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Case Report

Subhyaloid hemorrhage in cerebral malaria

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Cerebral malaria is one of the most serious manifestations of severe malaria in adults. The exact pathophysiology of the disease, however, is still elusive. The ocular fundus findings are supposed to reflect the pathological changes taking place in the cerebral tissue. In about 15% patients of cerebral malaria, retinal hemorrhages are seen[1]. They are multiple and bilateral, and the most common ophthalmoscopic finding in falciparum malaria[1,2]. Moreover, they increase in number with the severity of malaria[1,3]. Therefore, the examination of retinal details in patients with cerebral malaria serves as a diagnostic marker for the severity of disease. There are very few Indian studies on adult patients with cerebral malaria[1,2] emphasizing the importance of fundus examination which shows that physicians are making less use of this widely available diagnostic tool. We are reporting a case of cerebral malaria with bilateral retinal and subhyaloid hemorrhages—a rare finding encountered in adults suffering from cerebral malaria.

Case report: A 30 yr female reported in a state of impaired consciousness of 10 to 12 h duration. She had a history of intermittent high grade fever, abdominal pain and vomiting for last four days for which she was receiving oral chloroquine. On physical examination she was drowsy, glasgow coma scale (GCS) score of 10, and febrile having tachycardia, tachypnoea, marked pallor and mild icterus. There was mild hepatosplenomegaly, bi-basilar crepts on auscultation of chest, and bilateral extensor plantar response.

Laboratory investigations showed severe normochromic normocytic anemia (Hb 4.2 g/dL, hematocrit 12%) with increased retic count (4.5%). WBC count was 9,800/mm^3 and platelets were 1.05 lac/mm^3. Microscopic hematuria was detected on urine examination. On blood biochemistry, indirect hyperbilirubinemia (total bilirubin 4.02 mg/dL, indirect 3.14 mg/dL) and marginally deranged liver enzymes (SGOT 150 U/L and SGPT 86 U/L) were noted. Quantitative Buffy Coat test was positive for *Plasmodium falciparum*. Peripheral blood smear showed ring stages of *P. falciparum* with crenated RBCs and schistocytes. Ultrasonography of abdomen confirmed hepatosplenomegaly. Initial fundus examination using an indirect ophthalmoscope revealed bilateral normal optic disks and multiple intra-retinal hemorrhages scattered in the central retina. Subhyaloid hemorrhage was noticed in both eyes masking the fovea. Cerebrospinal fluid examination and CT scan of brain were normal.

Despite being managed intensively with injectable quinine, blood transfusion and supportive measures, condition of the patient deteriorated. She became increasingly drowsy (GCS score of 7) and developed respiratory distress. Chest X-ray showed newly developed alveolar shadows (Fig. 1) consistent with acute respiratory distress syndrome (ARDS) as were arterial blood gas analysis findings (pH 7.49, PaO_2 49.5 mm Hg, $PaCO_2$ 28.3 mm Hg, HCO_3–22.3 meq/L, SaO_2 84%). Repeat coagulation profile, renal and liver function tests were near normal. Patient was put on ventilatory support and given injectable Artesunate. Over the next three days she steadily improved, regained consciousness but complained of diminution of vision.

