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Plasmodium falciparum: inhibition/reversal of cytoadherence of Thai isolates to melanoma cells by local immune sera

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SUMMARY

The effect of sera on the cytoadherence *in vitro* of *Plasmodium falciparum*-infected erythrocytes to melanoma cells was examined. Sera from 19 healthy individuals living in endemic malarious areas in Thailand and 24 patients with *P. falciparum* malaria were tested against four local *P. falciparum* isolates. Out of 57 sera examined, 12 (21%) showed significant inhibition (> 50%) of cytoadherence for at least one isolate. Anti-malarial IgG antibody titres were determined for all 57 sera and although 11 of the 12 inhibitory sera had relatively high titres, 36 out of 47 sera with similarly high titres showed no significant inhibitory activity. Convalescent sera were no more effective than corresponding acute sera in inhibiting the cytoadherence of erythrocytes infected with any of the four heterologous isolates examined. Sera which significantly inhibited cytoadherence were also capable of reversing cytoadherence, and pooled plasma, from healthy individuals living in malarious areas, was effective in significantly reversing the *in vitro* cytoadherence of all the five parasite isolates examined. The results confirm the antibody mediated strain-specific nature of the inhibition of cytoadherence and stress the difficulty in selecting immune sera potentially useful for the immunotherapy of cerebral malaria patients in Thailand.

Keywords *Plasmodium falciparum* cerebral malaria cytoadherence melanoma cells

INTRODUCTION

Plasmodium falciparum infection in man is characterized by the sequestration of erythrocytes containing mature stages of the parasite in deep vascular beds (Clark & Tomlinson, 1949). Electron microscopic studies of immediate postmortem tissues have demonstrated the preferred sites of sequestration to be the brain and heart, where parasitized erythrocytes adhere to the post-capillary venular endothelium (MacPherson *et al.*, 1985). The resulting microcirculatory obstruction is thought to be the basis of complications such as cerebral malaria (Phillips & Warrell, 1986; Warrell, 1987).

An *in vitro* correlate of sequestration has been developed in which erythrocytes containing trophozoites and schizonts specifically bind to monolayers of endothelial cells (Udeinya *et al.*, 1981) or melanoma cells (Schmidt *et al.*, 1982). Using the melanoma cell binding assay (MCBA), cytoadherence has been shown to be not only inhibited, but also reversed by homologous immune serum (David *et al.*, 1983; Udeinya *et al.*, 1983). This observation could be reproduced *in vivo* where the infusion of immune serum into squirrel monkeys led to a sharp increase in the number of trophozoite- and schizont-infected erythrocytes in the peripheral blood within minutes of serum administration (David *et al.*, 1983). The parasitized erythrocytes that were flushed out were rapidly cleared, as the parasitaemia reduced drastically within 24 h of serum transfer and continued to decrease to undetectable levels without specific antimalarial therapy. These observations suggest an important role for antibodies in inhibiting and reversing cytoadherence, and raise the possibility of using intravenous immunotherapy as an emergency treatment of cerebral malaria. Cerebral malaria is the major complication of *P. falciparum* infections and still carries a mortality of 20–50% despite optimal medical management (Warrell *et al.*, 1982). In some parts of the world, particularly in Thailand, the extent of drug resistance is a major problem and many research groups are now actively looking to alternatives to quinine therapy.

Before seriously considering any immunotherapy trials in patients with cerebral malaria in Thailand, it was important to establish the following:

(1) Can immune serum from individuals in Thailand inhibit or reverse the cytoadherence of Thai *P. falciparum* isolates to melanoma cells? (2) What is the degree of parasite strain

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