Peripheral Gangrene in a Case of Complicated Falciparum Malaria

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Abstract
Peripheral gangrene occurring as a rare manifestation of complicated falciparum malaria in a 65 year old lady has been reported. Clinical features and pathogenesis are discussed.

Key words
Complicated falciparum malaria, Symmetrical peripheral gangrene, Disseminated intravascular coagulation.

Introduction
Symmetrical peripheral gangrene (SPG) is a rare clinical condition which manifests as acral ischaemic damage in two or more extremities without any evidence of obstruction or vasculitis of the relevant artery. This condition has been described in association with a multitude of medical conditions, commoner among them being infections, low output states like myocardial infarction, shock, congestive cardiac failure, or use of vasopressors such as dopamine. SPG is very rarely reported in falciparum malaria and only eight cases have been described in the literature, six of them from India. We report this case as a rare manifestation of complicated falciparum malaria.

Case report
A 65-year-old lady presented to our medical emergency department with history of high-grade fever with chills and rigors for 8-10 days and loss of consciousness for the last 24 hours. On examination, she was in altered sensorium (GCS-7) with mild dehydration. Pulse rate was 108/min., BP 100/70 mm Hg. with respiratory rate of 22/min. She was markedly pale and icteric. All peripheral pulses were palpable. She had hepatomegaly of 3cm below right costal margin and spleen just palpable below the left costal margin. Rest of the systemic examination was unremarkable.

Her peripheral blood smear was found to be positive for asexual forms of Plasmodium falciparum for which she was treated with intravenous quinine dihydrochloride 600 mg eight hourly and parenteral fluids. She regained her consciousness after 48 hours of treatment. However, on the 4th day of hospitalisation, she developed dusky discoloration on the middle and terminal phalanges of all the fingers of the right hand, and over the heel and middle toe of the left foot which progressed to dry gangrene in next 1-2 days (Fig. 1). On advice of the surgeons, she was started on low molecular weight dextran and pentoxifylline infusions. Two units of whole blood were transfused for correction of anaemia. By the 6th day of her hospital stay, her condition stabilised and her gangrene remained localised to the areas mentioned above. All her peripheral pulses remained palpable in all four limbs. She was

Fig. 1: Clinical Photograph showing gangrene in the phalanges of right hand, and over the heal and middle toe of left foot.
subsequently referred to the surgeons for amputation of gangrenous digits of the right hand following development of line of demarcation between gangrenous and healthy tissues.

Laboratory investigations showed: Hb. 3.2 g/dl and TLC 17,700/mm³ with 80% polymorphs. Peripheral blood smears were positive for *Plasmodium falciparum* with nucleated RBCs 14/100. Blood urea was 150 mg/dl and serum creatinine 1.4 mg/dl. The CSF examination was normal. Blood cultures were sterile. G6PD was not deficient. HbsAg, anti-HCV, anti-nuclear antibodies, rheumatoid factor, and cryoglobulins were negative. Blood coagulation profile was normal with platelet count of 1,56,000/mm³. Blood could not be tested for fibrin degradation products (FDPs). However evidence of disseminated intravascular coagulation (DIC) was seen in the skin biopsies obtained from the junction of normal and gangrenous areas. Fibrin deposits, almost occluding the lumen of all the dermal vessels, were seen alongwith perivascular infiltration. Echocardiography did not reveal any evidence of thrombus or vegetation.

Discussion

SPG has been reported in a multitude of medical conditions including falciparum malaria. Our patient had no clinical or laboratory evidence of other common causes of SPG such as sepsis, vasospastic conditions like Raynaud’s phenomenon, ergot poisoning, or vasopressor use. Also there was no evidence of vasculitis, cryoglobulinaemia, polycythaemia, or thrombocythaemia. Patient remained haemodynamically stable throughout. DIC is the most common pathogenic mechanism in majority of cases of SPG². All the cases of falciparum malaria with SPG² reported in the literature had evidence of DIC²-⁶. A functionally active but controlled coagulatory state exists in falciparum malaria even in uncomplicated cases⁷. Elevations in the concentration of FDPs reflecting the ongoing fibrinolysis have been documented⁸. Heavy parasitaemia triggering the coagulation pathway⁹, alterations in the lipid distribution across the surface membranes of the parasitised erythrocytes activating the intrinsic coagulation cascade¹⁰, and activation of the complement system¹⁰ have all been proposed as likely mechanisms for DIC in falciparum malaria. Sequestration of the parasitised erythrocytes in the microcirculation by molecular interactions with endothelial receptors, chiefly intracellular adhesion molecule-1 (ICAM-1) may occur⁸,¹¹. Rosetting of the uninfected erythrocytes around parasitised red cells also occurs and these multicellular aggregates further exacerbate the vascular obstructions caused by sequestration. Though the biochemical evidence of DIC was lacking in our patient, yet demonstration of the intravascular fibrin deposits in dermal vessels of the affected regions leaves no doubt about the presence of DIC as the pathogenic mechanism of SPG in this patient. The initial procoagulant stage of DIC is followed by the stage of consumptive coagulopathy with depletion of platelets, fibrinogen, and other coagulation proteins with widespread bleeding manifestations. However, DIC in this case may have been arrested in the initial procoagulant stage by effective management of falciparum infection with quinine dihydrochloride therapy before consumptive coagulopathy could set in. This would also explain the non-extension of the ischaemic damage while under observation in hospital. This association of complicated falciparum malaria with SPG, though very rare, is perhaps under-reported in literature.

References