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Case Report

Internal Medicine Section

Retinal Hemorrhages in Severe Non-cerebral *Plasmodium vivax* Malaria in an Adult

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ABSTRACT

Malaria is the most important parasitic diseases of humans and one of the leading causes of morbidity and mortality in tropical countries. Earlier *Plasmodium vivax* was considered as a benign infection, but now it is recognized as a cause of severe malarial disease. It causes severe malarial disease similar to those as *Plasmodium falciparum* including cerebral malaria, severe anaemia, severe thrombocytopenia, hepatic dysfunction, shock, acute respiratory distress syndrome (ARDS), acute renal failure, and pulmonary oedema. Malarial retinopathy includes retinal whitening, vessel changes, retinal hemorrhages and papilledema. However, retinal hemorrhages are very rare in *Plasmodium vivax* infestation. Hereby, we report a case of 30-year-old man, who presented with fever with chills and diminution of vision. He was found to have *Plasmodium vivax* infection with retinal hemorrhages. He was treated successfully with artisunate, primaquine and doxycycline, completely recovered after one month.

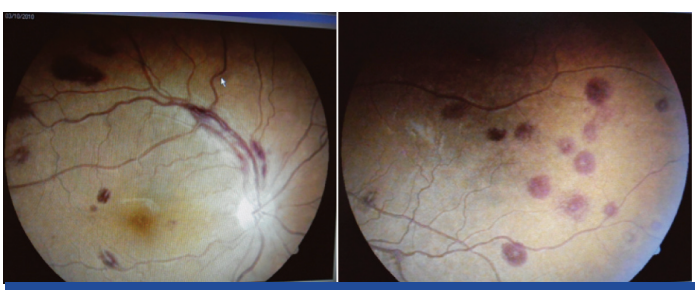
Keywords: Adult, Non-cerebral malaria, Retinopathy

CASE REPORT

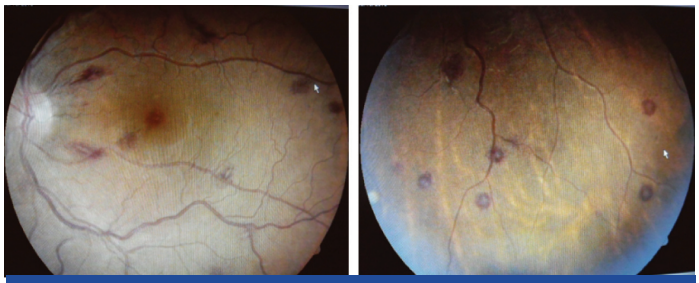
A 30-year-male admitted with seven days history of intermittent fever with chills. He had history of *Plasmodium vivax* malaria two months back and incompletely treated with chloroquine. Patient was not suffering from any chronic illness and had no addiction. He had no history of seizures or altered sensorium. On examination his temperature was 38.5ºC by axilla. The blood pressure was 120/80 mmHg, pulse rate 110 beats/min, regular and respiratory rate was 18 breaths/min. He had severe pallor, icterus, conjuctival hemorrhage and splenomegaly. Signs of meningeal irritation were absent. Cardiovascular and respiratory system revealed no significant abnormality.

Two days after admission in the hospital he had history of sudden painless decrease in the vision from both eyes. His visual acuity in left eye was 6/9 and 9/12 in right eye. External ocular muscle movements were normal. Both pupils were round, equal, regular and reacting to direct and consensual light stimulus. Fundus examination revealed multiple retinal hemorrhages with white center and roth spots in all quadrants of fundus of both eyes. Retinal vessels were found tortuous. Papilledema, retinal whitening and exudates were absent [Table/Fig-1,2].

