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Plasmodium vivax malaria: Is it actually benign?

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Summary Plasmodium vivax (Pv) malaria is being increasingly recognized as a cause of severe malaria in children.
Objectives: To describe the various severe manifestations associated with vivax malaria by retrospective analysis of records.
Methods: Children between the ages of 0 and 18 years with a confirmed diagnosis of Pv malaria monoinfection done by peripheral blood film (PBF) and/or rapid diagnostic test (RDT) admitted between June and September 2009 were included. Their clinical, hematological and biochemical manifestations were analyzed.
Results: Twenty-three patients of Pv malaria were retrospectively analyzed. Thrombocytopenia was present in 22 (96%) patients with counts less than 50,000/μL in 9 patients. Severe anemia (hgb < 5 mg/dl) was present in 8 (34%) patients. Cerebral malaria was present in 3 patients. Liver enzymes were elevated (>3 times normal) in 4 (17.3%) patients while jaundice (bilirubin > 2.5 mg/dl) was present in 2 patients (total bilirubin 5.2 mg/dl and 14.3 mg/dl). Renal dysfunction (creatinine > 3 mg/dl) was present in 6 (26%) patients with 2 patients showing severely deranged renal functions (blood urea 168 mg/dl, 222 mg/dl and serum creatinine 5.0 mg/dl, 5.6 mg/dl, respectively). Hypernatremia was present in one patient. One patient expired within 12 h of presentation because of severely deranged hepatic and renal dysfunction.
Conclusion: Pv malaria can lead to unusual and fatal complications. All new guidelines should include ''Severe Vivax malaria'' as a clinical entity. Further research into the etiopathogenesis and treatment would be important.

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Introduction

Plasmodium vivax (Pv) also called as benign tertian malaria accounts for more than 50% of infection in South East Asia region [1]. Although it is usually associated with benign course recent literature suggests that Pv can lead to serious manifestations [2—12] similar to Plasmodium Falciparum (Pf). The present report highlights the serious manifestation of Pv malaria in children from India.

Methods

Case records of children between 0 and 18 years of age with diagnosis of Pv malaria between June and September 2009 were retrospectively analyzed. Children with mixed infection with Pf/any other malarial species or any other associated infection were excluded. Diagnosis of Pv was confirmed by peripheral blood film (PBF) examination and/or rapid diagnostic test (RDT). Severe manifestations of malaria [13] like seizure, jaundice, coma, severe pallor, bleeding, oliguria, hypoglycemia, acidosis and ARDS were reviewed. Routine hematological and biochemical investigations were done in all patients.

Results

Among 232 patients of malaria infection presented to our hospital during study period, 110 (47%) were of Pf monoinfection, 108 (46%) of Pv monoinfection and 14 (6%) of mixed infection. Thirty-two patients of Pf monoinfection, 23 patients of Pv monoinfection and 5 patients of mixed (Pf and Pv) infection presented with severe manifestation were admitted. The record of these 23 patients of Pv monoinfection was retrospectively analyzed. Ten (44%) of these patients were female and mean age of presentation was 5.4 years (±3.67) with range from 1 month to 12 years [<1 year 4 (17%); 1—5 years 9 (39%); 5—10 years 7 (30%); >10 years 3 (14%)]. Seventy percent of the children had moderate malnutrition (as per World Health Organization classification) but there was no child with severe malnutrition. In four patients PBF was negative but RDT was positive while one patient had positive PBF but negative RDT.

Gastrointestinal symptoms (diarrhea, vomiting) were present in significant number (43.4%) of patients while seizures presented in 4 (17.3%) patients. Three patients with seizures had cerebral malaria but in fourth patient it was because of hypernatremia (173 meq/L). Hepatosplenomegaly was present in all patients with mean size of liver and spleen being 2.7 cm (SD ± 1.19 cm) and 2.4 cm (SD ± 1.6 cm) below costal margins, respectively. Various severe manifestations of vivax malaria have been described in Table 1. Severe anemia (<5 mg/dl) was present in 8 (34%) cases. Thrombocytopenia (less than $150 \times 10^3/\mu L$) was a very common (95.6%) manifestation while severe thrombocytopenia ($<50 \times 10^3/\mu L$) was present in 9 (39%) patients. Three patients who had platelet counts less than $10 \times 10^3/\mu L$ presented with bleeding manifestation in the form of petechiae and purpura which improved after platelet transfusion. Five (21%) patients presented with pancytopenia.

Two patients presented with jaundice. One of those had indirect hyperbilirubinemia (total bil. 6.2 mg/dl, indirect bil. 5.1 mg/dl) with normal liver enzymes (AST 35 IU/L, ALT 18 IU/L, ALP 240 IU/L) who improved subsequently. This patient had no feature suggestive of hemolytic anemia in the form of increased reticulocyte count, hemoglobinuria or decreased haptoglobin. The one with direct hyperbilirubinemia (total bil. 14.3 mg/dl, direct bil.

Table 1 Manifestations of severe malaria positive for Plasmodium vivax.

S. no.	Manifestation	No. (%) of patients ($n = 23$)
1	Severe anemia (<5 mg/dl)	8 (34.7)
2	Thrombocytopenia ($<150 \times 10^3/\mu L$)	22 (95.6)
3	Jaundice (bilirubin > 2.5 mg/dl)	2 (8.6)
4	Renal failure (creatinine > 3 mg/dl)	6 (26)
5	Cerebral malaria (Glasgow coma score < 9/14)	3 (13)
6	Disseminated intravascular coagulation	1 (4)
7	Deranged liver enzymes (>3 fold elevation)	4 (17.3)
8	Leucocytosis (>12,000/cumm)	3 (13)
9	Persistent vomiting	4 (17.3)
10	Multi organ dysfunction	1 (4)
11	Repeated generalized convulsions	4 (17.3)