

# CASE REPORT

## SYMMETRIC PERIPHERAL GANGRENE OF THE LOWER LIMBS IN A CASE OF COMPLICATED FALCIPARUM MALARIA

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**Abstract.** Association of symmetric peripheral gangrene (SPG) with falciparum malaria infection is a relatively uncommon clinical entity. Here we report a case of complicated falciparum malaria with SPG involving both lower limbs from the mid-calf downwards, probably due to antibody mediated vasculitis.

### INTRODUCTION

Though falciparum malaria is known for its various pernicious and atypical manifestations, peripheral vascular manifestations are rarely seen (Gopinathan and Subramanian, 1982). SPG was first described by Hutchinson in 1981 (Molos and Hall, 1985). Reported cases are few and are mostly from India. Sharma (1987) reported a case of cutaneous gangrene from Rajasthan (India) and a similar case was reported by Thapa *et al* (1987) in the same year from Chandigarh (India). Subsequently Anuradha *et al* (1999), Sharanabasawappa (2000), Kakati *et al* (2004), Thanachartwet *et al* (2006) and Agarwal *et al* (2007) reported cases of SPG in association with falciparum malaria from different parts of India. SPG is defined as symmetrical distal ischemic damage of two or more sites in the absence of large vessel obstruction. Though classically it accompanies various infectious diseases and decreased flow states, such as cardiogenic and hypovolemic

shock, it is seen in the presence of bacterial, viral and rickettsial infections. It is also reported as a complication of paraneoplastic syndrome, ergot poisoning, Raynaud's phenomenon, polymyalgia rheumatica, C-reactive protein deficiency and sickle cell disease. The condition may also be precipitated by the use of vasopressor drugs.

### CASE REPORT

A 12-year-old boy presented to the emergency department of Downtown Hospital in Guwahati, India with a history of high fever with rigors of 10 days duration, inability to stand or walk for 6 days prior to hospital admission with pain and change in color of the skin of both lower limbs for 2 days. There was no history of joint pain in the upper limbs, rash, hematuria or evidence of bleeding disorder suggestive of disseminated intravascular coagulation (DIC). There was no history of jaundice and the urine output was normal. The patient lives in a malaria endemic area (Tura district of Meghalaya, India) and had a previous history of fever in the past.

On physical examination, the patient appeared ill, was febrile, conscious, oriented, and

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had mild pallor. Dehydration, cyanosis, clubbing and icterus were absent. On admission the axillary temperature was 37.5°C, pulse rate was 76/minute, blood pressure 110/70 mmHg with a respiratory rate of 24/minute. Abdominal examination revealed mild hepatosplenomegaly. Examination of respiratory, cardiovascular and neurological systems were normal. On examination bluish black discoloration was present in both lower limbs from mid calf down with a line of demarcation (Figs 1 and 2). The area was cold to touch, the calf muscles were tender on palpation. Pain sensation was present at the ankle and above, but absent distal to the ankle. Posterior tibial and dorsalis pedis arterial pulsations were absent bilaterally, but femoral and popliteal arterial pulsa-

tions were normal. There were no changes in the upper limbs or nose. Peripheral pulsations in both upper limbs were normal. Trophic changes were seen in the distal parts of the toes and heels but scaling was minimal.

Laboratory examinations revealed a Hb of 7.0 g/dl, WBC was 17,600/mm<sup>3</sup> with 83% polymorphs, and the ESR 130 mm 1 hour. The peripheral blood smear revealed 200 ring forms and 5 gametocytes of *Plasmodium falciparum*/1,000 RBC. The rapid diagnostic test (Optimal) was positive for *Plasmodium falciparum*, the platelet count was 166,000/mm<sup>3</sup>, the prothrombin time (PT) was 17 seconds (control 17 seconds), the activated partial thromboplastin time (APTT) was 35 seconds (control 30-35 seconds), the bleeding



Fig 1



Fig 2

Fig 1,2—Symmetric peripheral gangrene of lower limbs showing bluish black discoloration from mid calf down with a line of demarcation.

time and clotting time were normal. Blood chemistry revealed a serum bilirubin of 0.9 mg/dl, the SGOT was 741 IU/l, the SGPT was 343 IU/l, the blood sugar was 101 mg/dl, the blood urea was 56.24 mg/dl and the serum creatinine was 0.82 mg/dl. The blood cultures (3 samples) were negative. Hemoglobin electrophoresis, protein C, protein S, fibrinogen level, fibrin degradation products, and serum electrolytes were normal. The sickling test, Mantoux test, HIV, VDRL, HBsAg and antiHCV test results were negative. Routine urine examination was normal and urine culture was negative. The anti-nuclear antibody (ANA) was positive and cytoplasmic anti-neutrophil cytoplasmic antibody (C-ANCA) was also positive. Perinuclear antineutrophil cytoplasmic antibody (P-ANCA), double stranded DNA, rheumatoid factor and C-reactive protein (CRP) were negative. Ultrasonography of the abdomen revealed mild hepatosplenomegaly. The chest X-ray and leg X-rays and 2D Echo were normal. Vascular Biopsy could not be done because the family did not give consent for biopsy. Color doppler revealed significant arterial narrowing >98% in both legs below the calf suggestive of arteritis. The abdominal aorta, renal, femoral and popliteal arteries were normal.

Treatment was started with iv quinine and supportive measures. After 5 days of treatment the patient became afebrile, began feeling better, the color of the skin and sensation improved at the ankles and above. The peripheral blood smear became negative for *Plasmodium falciparum* and the color doppler showed significant improvement. However there was no improvement in the color of the skin over the toes. The patient was referred to the pediatric surgery department and amputation of both feet was planned but the parents refused. The patient was discharged on oral quinine for a total of 10 days, oral iron and multivitamins. He was then lost to follow-up.

## DISCUSSION

Although the association between SPG and *Plasmodium falciparum* malaria is occasionally reported in the literature, it is a relatively rare complication of falciparum malaria. The most common cause of SPG is septicemia. Our patient had no clinical or laboratory evidence of septicemia or other possible causes of SPG, such as vasospastic conditions, Raynaud's phenomenon, ergot poisoning, diabetes mellitus or frost bite. There was no history of immunosuppression or the use of vesopressor agents. There was definite evidence of *Plasmodium falciparum* infection. In a patient reported by Anuradha *et al* (1999) features of DIC were evident on investigation without clinical manifestations of a bleeding disorder. Though DIC is commonly implicated in SPG it is based on laboratory documentation only and not on the clinical profile. According to Agarwal *et al* (2007) the cause of SPG is most likely due to interaction between parasite factors (cytoadherence, sequestration to micro circulation) and host factors (sluggish circulation because of dehydration and hypoxia due to anemia). Our patient did not have any clinical or laboratory evidence of DIC.

Sharma (1987) explained the possibility of vasculitis of cutaneous capillaries of the periphery by the malaria parasite in addition to an immune vasculitic reaction to the malaria antigen, which resulted in capillary occlusion and epidermal gangrene. Various autoantibodies, such as ANA and antineutrophil cytoplasmic antibodies (ANCA) develop in the presence of falciparum malaria infection (Yahya *et al*, 1997). In cases of repeated malarial infections in susceptible individuals vasculitis may develop through ANCA pathways (Pradhan *et al*, 2002). In our case the C-ANCA was positive, which in association of other antibodies may have caused vasculitis leading to SPG.

## ACKNOWLEDGEMENT

We are grateful to the authorities of the Downtown Hospital in Guwahati, India, for allowing us to publish this case report.

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