CEREBRAL MALARIA: A DIAGNOSIS OFTEN FORGOTTEN IN SINGAPORE

K T Tan
K Y Fong
V Kwok
J S Cheah

University Department of Medicine
Singapore General Hospital
Outram Road
Singapore 0316

K T Tan, MBBS, M Med, MRCP (UK)
Registrar

J S Cheah, MBBS (Hons), MD, FRACP
Head and Professor

Department of Medicine
Singapore General Hospital

K Y Fong, MBBS, M Med
Registrar

V Kwok, MBBS, M Med, MRCP (UK)
Consultant

SYNOPSIS

Since November 1982 Singapore has been declared as having achieved malaria eradication. However cases of imported malaria continue to be seen here. Although cerebral malaria is not a common diagnosis, cases of cerebral malaria continue to be seen. Prompt diagnosis and treatment is essential. We report 4 cases (1 fatal) of cerebral malaria seen over a period of 4 months at the Singapore General Hospital.

INTRODUCTION

On 22 November 1982, Singapore was certified by WHO as having achieved the status of malaria eradication (1). Although having achieved this status, cases of malaria are still seen and treated in Singapore. This is because the ease of international travel brings people of many different countries through Singapore. It is therefore not surprising that many cases of "imported malaria" are seen. In 1985 there were a total of 166 notified cases of malaria in Singapore. All these cases were "imported malaria" (2). Malaria and especially cerebral malaria with its high mortality rate is still an important diagnosis to remember in patients with fever and a history of travel outside Singapore. The four successive cases of cerebral malaria seen at Singapore hospital over a period of four months (June to October 1986) illustrate these points very well.

CASE REPORTS

Case 1

This was a 26-year old Burmese seaman who was admitted for cerebral malaria and died four hours later.

Two months before this admission, he had suffered a fracture of the radius and was treated in a hospital in Kenya. He was admitted two weeks later to a private hospital in Singapore. While in Singapore, he developed a high fever. Malaria was suspected and although initial blood films for malarial parasites were negative, it was positive for Plasmodium vivax three days after the onset of fever. He was then treated with oral Fansidar.

Two days after the diagnosis of Plasmodium vivax infection was made, the patient's condition deteriorated. He became comatose and on admission to this hospital, he was in Coma 4 (no response to noxious stimuli). Blood sugar level on admission was 23 mg/dl; it was corrected immediately with intravenous glucose. Blood film done was positive for Plasmodium falciparum. He collapsed soon after admission and died inspite of attempts to resuscitate him. A post-mortem confirmed that the cause of death was Cerebral Malaria.

Case 2

This was a 38-year old Algerian seaman who developed headache, fever with chills and rigors 11 days before admission. During this period, he was on board his ship and was treated initially with Clamoxyl. Two days later, when he had showed no improvement, Streptomycin and Novaquine were added. When his ship reached Singapore, he was sent to our hospital.

On admission, he was noted to be febrile, pale and jaundiced. He was also drowsy and had hepatosplenomegaly. Blood film was positive for Plasmodium falciparum and he was started on intravenous quinine hydrochloride. Blood urea level was 286 mg/dl and serum creatinine level was 2.8 mg/dl on admission. These levels subsequently became normal. He recovered uneventually and was discharged 10 days later.

Case 3

This was a 35-year old Indonesian seaman, who was brought to Singapore after being ill for 10 days in Indonesia. He presented with fever and chills 10 days before admission and was treated as a case of fulminant hepatitis in Indonesia. He was then noted to be febrile and jaundice and had been drowsy for 2 days before arriving in Singapore.

On admission, he was febrile and comatose responding only to deep pain. He was also jaundiced and had acidotic breathing. Initially meningitis was suspected but blood film were also examined for malaria parasites. Leptospirosis with acute renal failure was also considered in differential diagnosis. The blood film showed Plasmodium falciparum. He was started on intravenous quinine.

