Dear Sir:

A recent study reported that retinopathy is a characteristic feature of cerebral malaria caused by Plasmodium falciparum. Severity of retinopathy was related to risk of death and duration of coma in survivors. One characteristic feature of malaria related retinopathy were hemorrhages, which were present in 46% of patients with cerebral malaria. A previous study showed that the number of retinal hemorrhages correlated with the number of cerebral hemorrhages.

Recently, a case of dietary folate deficiency associated with bilateral retinal hemorrhages was reported, which confirmed previous similar observations. Congenital folate deficiency due to a homozygous mutation in the methylenetetrahydrofolate reductase (MTHFR) gene has been associated with cerebral hemorrhages. Folate levels were significantly lower in patients homozygous for this mutation and cerebral hemorrhages compared with patients without and controls. An investigation of serum and cerebrospinal fluid (CSF) folate levels in patients with cerebral malaria showed significantly reduced levels compared with controls. After successful treatment of the acute malaria episode, CSF folate levels increased significantly. This may indicate that folic acid deficiency is involved in the pathogenesis of retinal and cerebral hemorrhages in cerebral malaria. The mechanism by which folic acid deficiency causes retinal and cerebral hemorrhages in malaria does not seem to involve anemia, which in itself is a well-established cause of retinal hemorrhages regardless of the etiology of anemia. Patients with retinal hemorrhages in cerebral malaria had the same packed red blood cell volume compared with patients with cerebral malaria without retinal hemorrhages, and patients with severe malarial anemia in another study had less severe retinopathy compared with patients with cerebral malaria. Electron microscopic studies of cerebrovascular endothelium in folate-deprived rats showed cytoplasmic swelling and mitochondrial degeneration in the endothelium and degenerative changes in the cerebrocortical microvascular wall, which may predispose to hemorrhages.

Future research needs to investigate an association of folate deficiency and MRTHFR gene polymorphisms with retinal hemorrhages and disease severity in cerebral malaria.

REFERENCES


MICHAEL EISENHUT
Luton and Dunstable Hospital
Lewsey Road
Luton LU40DZ, United Kingdom
Telephone: 44-804-5127-027
E-mail: Michael_eisenhut@yahoo.com
anemia (excluding cerebral malaria), there are far fewer reti-
nal hemorrhages.\textsuperscript{3} The pathogenesis of retinal hemorrhage in
cerebral malaria seems to be associated with the presence of
coma, and only then anemia. Because Olumese and others
used fundoscopy through undilated pupils, they would have
only been able to see a small proportion of the total number
of retinal hemorrhages present in the patients they studied.\textsuperscript{4}

Given the presence of sequestered parasitized red blood
cells, vessel endothelial changes, and hematologic derange-
ment in cerebral malaria, there are many predisposing factors
for retinal and cerebral hemorrhage.

REFERENCES

1. Beare NA, Taylor TE, Harding SP, Lewallen S, Molyneux ME,
2006. Malarial retinopathy: a newly established diagnostic sign
2. White VA, Lewallen S, Beare N, Kayira K, Carr RA, Taylor TE,
2001. Correlation of retinal haemorrhages with brain haemor-
rhages in children dying of cerebral malaria in Malawi. Trans
3. Beare NA, Southern C, Chalira C, Taylor TE, Molyneux ME,
Harding SP, 2004. Prognostic significance and course of reti-
opathy in children with severe malaria. Arch Ophthalmol 122:
1141–1147.

NICHOLAS A. V. BEARE
Malawi-Liverpool-Wellcome Trust
Clinical Research Program
College of Medicine
Blantyre, Malawi

TERRIE E. TAYLOR
College of Osteopathic Medicine
Michigan State University
East Lansing, MI 48824

SIMON P. HARDING
St. Paul’s Eye Unit
Royal Liverpool University Hospital
Prescot Street
Liverpool L7 8XP, United Kingdom

SUSAN LEWALLEN
Kilimanjaro Center for Community Ophthalmology
Kilimanjaro Christian Medical Center Hospital
Tumaini University
Moshi, Tanzania

MALCOLM E. MOLYNEUX
Malawi-Liverpool-Wellcome Trust
Clinical Research Program
College of Medicine
Blantyre, Malawi