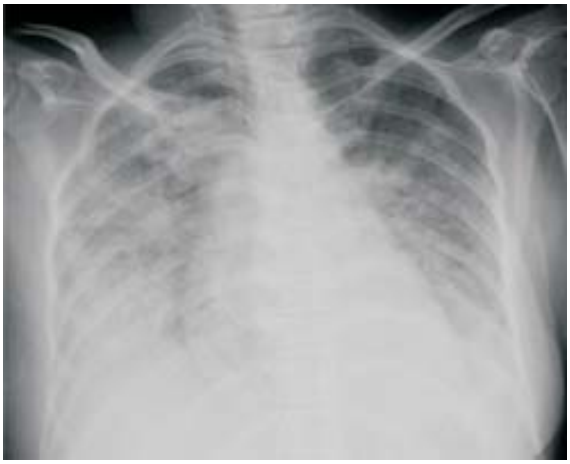


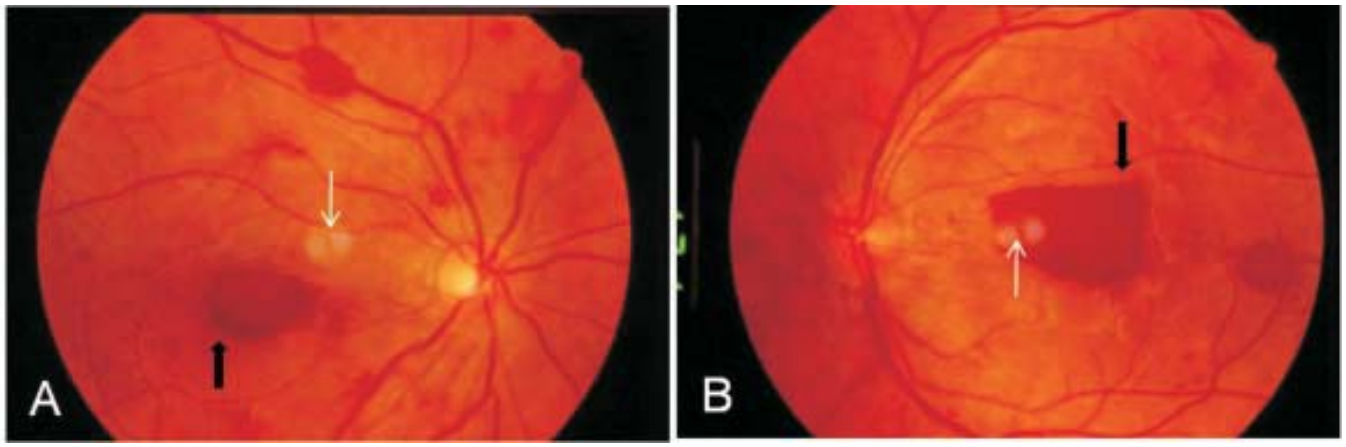
Fig. 1: Chest radiograph showing bilateral diffuse fluffy shadows, alveolar infiltrates, suggestive of ARDS.

On detailed ophthalmic examination, best-corrected vision was 6/6 in both eyes. The eyes were straight and ocular movements full in all directions of gaze. Conjunctiva showed marked pallor. Pupillary reactions to light were normal. Biomicroscopy and indirect ophthalmoscopy were performed to examine the retina. Fundus picture was same as seen previously. The peripheral retinal examination was normal. Fundus photography was done that complimented the ophthalmoscopic findings (Figs. 2 A&B). The patient was reassured and kept on regular follow-up. The vision in right eye was 6/18 and in left was 6/24 at six-week follow-up visit. Hemoglobin level improved to 9.4 g/dL. Funduscopy revealed absorbing subhyaloid hemorrhages, however, the intra-retinal hemorrhages disappeared completely. Almost a year after the attack of cerebral malaria, vision improved to 6/6 in both eyes.

Malaria is a parasitic disease common in tropical countries like India. Early detection and treatment are necessary to reduce the mortality. Cerebral malaria is the most dreaded complication of falciparum malaria and a leading cause of death (2 million annually worldwide). The pathogenesis of cerebral malaria remains obscure, but reduced microcirculatory flow caused by sequestration of parasitized rigid erythrocytes, neuronal injury by malarial toxins, excessive cytokine production and focal dysoxia leading to axonal dysfunction are the major contributors to neurological disability, coma and death[4].

The retinal and cerebral tissues are neuroectodermal in origin. There is structural and functional similarity between retinal and cerebral vasculatures. Therefore, a retinal vasculature insult in cerebral malaria gives information about the pathological changes taking place in the brain. A detailed dilated ophthalmic examination is, hence, mandatory for all the patients of cerebral malaria to assess the severity of disease[5].

The retinal manifestations of cerebral malaria in adults include retinal whitening, vessel changes, retinal hemorrhages and papillaedema[2,6]. Retinal hemorrhages and papillaedema are frequently encountered findings seen in the central retina. They are best visual-



Figs. 2 A & B: Fundus photographs of right eye (A) and left eye (B) showing multiple intra-retinal hemorrhages, subhyaloid hemorrhage (black arrows) and flare (white arrows).

ized on slit-lamp biomicroscopic ophthalmoscopy and/or indirect ophthalmoscopy due to a larger field of view and stereopsis than on direct ophthalmoscopy. Retinal whitening and vessel changes occur in the peripheral retina that invariably require indirect ophthalmoscopy. Our case, besides having cerebral malaria, had severe anemia and ARDS, diagnosed on the basis of the American-European Consensus Conference definition of ARDS[7], both of which could be detrimental to life. ARDS in severe malaria is mediated by immunomodulatory cytokines that lead to increased alveolar permeability[8]. During the course of illness, outpatient developed retinal manifestations of cerebral malaria in the form of widespread hemorrhages and bilateral subhyaloid hemorrhages.

The retinal hemorrhages are the earliest sign of cerebral involvement in falciparum malaria. There is a strong correlation between retinal hemorrhages and brain hemorrhages at autopsy[3,5,9]. The number of retinal hemorrhages on funduscopy increases with the severity of *P. falciparum* infection[1,3]. Subhyaloid hemorrhages are reported in cerebral malaria in children[3,10], but to the best of our knowledge, bilateral premacular subhyaloid hemorrhage in adults with cerebral malaria have not been reported so far. They may be considered as one of the features of falciparum malaria retinopathy and a cause for profound diminution of vision. This case highlights the importance of detailed binocular fundus examination by an ophthalmologist to detect the severity of cerebral malaria. Treating physician should be aware of the fact that all the cases of malaria with altered sensorium must undergo funduscopy by a trained oculist in order to detect even subtle retinal changes. Further, large prospective studies in adults are needed to establish subhyaloid hemorrhage as an indicator of severity in cerebral malaria.

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