Laboratory investigations are mentioned in [Table/Fig-3]. Hemogram on the day of admission revealed anaemia and thrombocytopenia. The peripheral blood film showed trophozoite ring of *Plasmodium vivax*. RBCs were normocytic normochromic with polychromasia and platelets were reduced. The antigen testing including parasite lactate dehydrogenase (LDH) tested positive for *Plasmodium vivax* and negative for *Plasmodium falciparum*. Confirmation of *Plasmodium vivax* and exclusion of *Plasmodium falciparum* was done by PCR. NS1 antigen and IgM antibodies were negative for dengue virus. The Chest X-ray and ECG were normal. Ultrasonography of abdomen showed mild hepatosplenomegaly. CT scan of head was done which had no significant abnormality. CSF examination and coagulation profile was normal. Urinanalysis was normal and blood culture was sterile. He was tested negative for HBsAg, Anti- HCV and HIV 1&2. In a case of *Plasmodium vivax* malaria these finding were suggestive of severe vivax disease. He treated with 120 mg Artisunate iv injections at 0, 12 and 24 h and then OD for seven days with 100 mg doxycycline orally for seven days. Two units of packed cell were transfused. After seven days CBC was repeated which revealed Hb 7.1gm/dl, total leukocyte count 7800/mm^3 and platelet 128000/mm^3. CRP was <6 mg/dL. He was discharged on primaquine 15 mg OD for 14 days. On follow up after 30 days, patient was asymptomatic with normal hematological parameters and normal vision. Retinal hemorrhages had absorbed completely.



[Table/Fig-1]: Right eye fundus



[Table/Fig-2]: Left eye fundus

DISCUSSION

Chloroquine, resistance relapses and greater transmission potential of *Plasmodium vivax* at low parasite densities may be responsible for severe and fatal complication of vivax malaria [1].

Retinal hemorrhages are frequently observed in *Plasmodium falciparum* infection, particularly with cerebral malaria in children but uncommon in non-cerebral malaria [2]. Malarial retinopathy includes various retinal changes and retinal signs in patients suffering from malaria. It includes retinal whitening, vessel changes, retinal

Parameters	Values	Reference value
Hb	3.6 g/dL	13.3-16.2 g/dL
TLC	9,240/mm^3	3.54-9.06×10^3/mm^3
DLC	N- 64%, L- 33%, E- 3%	N-40-70%, L20-50%, E-0-6%
Platelets	30,000/mm^3	165-415×10^3/mm^3
Blood sugar	110 mg/dL	65-95 mg/dL
Blood urea	90 mg/dL	7-20 mg/dL
Serum creatinine	1.5 mg/dL	06-1.2 mg/dL
S. Bilirubin-Total	2.54 mg/dL	0.3-1.3 mg/dL
Direct	0.52 mg/dL	0.1-0.4 mg/dL
AST	55 IU/L	12-38 IU/L
ALT	54 IU/L	7-41 IU/L
Total protein	6.7 g/dL	6.7-8.6 g/dL
S. Albumin	3.7 g/dL	3.5-5.5 g/dL
S. LDH	3886 IU/L	115-221 IU/L
S. Iron	140 µg/dL	70-140 µg/dL
TIBC	327 µg/dL	250-406 µg/dL
% Saturation	42.5.0%,	16-35%
S. Sodium	142 meq/L	136-146 meq/L
S. Potassium	4.5 meq/L	3.5-5 meq/L
S. Phosphorus	4.6 mg/dL	2.5-5.5 mg/dL
S. Calcium	8.8 mg/dL	8.5-10.5 mg/dL
S. alkaline phosphatase	125 IU/L	44-147 IU/L
C-reactive protein	>6 mg/dL	(0-6 mg/dL)
BT	1 min 30 sec	(normal up to 5 min)
CT	3 min	(normal up to 8 min)
PT	PT 13 sec	(control 13)
APTT	34.6 sec	(control 32.2) min
CSF	Sugar 56 mg/dL, Protein 35 mg/dL, RBC 0 cell/ml, WBC 02 cells/µL	Sugar (40-60) mg/dL, Protein (20-40) mg/dL, RBC 0 cell/ml, WBC (0-5) cells/µL

