Case report

Malaria: A cerebral approach

An increasing number of patients with severe complicated *Plasmodium falciparum* malaria are presenting to South African hospitals, having travelled through malaria-endemic countries from Central and East Africa. This report concerns an immigrant from Pakistan who developed severe cerebral malaria.

A 26-year-old Pakistani man arrived in Cape Town in December 2011, having flown to Dar es Salaam in Tanzania and then travelled overland through Mozambique. Three days after arrival he became unwell – he felt feverish, weak and shaky, which was followed by diarrhoea and vomiting. He was seen by a local general practitioner who did not test for malaria. A day later, he became confused and was taken by his friends to a primary level hospital, where a malaria smear proved positive. He was then urgently referred to secondary level care.

On examination he was jaundiced and pale, his temperature was 37.6°C, blood pressure (BP) 82/48 mmHg and pulse 82/min. His Glasgow Coma Scale (GCS) was 10/15. He exhibited neck stiffness and increased tone in the upper limbs bilaterally, with normal lower limb tone and extensor plantar responses; his pupils were equal and reactive to light. All other systems were normal; there was no hepato- or splenomegaly. *P. falciparum* malaria was confirmed on a thin blood film, with hyperparasitaemia of 13.8%. He was jaundiced, anaemic and thrombocytopenic with significant renal dysfunction (Table 1). A diagnosis of cerebral malaria was made, with possible bacterial meningitis.

Treatment with intravenous artesunate (2.4 mg/kg), intravenous ceftriaxone 2 g 12-hourly and judicious intravenous fluids was commenced and he was admitted to a secondary level intensive care unit (ICU). The following morning, he had a generalised tonic clonic seizure. His GCS dropped to 4/15 and failed to improve. He was intubated for airway protection and ventilated without sedation. An adrenaline infusion was required to maintain his BP. His GCS remained 2T for the next 72 hours and even though his malaria smear was negative after 3 days of artesunate, renal and liver function deteriorated rapidly (Table 1).

Based on his poor neurological prognosis and worsening multi-organ failure, he was refused tertiary level ICU admission on day 4 according to local ICU admission policy. However, on day 5 he began to improve neurologically, showing a subtle flexion response to deep pain stimulation. Consequently, he was accepted by the tertiary ICU. Dialysis was commenced and he continued inotropic support. He required thirteen red packed cells in total to maintain his haemoglobin (Hb). Despite developing a ventilator-associated pneumonia, his condition steadily improved. His GCS returned to 15/15. Liver and renal function steadily normalised, such that dialysis could be stopped by day 16 in ICU. He completed artemisinin-based combination therapy for 3 days with Coartem® (arthemeter and lumefantrine). He was finally extubated after 3 weeks and discharged from the ICU. Four days later, he walked out of hospital with normal kidney, liver and haematological parameters. At follow-up, he was well and had no neurological sequelae.

The 2011 World Malaria Report confirms 216 000 000 malaria cases in 2010 with 665 000 deaths.[1] Cerebral malaria, a prominent manifestation of falciparum malaria, carries a 15 - 20% mortality which rises above 30% with multi-organ involvement.[2] It is caused predominantly by sequestration of infected red blood cells within the cerebral mircrocirculation.[3] Artesunate, a derivative of the ancient Chinese herb qinghaosu (artemisinin), has

Table 1. Laboratory results

	Admission (day 0)	Tertiary ICU admission (day 5)	Discharge (day 32)
Hb (g/dl)	6.9	6.9	9.2
Platelets	41	147	374
White cell count	9.0	14.9	
Urea (mmol/l)	18.4	48.3	8.4
Creatinine (µmol/l)	155	626	90
HCO_3 (mmol/l)	22.7	16.1	25.6
Parasite load	13.8% (*P. falciparum*)	Clear	
ALT (U/l)	29	128	70
INR	1.3	1.1	
CSF	Protein: >2; polys: 3; lymphs: 24; RBC: 10 000		
HIV	Negative		
CT brain		Normal	

been shown to have a mortality benefit of 34.7% over quinine in adults and 22.5% in children with severe falciparum malaria.[2,4] It also has few side-effects, does not require dosage adjustment in renal failure and is easily administered. However, it is not yet registered for use in South Africa, so access is limited to an access programme introduced in January 2010, under Section 21 of the Medicines and Related Substances Act.[5]

This patient's case provides a number of important learning points with regard to falciparum malaria. Firstly, malaria should be considered in the diagnosis of any patient with fever returning from a malaria-endemic area and investigated as a medical emergency. Secondly, clinicians should be aware that signs of meningitis are not consistent with malaria and either suggest a secondary bacterial infection in someone with proven malaria or an alternative diagnosis. Thirdly, the use of intravenous artesunate has a substantial survival advantage over quinine and is available in South Africa through an expanded access Section 21 programme. Lastly, such patients present complex clinical problems, often with multi-organ failure, and are best managed in a tertiary level ICU by experienced critical care physicians and infectious diseases specialists.

Richard Court, MB ChB, DipHIVman (SA)
Medical Registrar, Department of Medicine, University of Cape Town

David Stead, MB ChB, FCP (SA), DipHIVman (SA)
Senior Registrar, Division of Infectious Diseases and HIV Medicine, Department of Medicine, UCT and Groote Schuur Hospital, Cape Town

Karen Barnes, MB ChB, MMed (Clinical Pharmacology)
Professor, Division of Clinical Pharmacology, Department of Medicine, UCT and Groote Schuur Hospital

Clint Cupido, MB ChB, FCP (SA)
Head of Medicine, Victoria Hospital, Wynberg, and Senior Lecturer, Department of Medicine, UCT

Ivan Joubert, MB BCh, DA (SA), FCA (SA)
Director and Head, Critical Care, UCT and Groote Schuur Hospital

Marc Mendelson, PhD, FRCP, DTM&H
Principal Specialist and Head, Division of Infectious Diseases and HIV Medicine, Department of Medicine, UCT and Groote Schuur Hospital

Correspondence to: R G Court (richardcourt@mweb.co.za)

References available at www.cmej.org.za

SINGLE SUTUTRE

Epidemic of plain packaging to curb smoking uptake

Here's a potential epidemic worth celebrating. Australia's High Court has upheld 'plain packaging' legislation for cigarettes – a move that some say will see the practice sweep through the world. The legislation forces cigarette packages to carry prominent health warnings and a plain font over an olive green background – logos would no longer be allowed.

'The ramifications really are immense,' says Mike Daube at Curtin University in Perth, Western Australia. 'There's a domino effect in tobacco control.' Daube says there will now be an 'epidemic of plain packaging' across the globe. He says bans on smoking on flights seemed impossible but they spread once one airline took the plunge.

According to Jonathan Liberman, director of the McCabe Centre for Law and Cancer in Melbourne, Australia, the decision will have a global impact. '[It shows] that all the tobacco companies' arguments came to naught and the world needs to consider the arguments in that light.'

Whether that impact extends to the USA remains to be seen. 'The US is a unique situation,' says Kevin Outterson of Boston University School of Law, who specialises in healthcare policy.

He says the US Supreme Court is 'openly suspicious' of precedents set in other countries. Moreover, it has come to consider 'commercial speech' as protected under the first amendment right to free speech. 'Many countries in Europe and elsewhere are proposing similar legislation and have been faced by similar claims that this is somehow an expropriation of the tobacco companies' intellectual property rights,' says John Burman, senior legal adviser at Cancer Research UK. He says the Australian decision can be cited in US and UK courts, and he thinks it is likely to have some influence.

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