Letters to the Editor

Hypoglycaemia and cerebral malaria

Sir,
We read with interest Dr Kiire's paper¹ but beg to disagree with him on two points.

It is difficult to see how 44 ring forms of *P. falciparum* per 300 white blood cells could be considered as a strongly positive result, and therefore imply a heavy infection. A leucocyte count over 10,000/ μ l occurs in under 3% of malaria cases.² Nevertheless, if the white blood cell count of Dr Kiire's patient were of this magnitude, his parasite count would be but 1,466 asexual blood forms per microlitre; while this can obviously be associated with a lethal outcome, it cannot be considered as a high, or even medium, degree of parasitaemia in falciparum malaria.

We do not discern the basis for Dr Kiire's assertion that 'This probably represented yet another example of chloroquine failing to save life'. As the patient had apparently vomited most of the chloroquine that had been administered before admission, and as he died 3 hours after admission, there is no firm reason to postulate a lack of effectiveness of chloroquine in this case. By the same token, the author was probably not implicating chloroquine as a cause or co-factor of the hypoglycaemia, although this drug is known to inhibit the degradation of insulin,³ and has even been used to reduce the dose of insulin employed in a case of severe insulin resistance.⁴ However, chloroquine has not been known to cause hyperinsulinaemia in malaria.⁵

Hypoglycaemia in falciparum malaria occurs in two groups of patients: those with severe disease, and/or women who are pregnant, or who have recently delivered,⁵ usually (but not always) associated with the therapeutic administration of quinine.^{6–9} Cases however have been reported where both quinine and pregnancy were absent; these instances of hypoglycaemia seem to be associated with renal failure, cerebral malaria, or both.⁸

The finding of asexual parasitaemia in a patient with impaired consciousness does not seal the diagnosis of cerebral malaria,¹⁰ and other conditions have to be excluded. The examination of the cerebrospinal fluid is not sensitive or specific enough to diagnose or exclude many causes of coma.¹¹ Therefore, it is unfortunate that, although an autopsy was performed in this case, no details were given of the central nervous system condition in it.

Falciparum malaria resistant to chloroquine has been reported from Zimbabwe since 1984,¹² and although its extent is presently unknown,¹³ the author is probably right in that quinine by infusion should be used in severe malaria cases in areas of resistance to the 4-aminoquinolines.¹⁴ The absence of this is in the circumstances of the case reported, however, cannot be construed as the reason for the patient's death.

C.F. Ramos Filho
P.F.A. Lopes
S.F.V. Martins

Department of Preventive Medicine
Federal University of Rio de Janeiro
21941. Rio de Janeiro
Brazil

References

1. Kiire, C.F. Hypoglycaemia and cerebral malaria. *Postgrad Med J* 1986, **62**: 401–402.
2. Ramos Filho, C.F. *Malária em Área Não-Endêmica. Estudo Clínico e Epidemiológico de 250 Casos Observados no Rio de Janeiro*. Thesis, p. 198. Federal University of Rio de Janeiro, Rio de Janeiro.
3. Misbin, R.I. & Almira, E.C. The fate of insulin in rat hepatocytes. Evidence for the release of an immunological active fragment. *Diabetes* 1984, **33**: 355–361.
4. Blazar, B.R., Whitley, C.B., Kitabchi, A.E. *et al.* In vivo chloroquine-induced inhibition of insulin degradation in a diabetic patient with severe insulin resistance. *Diabetes* 1984, **33**: 1133–1137.
5. WHO (World Health Organization) Malaria Action Programme. Severe and complicated malaria. *Trans R Soc Trop Med Hyg* 1986, **80**: (supplement), 1–50.
6. Fisher, C.W.S. Clinical curio: acidosis and hypoglycaemia in malaria. *Br Med J* 1983, **286**: 1261.
7. Migasena, S. Hypoglycaemia in falciparum malaria. *Ann Trop Med Parasitol* 1985, **77**: 323–324.
8. White, N.J., Warrell, D.A., Chanthavanich, P. *et al.* Severe hypoglycemia and hyperinsulinemia in falciparum malaria. *N Engl J Med* 1983, **309**: 61–66.
9. Looareesuwan, S., Phillips, R.E., White, N.J. *et al.* Quinine and severe falciparum malaria in late pregnancy. *Lancet* 1985, **ii**: 4–8.
10. Warrell, D.A., Looareesuwan, S., Warrell, M.J. *et al.* Dexamethasone proves deleterious in cerebral malaria. A double-blind trial in 100 comatose patients. *N Engl J Med* 1982, **306**: 313–319.
11. Marton, K.I. & Gean, A.D. The spinal tap: a new look at an old test. *Ann Int Med* 1986, **104**: 840–848.
12. WHO (World Health Organization). World Malaria Situation 1984. *World Health Stat* 1986, **39**: 171.
13. Mutambu, S.L., Dallas, A.B.C. & Olweny, C.L.M. Chloroquine-resistant *Plasmodium falciparum* malaria in Zimbabwe. *Br Med J* 1986, **292**: 522.
14. Bruce-Chwatt, L.J., Black, R.H., Canfield, C.J., Clyde, D.F. & Peters, W. In *Chemotherapy of Malaria*, 2nd edition. World Health Organization, Geneva, 1982, pp 143–145.

