Fatal falciparum malaria in Canadian travellers

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This article has been peer reviewed.

Can Med Assoc J 1997;156:1165-7

Abstract

THE AUTHORS REPORT 2 CASES of severe falciparum malaria in Canadians that had fatal outcomes. In the first case a man presented to a local hospital shortly after returning from Africa, but a diagnosis of malaria was not considered. He was transferred to a secondary and then to a tertiary care facility, where he subsequently died. Intravenous quinidine therapy, the treatment of choice, was unavailable at all 3 hospitals. In the second case, a woman taking chloroquine prophylaxis while visiting Nigeria developed cerebral malaria and died. These cases illustrate critical management issues: appropriate advice on malaria prevention before departure; consideration of malaria in all febrile people returning from an endemic area; ready access to parenteral therapy for severe malaria in Canadian hospitals; and an increase in awareness of travel medicine among family physicians.

Résumé

LES AUTEURS SIGNALENT 2 CAS de paludisme à falciparum grave chez des Canadiens, dont l'issue a été fatale. Dans le premier cas, un homme s'est présenté à un hôpital local peu après son retour d'Afrique, mais on n'a pas pensé à diagnostiquer une attaque de paludisme. Il a été transféré à un établissement de soins secondaires et, ensuite, de soins tertiaires, où il est décédé. La thérapie à la quinidine par voie intraveineuse, traitement de choix, n'était pas disponible aux 3 hôpitaux. Dans le deuxième cas, une femme qui prenait de la chloroquine prophylactique pendant un séjour au Nigéria a contracté une forme cérébrale de malaria et en est morte. Ces cas illustrent des problèmes critiques de prise en charge : conseils appropriés sur la prévention du paludisme avant le départ, possibilité de paludisme chez toutes les personnes fiévreuses qui reviennent d'une région endémique, accès facile à une thérapie parentérale contre le paludisme grave dans les hôpitaux canadiens et sensibilisation accrue à la médecine des voyages chez les médecins de famille.

With the resurgence of drug-resistant malaria worldwide and with current travel and immigration patterns, imported drug-resistant malaria is an increasing problem in Canada.[1–4] In 1995, 621 cases of malaria were reported in Canada, representing an increase of 44% from the 430 cases reported in 1994. This is likely an underestimate of the true incidence of malaria, since only one-third to one-half of cases are believed to be reported to public health officials.[1]

About 90% of travellers who acquire malaria will not become symptomatic until they return home.[1,5] Delays in diagnosis and treatment increase morbidity and mortality.[1,5,6] Therefore, it is necessary to recognize cases promptly, to identify species accurately and to provide appropriate initial management. However, recent studies indicate that several problems exist in the recognition and management of malaria in Canada.[2–4] The following 2 cases illustrate that these problems, combined with the unavailability of treatment for severe malaria, can result in fatal outcomes.

Case reports

Case 1

A previously healthy 66-year-old man travelled through South Africa and Zimbabwe. He did not seek advice about malaria prevention before travelling but did begin proguanil and chloroquine prophylaxis while on route from Johannesburg to Victoria Falls. Shortly after returning to Canada he had gastrointestinal upset and stopped taking the antimalarial drugs. About 1 week later he had nausea and headaches. Five days later his condition deteriorated, and he was found unresponsive and incontinent of urine.

At a local hospital the man was noted to be afebrile, disoriented, tachypneic and in atrial fibrillation. Blood work revealed hypoglycemia and acidosis; a complete blood count was not performed at that time. He was transferred to a larger, regional hospital. A complete blood count there revealed a thrombocyte count of 21 (normally 150–400) $\times$ 10^9/L, and a blood smear indicated 50% parasitemia with *Plasmodium falciparum* (Fig. 1). No quinidine was available for parenteral treatment; instead, 1500 mg of mefloquine and 3 tablets of sulfadoxine–pyrimethamine were given orally.

The patient was transferred to a regional tertiary care hospital 10 hours later for parenteral quinidine therapy. Upon arrival he was in coma and acute renal failure. The regional hospital no longer stocked the drug, and quinine for intravenous use was received from National Defence on an urgent basis. The patient was managed with exchange transfusion, parenteral quinine therapy and doxycycline. Irreversible shock developed, and he died the following day. Postmortem examination confirmed typical findings of severe and cerebral malaria.[6]

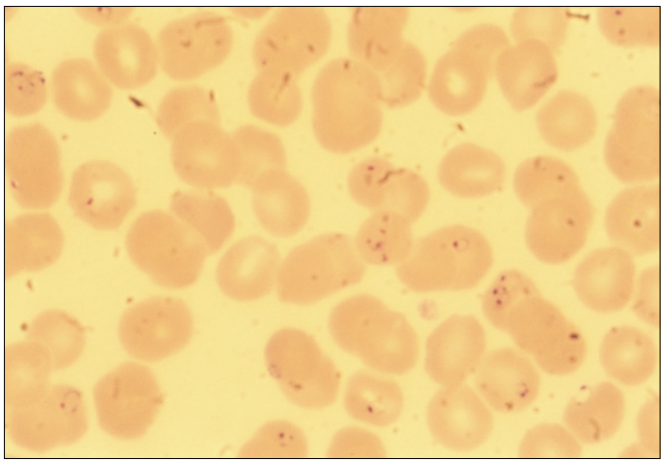

Fig. 1: Thin blood film showing about 50% parasitemia in 66-year-old man in whom severe falciparum malaria developed after his return from Africa.

