CASE REPORT

Symmetrical peripheral gangrene due to *Plasmodium falciparum* malariaNasar Abdali,¹ Azharuddin Mohammed Malik,¹ Athar Kamal,¹ Mehtab Ahmad²¹Department of Medicine, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India²Department of Radiodiagnosis, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

Correspondence to

Dr Azharuddin Mohammed Malik,
malikazharuddin@gmail.com

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SUMMARY

A 45-year-old man presented with a 4-day history of high-grade fever with rigours and a 2-day history of painful bluish black discolouration of extremities (acrocyanosis). He was haemodynamically stable and all peripheral pulses palpable, but the extremities were cold with gangrene involving bilateral fingers and toes. Mild splenomegaly was present on abdominal examination but rest of the physical examinations were normal. On investigating he was found to have anaemia, thrombocytopaenia with gametocytes of *Plasmodium falciparum* on peripheral blood smear. His blood was uncoagulable during performance of prothrombin time with a raised D-dimer. Oxygen saturation was normal and the arterial Doppler test showed reduced blood flow to the extremities. A diagnosis of complicated *P. falciparum* malaria with disseminated intravascular coagulation (DIC) leading to symmetrical peripheral gangrene was performed. Artemisinin combination therapy was started and heparin was given for DIC. A final line of demarcation of gangrene started forming by 12th day.

BACKGROUND

Malaria is one of the major health problems worldwide affecting nearly 300–500 million people causing 1–2.7 million deaths per year.¹ Symmetrical peripheral gangrene (SPG) usually manifests as symmetrical involvement of two or more extremities without large vessel obstruction. This is may be due to sepsis, low cardiac output states especially with the use of vasopressors, vaso-spastic conditions, myeloproliferative disorders or in hyperviscosity syndrome.² SPG can also be a rare manifestation of *Plasmodium falciparum* malaria, which is mainly attributed to disseminated intravascular coagulation (DIC).³ We report a case of SPG caused by *P. falciparum*.

CASE PRESENTATION

A 45-year-old man, a farmer by occupation, non-smoker and non-alcoholic presented with a 4 day history of high-grade fever with rigours and a 2 day history of painful bluish black discolouration of the extremities (acrocyanosis) (figure 1). There was no history of diabetes mellitus, hypertension, recent trauma to limbs, exposure to cold, drug intake and rashes over body or bleeding from any site. He was haemodynamically stable though his peripheries were cold with gangrene involving bilateral fingers and toes. All of his peripheral pulses were palpable with no radioradial or radiofemoral delay. His respiratory and cardiovascular

Figure 1 Clinical photograph of the patient showing established gangrene with visible line of demarcation in the fingers of bilateral hands and pre-gangrenous changes in bilateral toes; also seen are the purpuric spots on the legs.

system examinations were normal; however, mild splenomegaly was present on per abdominal examination.

INVESTIGATIONS

The patient's haemoglobin was 8.2 g/dL, total leucocyte count $8.2 \times 10^3/\text{mm}^3$, platelets $18\,000/\text{mm}^3$, prothrombin time was unmeasurable (blood not coagulable), liver transaminases were raised with aspartate transaminase of 212 IU/L and alanine aminotransferase 227 IU/L. D-dimer was 2.2 mg/L FEU (fibrinogen equivalent units). Rest of the biochemical investigations were normal with a random plasma glucose of 110 g/dL, blood urea 24 mg/dL and serum creatinine 1.3 mg/dL. Peripheral smear showed gametocytes of *P. falciparum*. Total parasite load was $70\,000/\mu\text{L}$. Ultrasonography of the abdomen suggested mild splenomegaly. Arterial Doppler of the lower limbs revealed normal flow in the femorals and the popliteal, with slightly reduced flow in the dorsalis pedis with no distal flow bilaterally. In the upper limbs, the peak systolic velocity was decreased with sluggish flow in the proximal arteries with no flow in the distal arteries bilaterally. MR angiography of the upper limbs showed no focal/diffuse stenosis or arterial wall thickening/enhancement in any large vessel of the extremities; however, it showed absent terminal flow in the distal arteries in bilateral upper and lower limbs (figure 2). The patient had normal chest X-ray, echocardiography and negative anti-nuclear autoantibodies, Scl-70, anticardiolipin antibody, dengue serology and viral hepatitis markers.

TREATMENT

A diagnosis of complicated *P. falciparum* malaria with malarial hepatitis, anaemia and DIC was performed. The patient was treated with intravenous fluids; intravenous artesunate was started along with

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Figure 2 MR angiogram of the bilateral upper limb showing normal visualisation of arteries and veins of the forearm and palm. However, there is absent terminal flow in the digital arteries especially of the left hand.

oral mefloquine. Intravenous ceftriaxone was given for the prevention of Gram-negative septicaemia. Fresh frozen plasma was transfused to normalise International Normalised Ratio after which heparin was started.

OUTCOME AND FOLLOW-UP

The patient became afebrile 3 days after admission and the progression of gangrene stopped after 4 days. He was managed conservatively and a line of demarcation of gangrenous portion of the fingers started becoming apparent by 12th day. There was adequate return of circulation to the toes and there was no line of demarcation in the toes. The patient was apprised regarding the development of autoamputation of the affected fingers and was attached with the plastic and reconstructive surgery department for further rehabilitation of his hand.

DISCUSSION

SPG is defined as symmetrical ischaemic damage at two or more peripheral sites in the absence of large vessel obstruction.² SPG is commonly due to the underlying DIC accounting for about 85% of all cases and it can be considered a peripheral manifestation of DIC.⁴ DIC causing SPG may be secondary to sepsis, viral fever such as dengue and uncommonly due to complicated malaria.^{3–5} Apart from DIC other causes leading to SPG are complication of hyperviscosity syndromes, ergotism, inherited prothrombotic disorders, hypovolemic shock and administration of vasopressors such as norepinephrine.⁶

Although the precise mechanism of DIC due to *P. falciparum* is not well understood, excessive antigen load caused by severe parasitaemia leading to complement system activation and triggering the coagulation pathway has been proposed.⁷ Alteration in the lipid distribution of the inner and outer surface of the erythrocyte membrane has also been proposed to cause procoagulant activity as well as microvascular obstruction.⁸ The

presence of SPG portends a poor prognosis with high mortality and amputation rates.⁹ Treatment of SPG is largely empirical with treatment of the underlying cause. Use of vasopressors as well as early amputation should be avoided giving time for the formation of a line of demarcation and resolution of any associated infection.⁶ Cautious use of heparin can be useful for associated DIC. Other modalities that can be tried are sympathetic ganglion blockade, intravenous vasodilators such as nitroglycerine, phentolamine and prostaglandin (epoprostenol). However, papaverine, dextran and hyperbaric oxygen therapy have not been shown to be beneficial.¹⁰

Learning points

- ▶ Symmetrical peripheral gangrene (SPG) may occur in patients with *Plasmodium falciparum* malaria.
- ▶ SPG is usually a marker of underlying disseminated intravascular coagulation in these patients.
- ▶ Presence of SPG is associated with significantly adverse prognosis.
- ▶ Management of SPG is unsatisfactory with many patients ending with amputations, early diagnosis and management of the underlying condition has the potential to improve prognosis.

Contributors NA, AMM and AK were involved in patient evaluation and care, MA was involved in the performance of diagnostic studies such as MRA and colour Doppler. All authors contributed to manuscript preparation and approval.

Competing interests None.

Patient consent Obtained.

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