This letter has been shown to Dr Kiire who replies:

Sir,
It is dangerous to extrapolate clinical findings from one area of the world to another. For instance, a leucocyte count over 10,000/ μ l in malaria cases is not uncommon in this part of the world. This patient had a leucocyte count of 25,000/ μ l giving a parasite count of 3665 asexual blood forms/ μ l.

The second point of disagreement is my assertion that this patient's death was yet another example of chloroquine failing to save life. It is my contention that chloroquine would have been inappropriate even if the patient had not vomited or had lived more than three hours after admission. The basis for advocating quinine is that we have chloroquine

resistance in Zimbabwe¹ and quinine infusion for severe malaria cases in areas of resistance to the 4 aminoquinolines has been recommended.²

The pathophysiology of hypoglycaemia complicating cerebral malaria was fully discussed in my paper and nowhere did I implicate chloroquine as a cause or co-factor of the hypoglycaemia in this patient. Indeed, as Dr Ramos Filho and his colleagues point out, chloroquine has not been known to cause hyperinsulinaemia in malaria.³

Finally, I fully agree with the assertion that asexual parasitaemia in a patient with impaired consciousness does not seal the diagnosis of cerebral malaria.⁴ This could not be more true than here in Africa where we have a tremendous degree of experience with this clinical presentation. Other conditions have to be excluded, and this was done in this case. We were even fortunate to have an autopsy (rare in this part of the world) which did not reveal any other cause of coma or death. Obviously, only essential data were given in the case report.

C.F. Kiire,
Department of Medicine,
University of Zimbabwe,
P.O. Box A178,
Avondale,
Harare,
Zimbabwe.

References

1. Matumbu, S.L., Dallas, A.B.C. & Olweny, C.L.M. Chloroquine-resistant *Plasmodium falciparum* malaria in Zimbabwe. *Br Med J* 1986, **292**: 522.
2. Bruce-Chwatt, L.J., Black, R.H. Canfield, C.J., Clyde, D.F. & Peters, W. In *Chemotherapy of Malaria*, 2nd edition. World Health Organization, Geneva, 1982, pp 143–145.
3. WHO (World Health Organization) Malaria Action Programme. Severe and complicated malaria. *Trans R Soc Trop Med Hyg* 1986, **80** (Suppl): 1–50.
4. Warrell, D.A., Looareesuwan, S., Warrell, M.J. *et al.* Dexamethasone proves deleterious in cerebral malaria. A double-blind trial in 100 comatose patients. *N Engl J Med* 1982, **306**: 313.

Myocardial hypertrophy, fibrosis and infarction following exposure of the heart to radiation for Hodgkin's disease.

Sir,
The histopathological illustration accompanying our recent communication on cardiac disease following radiation for Hodgkin's disease (*Postgraduate Medical Journal*, 1986 **62**, 1055–1058), although submitted in the conventional positive form was printed as a negative giving an appearance similar to that of an X-ray film. It is interesting to observe histopathology illustrated in the manner of diagnostic imaging and to recall that the distinction made in optics between object and image has its parallel in the diagnostic sciences where the

pathological disciplines study actual tissue (object) while the radiological sciences study images. This distinction may have, in the past, given rise to the idea that pathology was based on objectivity and radiology on imagination but recent improvements in the quality and variety of diagnostic imaging techniques have blurred the distinction. However, illustrating pathology by the image reversal conventions of radiology does not convey any additional information so that we must take a negative view of this development in histopathological imaging.

D.S. O'Briain,
Department of Pathology,
St. James's Hospital,
James's Street,
Dublin 8
Ireland

Effects of the opiate antagonist naloxone on learning and memory in patients with multi-infarct dementia.

Sir,

The endogenous opioids have recently been implicated in learning and memory mechanisms in both animals¹ and humans,² and naloxone was reported to improve memory functions in a subgroup of patients with senile dementia of the Alzheimer's type.² We thus tested the effects of acute naloxone administration in 8 drug-free patients (aged 60–81 years) who met DSM-III criteria for multi-infarct dementia (MID) with Hachinski scores greater than 7 and with Mini-Mental States scores of 14–26. In all subjects diagnosis was supported by characteristic head computed tomographic (CT) findings. Subjects were tested twice off and on 1.2 mg i.m. of naloxone, on selected scales of the Wechsler Memory Scale (WMS) and on 12 item list learning task using the Bushke-Fuld Selective Reminding Procedure. The order of the drug and drug-free testing was counterbalanced. No significant ($P < 0.05$) effects were found on the WMS and on the list learning task following 30 and 60 minutes respectively, of naloxone administration.

These findings suggest that administration of opiate receptor antagonists may not be useful in the management of memory and learning functions in MID patients, and are consistent with recent reports demonstrating significant correlation between the severity of dementia and reduced CSF beta-endorphin levels in MID patients.³

Reuven Sandyk¹
James Allender²
Colin R. Bamford¹
Departments of ¹ Neurology
and ² Psychiatry
University of Arizona,
Health Sciences Center,
Tucson, Arizona 85724, USA.

References

1. Izquierdo, I. Effect of naloxone and morphine on various functions of memory in the rat: possible role of endogenous opiate mechanisms in memory consolidation. *Psychopharmacology* 1979, **66**: 199.