Case 2

A previously healthy 45-year-old woman travelled with her family to Nigeria for 1 month. On the advice of her family physician she and her family began chloroquine prophylaxis before their departure and by history were fully compliant. No personal protection measures such as insect repellents or bed nets were used. Three weeks after arriving in Nigeria the woman developed general malaise, diarrhea and back pain. She was assessed by a local physician after fever, chills, rigors and delirium developed. Initial therapy consisted of analgesia and diazepam despite a presumptive diagnosis of malaria. Results of a thick blood film received the following day revealed *P. falciparum* malaria. Her level of consciousness deteriorated, and jaundice developed. Treatment was switched to intravenous hydration and parenteral chloroquine therapy. The woman went into coma and died of cerebral malaria 2 days later. These findings were confirmed by postmortem examination following the return of her body to Canada.

After returning to Toronto the woman's 3 children (ages 12, 16 and 16) were found to have *P. falciparum* malaria while still taking the chloroquine prophylaxis. They were admitted to hospital, with parasitemias of 0.5% to 3%. Each was treated with quinine (600 mg orally 3 times daily for 3 days) and doxycycline (100 mg orally twice daily for 7 days). Therapeutic response was slow, but by day 5, thick blood smears showed no signs of the parasite.

Comments

These cases highlight important problems in the prevention, diagnosis and management of malaria in Canadian travellers that can result in fatal outcomes. First, people must receive accurate advice regarding malaria chemoprophylaxis and the use of personal protection measures before they travel to endemic areas. Although most Canadians do seek pretravel advice from their family physicians, a recent study of 83 cases of malaria showed that many travellers were prescribed innappropriate drugs and few were advised about personal protection measures.[4]

Because of widespread drug resistance, chloroquine is no longer effective for malaria prophylaxis in most endemic areas. Chloroquine plus proguanil is only 60% to 70% effective in sub-Saharan Africa, but mefloquine or doxycycline provides substantial protection in this region.[5] Because of a constantly changing situation with drug-resistant malaria, physicians providing pretravel advice must keep up to date regarding current recommendations.[5] Alternatively, travellers should be referred to tropical medicine or travel specialists.

As evident in the second case, treatment of malaria in developing countries may not be reliable, especially since local physicians may be unfamiliar with the disease response and outcome in a nonimmune patient population. Chloroquine therapy was inappropriate for the initial management of falciparum malaria in this patient. Her death and the high attack rate in her family underscore the need for appropriate chemoprophylaxis use by Canadian travellers.

Fever after travel to or through a malaria-endemic area must be considered to indicate malaria, in particular *P. falciparum* malaria, until proven otherwise. Delays in diagnosis and treatment increase the risk of complications and death.[1,5,6] Falciparum malaria in a nonimmune patient constitutes a medical emergency and generally requires admission to hospital for initial management and follow-up.[5,6] The treatment of choice for severe or complicated cases is parenteral quinidine gluconate therapy.[5] Although readily available in the past for the treatment of cardiac arrhythmias, quinidine has been replaced by newer antiarrhythmic agents. As a result, many hospitals have stopped stocking this drug in their pharmacies. Two recent deaths from malaria in the United States were at least partially the result of delays in obtaining quinidine for intravenous therapy.[7,8] In the first case we report, none of the 3 hospitals to which the patient was admitted had quinidine available for parenteral use. Although the alternative — parenteral quinine dihydrochloride therapy — is available through Emergency Drug Release (tel. 613 941-2108), there may be unacceptable delays in acquiring this drug because of the time taken for processing requests and delivering the drug to the hospital.

To determine the current availability of quinidine and quinine for intravenous use we surveyed secondary and tertiary care hospitals in Ontario and tertiary care hospitals elsewhere in Canada. In Ontario, only 4 of the 11 secondary care hospitals and 6 of the 12 tertiary care hospitals had the drugs on their formularies. In eastern and western Canada 4 of 6 and 2 of 4 tertiary care hospitals respectively had the drugs on their formularies. Overall, only 36% (4/11) of the secondary care and 55% (12/22) of the tertiary care hospitals surveyed had the drugs on their formularies. In 2 of the hospitals, although quinidine was on the formulary, no drug was stocked in the pharmacy; therefore, the appropriate treatment was available at only 45% of the tertiary care hospitals surveyed. Directors of hospital formularies need to ensure that parenteral therapy for severe malaria remains readily available.

In summary, imported malaria is an important problem in Canada. To prevent additional deaths from malaria people must receive appropriate advice on prevention before travelling to endemic areas. Malaria must be suspected in all febrile people returning from endemic areas and should be considered a medical emergency requiring prompt diagnosis and therapy.

This study was supported by a grant from the Physicians Services Incorporated Foundation and the Judy Kalu Memorial Fund.

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