He was also found to have acute renal failure and anemia. Serum urea, creatinine, and haemoglobin were 615 mg/dl, 18 mg/dl, 7.9 mg/dl respectively on admission. He required peritoneal dialysis and was in a drowsy state for 3 days before becoming conscious and rational. His renal function returned to normal and he also made full recovery although after a rather protracted hospital stay.

Case 4

This 45-year old Indian lady was a tourist from India. She had a history of fever, chills and rigors for one week prior to admission. She also had nausea and vomiting and passage of tea coloured urine. She was noted to be jaundiced by a general practitioner and referred to hospital as a case of viral hepatitis.

On admission, she was noted to be rather drowsy and febrile. The possibility of hepatic encephalopathy or leptospirosis was considered. Blood films were examined for malarial parasites and this showed Plasmodium falciparum. She also had evidence of intravascular hemolysis and was given blood transfusion.

She was treated with intravenous quinine hydrochloride. She recovered uneventfully and was discharged 10 days later.

DISCUSSION

These 4 cases serve to illustrate a number of important points.

All 4 patients were foreigners. Three were seamen who had travelled in various places in South East Asia as well as Africa and one was a tourist who had flown to Singapore from India. Malaria must be suspected in patients who present with high fever and have a history of travel outside Singapore. Blood film must be examined for malarial parasites as physical signs are not specific for malaria. It is vital that blood films (thick or thin) should be read by trained technicians, otherwise the diagnosis may be missed as illustrated in Case 1.

In 2 of the patients, fulminant hepatitis with encephalopathy was the initial diagnosis as they had fever, jaundice and changes in sensorium. If cerebral malaria is not considered in differential diagnosis and blood film for parasites not examined, the diagnosis can easily be missed or seriously delayed.

In Case 1 (the patient who perished) there was delay in diagnosis. Although he was already in Singapore for one month before developing fever, this is not inconsistent with imported malaria as symptoms may be delayed for up to six months (3). Although malaria was suspected, the blood film was noted to be negative until 3 days after the fever started. This is again not uncommon as it is often necessary to send multiple blood film samples before the diagnosis can be dismissed. This case further demonstrates a point that mixed infections are not uncommon. This patient was found to have Plasmodium vivax infection and treated with Fansidar but later perished from Plasmodium falciparum infection which was probably not sensitive to Fansidar.

It is noteworthy that in Case 2 the patient was treated empirically while he was on board the ship with Chloroquine but did not respond. This case together with Case 1 illustrates the fact that Chloroquine resistant strains of Plasmodium falciparum are now prevalent in this part of the world and Fansidar resistant malaria is also not unexpected (3,4). In patients who are seriously ill with falciparum malaria it is prudent to assume that they are Chloroquine resistant and treated accordingly (5,6). All 4 patients were treated with intravenous quinine hydrochloride and apart from the first patient who perished soon after admission the other 3 recovered.

Case 1 also illustrates an important fact that hypoglycaemia is not an uncommon complication of cerebral malaria (5.7). The failure to recognize this complication can be fatal. However, it is not possible to predict when hypoglycaemia will occur as in cerebral malaria the patient's sensorium is altered and signs of hypoglycaemia can be masked. It is therefore important to monitor the blood sugar of these patients regularly for hypoglycaemia till their sensorium

recovers. It should also be remembered that hypoglycaemia may also be a result of treatment with quinine as well as quinidine (8).

Cerebral edema is another complication of cerebral malaria. Two of our patients had CT Scan of brain done (Case 2 and 3). Both scans were normal. However it is known that CT Scan of Brain may not accurately reflect whether the patient has cerebral edema (9). The use of dexamethasone to treat cerebral edema is controversial. So far evidence from a controlled trial published in 1982 by Warrell et al is against the use of dexamethasone (6).

Case 3 and 4 also illustrate two other important complications that can occur in patients infected by Plasmodium falciparum. The patient in Case 3 suffered from renal failure as a result of blackwater fever and required a period of dialysis. Case 4 developed intravascular hemolysis and required blood transfusion (5). Both patient were subsequently well on discharge.

In conclusion a high index of suspicion, early diagnosis and awareness of complications of cerebral malaria are all important in preventing deaths due to this treatable disease.

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