West African Malaria

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SUMMARY: *Plasmodium falciparum* malaria poses an increasing risk to travellers to West Africa. The development of chloroquine resistant in West Africa has further compounded the risk. Two cases of falciparum malaria from Sierra Leone are presented. One represents the classic missed case and the other a probable case of chloroquine resistant (RI vide infra) falciparum malaria. These cases highlight the danger of the missed or late diagnosis; the need for chemoprophylaxis, even in emigrants; the threat posed to the international traveller by malaria; and the problem of chloroquine resistant *Plasmodium falciparum* (CRPF) malaria from West Africa. The position of *Plasmodium falciparum* malaria in West Africa is reviewed along with the problem caused by chloroquine resistance.

Introduction

Travellers to West Africa are at considerable risk of contracting malaria, principally *Plasmodium falciparum*. In the first half of 1990, five hundred and sixty cases of malaria originating in Africa were reported to the Malaria Reference Laboratory, of which eighty two percent were due to *Plasmodium falciparum* (1-2). In the first two quarters of the same period the percentage of *Plasmodium falciparum* malaria originating from West Africa was 51% and 46% respectively of all African malaria cases (1-2). The increasing risk from *Plasmodium falciparum* in West Africa has been documented by Phillips-Howard et al (3), who showed that the number of reported cases rose from 147 in 1977 to 409 in 1986, and that over the same time period, the proportion of all reported cases of malaria caused by *Plasmodium falciparum* rose from one fifth to one third. The increase is partly explained by the development of chloroquine resistant strains in West Africa, something which is well reported in the literature (4-10). The number of reported cases continues to rise; for the period July 89 - June 90, just over 500 were reported. We report two cases which illustrate the risks faced by travellers to West Africa from *Plasmodium falciparum* malaria; one represents the classic missed case and the other, a case of possible CRPF malaria in Sierra Leone.

Case Reports

A married couple, both natives of Sierra Leone, made their annual visit to Freetown, Sierra Leone in November. Both had resided in the UK for more than ten years. They stayed with relatives in Freetown and remained in residential areas only. Neither took malarial prophylaxis. They returned to the UK in early December.

Case 1

The wife, aged 46 years, fell ill seven days after their return with fever, diarrhoea, vomiting and progressive prostration. Two civilian doctors visited over this period and diagnosed influenza. Admission was requested by a third doctor when the patient was moribund with high fever, anaemia, dehydration and jaundice. She was unresponsive to all stimuli, with deep pain, reacting with small withdrawal movements and grunting. Blood films confirmed the diagnosis of *Plasmodium falciparum* malaria, and showed a severe normocytic, haemolytic anaemia (Hb 4.6 g/dl). The level of parasitaemia was assessed to be 2% but this was felt to be an underestimate in view of the severe degree of haemolysis. The platelet count was normal (150 x10^9 / dm3) and the ESR was raised at 115 mm/1st hour. In addition, there was severe hyponatraemia (120mmol/l), hypokalaemia (3,3 mmol/ l), hypoalbuminaemia (28g/l) and elevated hepatic transaminases (AST 130 IU/L ; ALT 150 IU/L). Urinalysis showed heavy haemoglobinuria. Arterial blood analysis showed a severe metabolic acidosis and hypoxia. Treatment comprised high dose intravenous quinine, initially in a loading dose of 20mg/kg body weight reducing to 10mg/kg given over four hours every eight hours; corticosteroids, blood transfusion and urinary alkalinisation with intravenous 4.2% sodium bicarbonate. Intravenous hydrocortisone (100mg qds) was administered in view of the degree of haemolysis. Oral quinine (600mg 8 hourly) was instituted after 3 days followed by three tablets of Fansidar (pyrimethamine 25mg plus sulfadoxine 500mg) without recrudescence. Clearance of parasites was confirmed by serial blood films. Recovery was fortunately complete.

Case 2

Her husband, a serving RAF officer aged 47 years, had had blood smear positive *Plasmodium falciparum* malaria whilst in Sierra Leone and received treatment with chloroquine, initially administered in-
tramuscularly followed by a standard course of oral chloroquine. He did not suffer any diarrhoeal illness during this time. Consequently there was nothing to suggest that there had been malabsorption of chloroquine, and he had complied with the treatment course. He became unwell 23 days after returning to UK with headache, fever and malaise. Investigation showed a moderate anaemia (Hb 10gm/dl) and blood films confirmed the presence of *Plasmodium falciparum*, with a low level parasitaemia (0.5%). Chloroquine resistance (RI *vide infra*) considered highly probable and he was treated with a standard course of oral quinine sulphate (600mg 8 hourly) for seven days followed by Fansidar (3 tablets), without recrudescence.

