspherocytes. Quinine associated haemolytic uremic syndrome is known to occur. Two children had positive direct Coomb’s test with the smear showing agglutination of red cells around the parasitized RBC ruling out a false positive test as previously reported in literature. Respiratory complication in *P. vivax* malaria seem to be underdiagnosed. Acute non-cardiogenic pulmonary oedema, ARDS, acute pulmonary injury and interstitial pneumonia are some of the reported complications. Small airway obstruction, gas exchange alteration, increased phagocytic activity and accumulation of pulmonary monocytes are the suggested mechanisms. In our study group, three maternal deaths occurred due to ARDS. The diagnosis was based on blood gas analysis, chest radiograph and normal central venous pressure. The patients had heavy parasitaemia with WBC agglutinates which showed phagocytosed parasites. It is postulated that these WBC agglutinates produce the ARDS. None of the patients presented with cerebral malaria.

This paper highlights that thrombocytopenia, hepatic dysfunction, renal involvement and ARDS do complicate benign tertian malaria. Close monitoring of such patients for respiratory complications should be done since ARDS appears to be associated with a fatal outcome and aggressive exchange transfusions to decrease the parasitic load and WBC agglutinates may be beneficial and life-saving.

References


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