Chloroquine Resistant Malignant Subtertian Malaria Unmasked by Systematic Steroid Therapy

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SUMMARY: We report a case of a Nepalese who developed a recrudescence of malignant falciparum malaria whilst taking systemic corticosteroids. The malaria was resistant to chloroquine at the RI level, the first such case reported from BMH Dharan.

Case Report

Introduction

Corticosteroid therapy has many dangers especially when used in large doses in patients from tropical or subtropical areas. The risk of a recrudescence of pulmonary tuberculosis is well recognised but the reawakening of an immunologically suppressed parasitic infection is less widely appreciated. In this case we feel a prednisolone-induced degradation of cell-mediated immunity was a crucial factor in the recrudescence of previously immunologically suppressed infection with *Plasmodium falciparum*. The parasite was resistant to chloroquine at the RI level, the first such case to be recorded at BMH Dharan.

Clinical Details

A 35 year old Nepalese man was admitted to BMH Dharan in a grossly emaciated state due to pulmonary tuberculosis of six months duration. He had been a resident of Assam for the previous 15 years. Examination revealed widespread pulmonary crepitations and evidence of marked weight loss but no other abnormal signs. He was afebrile. Chest x-ray revealed cavitating tuberculosis throughout both lung fields. In addition he had a microcytic anaemia (haemoglobin 5.6 gm/dl) and numerous ova of hookworm in his faeces.

He was commenced on streptomycin 0.75g daily, INAH 300 mg daily, rifampicin 450 mg daily and pyrazinamide 500 mg three times daily. In addition he was given buprenorphine and because of his very poor general condition prednisolone 20 mg thrice daily. By the seventh day he was improved and the prednisolone was reduced to 10 mg three times daily. He continued to improve and remained afebrile until day 30 when he suddenly had a severe rigor accompanied by malaise and

headache. His temperature spiked briefly to 40°C. Two further brief paroxysms of high fever occurred at intervals of 30-40 hours. Thick and thin blood films revealed a low grade *Plasmodium falciparum* parasitaemia. The steroid therapy was rapidly reduced to nil and chloroquine given by mouth 600 mg followed by 300 mg six hours later then 150 mg twice daily for two days. Within two days of chloroquine therapy the rigors and spiking fevers ceased although a low grade pyrexia, never exceeding 38°C and probably due to the tuberculosis persisted. Two repeat blood films showed no evidence of malaria parasites. He continued to improve gradually until 12 days after the end of the chloroquine therapy when the periodic fever recurred. Thick and thin blood films confirmed a recurrence of the falciparum parasitaemia. He was then given oral quinine 600 mg twice daily for four days followed by fansidar three tablets as a single dose which affected rapid and permanent cure of the malaria. The anti tuberculosis therapy was continued with good effect.

Discussion

Chloroquine resistant falciparum malaria is an increasing problem in many parts of the world. It is well established in the north-eastern part of the Indian subcontinent in areas close to or bordering Nepal such as Bangladesh and the Indian states of Assam, Orissa, Uttar, Andhra and Madhya Pradesh¹. The distribution of chloroquine resistant malaria in Nepal itself is poorly documented but cases have been reported from the Makwanpur district south of Kathmandu¹. As Uttar Pradesh borders south central Nepal that area of the Terai zone must be regarded as highly suspect. All types of malaria are uncommon in the area around BMH Dharan (Koshi zone) and as far as we can tell no cases of chloroquine resistance have been recorded previ-

ously. We feel the patient almost certainly contracted malaria in Assam but remained asymptomatic because of acquired immunity. The presence of such a case in BMH Dharan has important implications with regard to the management of future cases of falciparum malaria. Patients from areas of known chloroquine resistance, those from the east and central Terai zone or the far east of Nepal should probably be regarded as potentially chloroquine resistant and treated primarily with quinine plus fansidar. Some considerations might be given to a treatment policy which assumes chloroquine resistance in all patients from Nepal and north-eastern India rather than risk the delay consequent upon chloroquine failure.

Although the emergence of clinical malaria thirty days after the initiation of high dose prednisolone does not prove a causal relationship it seems probable that such a relationship existed. The immune response to malaria is complex and incompletely understood². Both humoral and cell mediated mech-

anisms, particularly T-lymphocytes are involved². The patient's immunocompetence was probably already compromised by the undernutrition due to the pulmonary tuberculosis³. Prednisolone which impairs cell-mediated immunity probably produced a critical degradation in the latter allowing the recrudescence of the previously suppressed malaria. This highlights another potential hazard of steroid therapy to patients potentially harbouring dangerous invasive parasites. Army physicians dealing with patients from all over the globe and especially those treating Gurkha soldiers and families need to be especially vigilant.

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