CASE REPORT

ARTEMETHER SAVED A PATIENT WITH SEVERE FALCIPARUM MALARIA AFTER QUININE TREATMENT FAILURE (R III TYPE OF QUININE RESISTANCE)

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Quinine has been one of the most effective drugs for the treatment of malaria since its introduction into clinical use several centuries ago. It is the drug of choice in severe falciparum malaria. Although the efficacy of the drug has gradually declined against malaria strains in various parts of Southeast Asia, resistance has not yet become a worldwide problem. Treatment failures from quinine in most cases, are low grade resistance (R I or R II type of response) which are mostly due to inadequate drug dosage (compliance reason). We report a successful treatment with artemether, in a patient with severe falciparum malaria after treatment failure from quinine (R III type of resistance).

In April 1993, we encountered a case of R III type of quinine resistance. A male British patient, 37 years old tourist, had visited Trat Province aproximately 10 days prior to admission. The patient had never been ill with malaria previously.

Five days before his addimission to the Bangkok Hospital for Tropical Diseases, Thailand, he had fever, bodyache and headache, followed 3 days later, by severe headache, high fever, chills and nausea. He was then admitted to a private hospital in Bangkok with a parasite count of 281,000/μl; gametocyte was seen. On admission to the hospital, he was well nourished, ambulatory, and alert, with slightly jaundice. He had adequate urinary output. No other sign of kidney failure was seen. He was immediately treated with quinine 600 mg intravenously every 8 hours. During the course of treatment, the patient had watery diarrhea 2 times. After 36 hours, his condition progressively declined; he became drowsy with vomiting and high fever but urine output was still adequate (100 ml/hour). He was then transferred to the Bangkok Hospital for Tropical Diseases after 5 doses of quinine.

On admission to our hospital, his parasite count rose to 602,700/μl (21% parasitemia). The patient was drowsy, dehydrated, with a temperature of 38.5°C, pulse rate of 100/minute, and blood pressure of 110/70 mmHg. The consciousness rapidly deteriorated; he became stuporose during transfer from the Outpatient Department to the ward and developed coma within 1 hour. He was anemic and slightly jaundiced. The creatinine on admission was 4 mg% with urinary output of 100 ml/hour. The patient was treated with artemether 300 mg intramuscularly, followed by 100 mg every 24 hours for another 4 doses. On the following day after admission, the creatinine rose to 6 mg%. Hemodialysis was then performed despite adequate urinary output. The patient gained consciousness 2 days after treatment. His parasite and fever cleared at 108 and 119 hours after treatment, respectively. He was discharged 10 days after admission. On discharge, he was slightly anemic, with no jaundice but serum creatinine was still 3.4 mg%. During follow-up at 14 day after treatment he was well and creatinine declined to 2.15 mg%. He was able to leave Thailand the following week in good condition.

Plasma quinine level on admission to the Bangkok Hospital for Tropical Diseases was 19.3 μg/ml (approximately 8 hours after the last dose of quinine). This is considered to be trough concentration; maximum concentration must have been much higher. The plasma quinine concentration in this patient should have been adequate (White *et al*, 1983). The MIC for quinine in Thailand has been documented as 10 μg/ml (White *et al*, 1983).

This is a confirmed case of R III type of quinine resistant falciparum malaria in Thailand with adequate plasma quinine concentration. In a previous study

(Looareesuwan *et al*, 1990), the first case of R III type of quinine resistant *P. falciparum* was reported after a full course of intravenous treatment, but a low level of plasma quinine concentration was detected, and therefore the explanation for the apparent drug resistance appeared to be due to pharmacokinetic factors rather than true resistance. In Vietnam and Cambodia (Giboda and Denis, 1988), existence of type III pattern of drug resistance to quinine had been documented; however, adequacy of quinine concentration had not been confirmed and thus the causes of treatment failure could be either from pharmacokinetic factors or true resistance. True resistance can only be confirmed through plasma quinine level monitoring.

It was fortunate that we treated this patient with artemether. Arthemether (as well as artemisinin and artesunate) has been shown to be a rapidly acting antimalarial; the action is faster than any other existing antimalarials (Karbwang *et al*, 1992a; Karbwang *et al*, 1992b; Taylor *et al*, 1993; White *et al*, 1992). We could have lost this patient if artemether was not available in our hospital. We suggest that artemether or artesunate should be made available in this type of situation where multiple durg resistant falciparum malaria is spreading. We can no longer rely on quinine alone for severe malaria.

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