Falciparum malaria resistant to prophylactic and therapeutic doses of chloroquine phosphate is widespread in Southeast Asia, especially in Vietnam, and occurs in South America, especially in Colombia and Brazil. This development is truly calamitous, since what was almost an ideal drug is becoming of limited value. All malariologists have dreaded the day when chloroquine-resistant malaria from Africa would appear. Alas, evidence presented in two case reports would indicate that the day is here.

Report of a Case

A 49-year-old zoologist who had traveled extensively throughout the world, including Africa, was in generally good health and gave no history of previous malaria. On Feb 25, 1978, he left the United States, taking a group of civilians on a tour of the Kenya highlands. He remained there 17 days and returned to New York on March 17. Two weeks before departure, he began taking chloroquine phosphate (Aralen Phosphate), prophylaxis 500 mg once a week, which he took faithfully during his stay in Africa, definitely for two weeks after his return, and probably for four additional weeks, since he knew that the proper span was five to six weeks. (He believes that he took the medication but cannot remember for certain.)

On May 5, following four days of fever and chills, falciparum malaria was diagnosed. My identification of the species was confirmed by two sources. His condition was treated with 2.5 g of chloroquine phosphate, and he showed prompt clinical recovery.

He was hospitalized again on June 15, following two days of symptoms of malaria, including fever. Falciparum malaria was diagnosed a second time. He was treated with 3.0 g of chloroquine phosphate during a four-day period and showed rapid response and parasite clearing. The chloroquine phosphate therapy, 500 mg once a week, was maintained for five weeks. The last dose was taken on July 27.

On Aug 22, the patient again had symptoms of malaria and was admitted to the New York Hospital, where blood smears disclosed ring forms, including many aplastic forms, of falciparum malaria. Cultures of blood taken the night of admission were made. Four days later, crescent forms appeared. Blood taken on Aug 27 for testing at the Center for Disease Control by the immunofluorescent technique showed the following titers: Plasmodium falciparum, 1:1,024; P vivax, 1:257; and P malariae, 1:64.

After taking 3.0 g of chloroquine phosphate in a four-day period with prompt clinical recovery, the patient was treated for five days with pyrimethamine, 50 mg daily, and sulfadiazine, 4.0 g daily. He has remained well since Oct 16, 1978, and is still under clinical observation.

Comment

That the patient had an infection with falciparum malaria is incontrovertible. Was his infection a drug-resistant one? Foreshortening of his initial prophylaxis might have precluded such a claim for the first attack. But malaria recurred following adequate therapy for the second attack, and the suppressive cure (500 mg of chloroquine phosphate for five weeks) justifies the conclusion that this patient's falciparum malaria was indeed drug resistant.

The patient's capacity to absorb chloroquine is normal, as indicated by the rapid response to therapeutic doses for each attack. Cultures of the parasites have been inoculated into monkeys in the hope of establishing a primate infection so that further drug-response studies can be made.

Report of a Case

A 29-year-old man had traveled in Africa (first in North and Central Africa, then in East Africa, Kenya, and Tanzania) for three months, May, June, and July, of 1975. Since his wife had Hodgkin's disease and had had a splenectomy, both were careful to take regularly 500 mg of chloroquine phosphate once a week. On three occasions on the day prior to taking chloroquine, he had a temperature of 38 to 39 °C with chills.

For five weeks after returning to the United States, he continued to take the drug. When seen on Aug 19, 1975, ten days after his last dose of chloroquine, smears for malaria were negative. However, blood taken that day and tested later by the indirect immunofluorescent technique at the Center for Disease Control eventually disclosed the following titers: P falciparum, 1:4,096; P ovale, 1:64; and P malariae, 1:1,024. On Aug 26, 17 days after his last dose, a temperature of 39 °C developed.

Two days later he was admitted to the New York Hospital with a temperature of 40 °C, a palpable spleen tip, and blood smears positive for ring forms of P falciparum. He was given 3.0 g of chloroquine phosphate orally during a three-day period and experienced prompt clinical recovery. On the possibility that he had a mixed infection, he was advised to take primaquine phosphate for 14 days and was discharged. Symptoms have not recurred. His wife never had any clinical or laboratory evidence of malaria.

Conclusion

This report of chloroquine-resistant malaria must not be used to alter immediate advice given to patients going to Africa, especially East Africa, or other parts of the malarious world. The prophylactic dosage remains 500 mg once a week from the week before departure until five or six weeks after return. However, clinicians should be alert to the possibility that even those who have adhered to the recommended regimen may not escape falciparum malaria.

Harry Most, MD, of New York University Medical College confirmed identification of falciparum malaria. This identification was also confirmed by the Center for Disease Control, Atlanta. Phuc Nguyen-Dinh, MD, of Rockefeller University, New York, took cultures that grew malaria parasites. He later shared the material with Carlos C. Campbell, MD, of the Center for Disease Control.

References