[Table/Fig-3]: Laboratory Investigations at the time of admission. Hb-Hemoglobin, TLC-Total Leukocytes count, DLC-Differential Leukocytes count, N-Neutrophils, L-Lymphocytes, E-Eosinophils, MCV-Mean Corpuscular Volume, MCH- Mean Corpuscular Hemoglobin, AST-Aspartate aminotransferase, ALT-Alanine aminotransferase, LDH- Lectate Dehydrogenase, TIBC-Total Iron Binding Capacity, BT- bleeding time, CT- clotting time, PT- prothrombin time, APTT- activated prothrombin time, CSF- Cerebrospinal fliud.

hemorrhages and papilloedema. Retinal hemorrhages are very rare in *Plasmodium vivax* infestation [3-5]. The visual defects are usually reversible with complete recovery after treatment but rarely may be irreversible [6].

Malarial retinopathy is predominantly found in patients suffering from *Plasmodium falciparum* infestation with cerebral malaria in children but it can also be found in other form of malaria. Malarial retinopathy has also been found in adults with severe malaria and rare in *Plasmodium vivax* infestation [7]. It is characterized by retinal whitening (macular or perimacular), vessel changes (white or orange), retinal hemorrhage (particularly with white centres) and papilledema. Among these four changes, retinal whitening and vessel changes are specific and diagnostic of severe malarial disease [8]. The incidence of retinal haemorrhages was found in 46% cases of cerebral malaria [9]. This incidence was around 60% in children with cerebral malaria and was lower in less severe malarial disease [2].

Lewallen et al., [10] observed that the sequestration of many de-hemoglobinized late stage parasitized erythrocytes via cyto-adherence in the retinal microvasculature is considered as a cause of characteristic white and orange appearances of retinal vessels in severe malaria. This pattern of de-hemoglobinization is consistent with the clinical findings. Beare et al., [11] explained retinal whitening because of loss of retinal transparency. Retinal whitening appears as discrete areas of pale discolouration of the retina due to capillary non-perfusion on fluorescein angiogram. Micro vascular occlusion due to sequestration of infected erythrocytes leads to reduced perfusion, hypoxia and oncotic cell swelling which is responsible for retinal whitening.

Plasmodium falciparum is responsible for most cases of severe malarial disease with retinal hemorrhages because of sequestration, cytoadherence and rosseting phenomenon [12]. In *Plasmodium vivax* malaria the mechanisms of development of retinal hemorrhage and severe diseases are not well defined. In vivo *Plasmodium vivax* infected RBCs are known to cause cytoadherence on human lining endothelial cells and placental tissue, though this phenomenon is lower than that with *Plasmodium falciparum* infected RBC [13]. Apart from these, accompanied thrombocytopenia and anaemia may be responsible for retinal hemorrhage as a confounding or even a sole cause. Retinal haemorrhage may be due to causes other than malaria in endemic areas where incidental asymptomatic parasitemia may be found [7].

Systemic inflammatory response is also increased in patient with severe *Plasmodium vivax* disease. There is increase in the C reactive protein, plasma tumor necrosis factor and interferon gamma levels [14].

Retinal hemorrhages in these patients usually absorbed spontaneously over the period of one to four weeks without retinal sequelae [9] and visual defect improved completely after successful treatment of malaria. Few cases have been reported with irreversible visual defects [7]. Our patient had peripheral parasitemia, severe anaemia, thrombocytopenia, hepatic dysfunction, mild renal dysfunction, raised CRP level and multiple retinal hemorrhages with white center. After successful treatment of malaria, he gained normal vision with normal visual acuity after one month. Thus we assume that severe vivax disease was responsible for retinal hemorrhages.

CONCLUSION

Characteristic features of Malarial retinopathy including number of retinal hemorrhages could be useful tool in the diagnosis of severe malaria, and these factors directly correlates with the severity and prognosis of malarial disease. Thus every patient of severe malaria should be checked for presence of retinal hemorrhages, even in adult patients with non-cerebral *Plasmodium vivax* disease and the patient who presented with unexplained retinal hemorrhage and fever should be evaluated for malaria.

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