Discussion

These two cases illustrate the continued need for vigilance amongst doctors in dealing with those patients returning from West Africa. The lady represents the classical missed case and shows that emigrants cannot be considered semi-immune (11). The use of prophylaxis in this group is to be strongly encouraged. Travellers to West Africa, including Sierra Leone, will be exposed to drug resistant parasites. At present, data on chloroquine resistance in Sierra Leone is scarce, but our second case suggests it is likely to present as a clinical problem. Re-infection may have occurred but chloroquine resistance seems equally probable. The patient had not suffered a diarrhoeal illness and thus malabsorption of chloroquine is not felt to be likely. Unfortunately we were unable to test the sensitivities of parasite isolates and therefore the assumption of chloroquine resistance is not proven.

Chloroquine resistance was first described in Colombia in 1961 (12). In Africa resistant parasites were initially encountered in 1978 in cases from Kenya and Tanzania (13). Chloroquine resistant malaria spread rapidly throughout East Africa and is a well recognised problem. In recent years drug resistant parasites have spread up the West Coast of Africa. Problems have been encountered in Angola (1984) (14), Gabon (1984) (15), Cameroon (1985) (16), Nigeria (1986) (17), Ghana (1986) (18), Benin (1986) (19) and The Gambia (1987) (20). Chloroquine resistance has been subdivided into different degrees by the World Health Organisation on the basis of the response to a standard dose of chloroquine base of 25 mg/kg body weight (21): RI - clinical cure with clearance of parasitaemia for 2 consecutive days followed by a relapse up to 28 days after therapy; RII - a 75% reduction in parasitaemia during the first 48 hours of therapy but without a clearance of the parasitaemia; and RIII - less than 75% reduction or an increase in the parasitaemia in the first 48 hours of therapy. Therefore, an initial response to chloroquine does not rule out drug resistance, which may present late in the cases of RI resistance, exemplified by our case. To date the resistance reported from West Africa has been of the RI or RII type.

It is well recognised that no drug regime offers total protection from infection (22). Cases of proven malaria have occurred in patients who have conscientiously taken their prophylaxis — so-called breakthrough malaria. Therefore in addition to appropriate chemoprophylaxis, it is of primary importance that physical protection measures to decrease the likelihood of being bitten are taken. However the need for appropriate chemoprophylaxis is stressed. The current recommendation for travellers to West Africa is to take chloroquine (Nivaquine) 300mg base weekly plus proguanil (Paludrine) 200mg daily. The regime should be started one week prior to travel to a malarious region and continued for twenty eight days after return. Service personnel should be issued with a malaria warning card (F Med 568) before returning from a malarious area.

The recommended treatment of *Plasmodium falciparum* malaria acquired in West Africa has been changed as a result of the emergence of chloroquine resistance and chloroquine is no longer regarded as a first line drug (22). Oral or intravenous quinine, depending on the severity of the case, should be used instead. It is desirable to perform *in vitro* testing of parasite isolates, if facilities are available, in order to detect the spread of resistant strains. Fansidar is given, after completion of the quinine course, to effect a radical cure. If the patient has travelled from an area of known Fansidar-resistance, or if the patient is sulphonamide hypersensitive, the use of tetracycline is advised.

There are between five and ten deaths from falciparum malaria in the UK each year. In the Armed Services special teaching is given to Medical Officers about the diagnosis and treatment of malaria. However, it is important to realise that the diagnosis of falciparum malaria depends upon the doctor thinking of the possibility. Cases of breakthrough malaria from West Africa are likely to increase in number and patients returning from malarious regions must have blood films examined for parasites.

In conclusion these cases demonstrate the danger of not taking malarial prophylaxis; the threat posed to the international traveller by malaria; the danger of delayed or missed diagnosis of malarial; the risk of breakthrough malaria in travellers from West Africa; and the need for all doctors to be aware of the increasing threat posed by chloroquine resistance in travellers returning from West Africa.

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