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Case Report

Symmetrical peripheral gangrene in an atypical case of *Plasmodium falciparum* malaria with HIV coinfection

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ABSTRACT

Malaria is a vector-borne tropical disease well known for causing a multitude of complications. One such rare but familiar complication is symmetrical peripheral gangrene (SPG). SPG is a distinct entity resulting from a horde of infectious and non-infectious illnesses. We report the case of a 32-year-old male infected with *Plasmodium falciparum* malaria and Human Immunodeficiency Virus who presented to us with renal failure and developed SPG of both feet 3 days into admission.

Keywords: Symmetrical peripheral gangrene, Falciparum malaria, Human immunodeficiency virus

INTRODUCTION

Symmetrical peripheral gangrene (SPG) is defined as ischemia of the distal parts of two or more limbs unaccompanied by any major arterial obstruction or arteritis.[1] A multitude of infective and non-infective conditions can give rise to SPG. These include bacteria, viruses, parasites, vasopressive, or vasospastic drugs (Dopamine, adrenaline, nor-adrenaline, and ergotamine), shock, and hypercoagulable states. The common mechanisms for the causation of SPG which prevail in these conditions are stasis and hypercoagulability culminating in obstruction of the microcirculation.[2] This leads to digital ischemia. Falciparum malaria is complicated by disseminated intravascular coagulation (DIC) and occlusion of microcirculation by both microthrombi and parasitized erythrocytes which rarely may cause SPG.[3-5]

CASE REPORT

A 32-year-old male presented to the medical emergency with chief complaints of abdominal pain, loose stools, and oliguria for 3 days. There was no history of fever. He was pale, drowsy, and tachycardiac on examination with a Glasgow Coma Scale of 13/15, pulse rate of 110/min, regular, and all the peripheral pulses were felt. His blood pressure was 90/60 mmHg and his random blood sugar was 118 mg%. His cardiovascular, respiratory, and per abdominal examinations did not detect any abnormality. His hemoglobin was 8 g%, total leukocyte count was 10,000/μL, platelets were 40,000/μL, aspartate transaminase/alanine transaminase: 396/406 IU/L, Kidney function test: urea/creatinine were 328/7.67 mg/dL. The initial peripheral smear was only suggestive of normocytic normochromic anemia. In the course of the admission, his hemoglobin started declining rapidly without bleeding. His serum lactate dehydrogenase was 3000 and haptoglobin was undetectable. He tested positive for Histidine Rich Protein-2 (HRP-2) antigen and the peripheral smear of the quantitative buffy coat revealed trophozoites and gametocytes of *Plasmodium falciparum*. He was treated with an injection of Artesunate, Clindamycin, and underwent dialysis. His sensorium started improving. On day 3 of admission, he developed black discoloration of the toes of both his legs [Figure 1]. On local examination, the toes of both his legs had turned black, were cold, and had normal pulses. The discoloration gradually progressed to involve the forefeet. There was no history of rash on the face or body, recurrent oral ulcers, joint pain, claudication, Raynaud phenomenon, hypertension, or diabetes mellitus. There was a history of alcohol use but he had been reformed for more than 2 months and denied intake after that. The urinary toxicological screen was negative. Arterial and venous Doppler of both the lower limbs was normal. Coagulation profile revealed disseminated intravascular coagulation (DIC): Prothrombin time (PT) was 30 s, activated partial thromboplastin time (aPTT) was 66 s, International normalized ratio (INR) was

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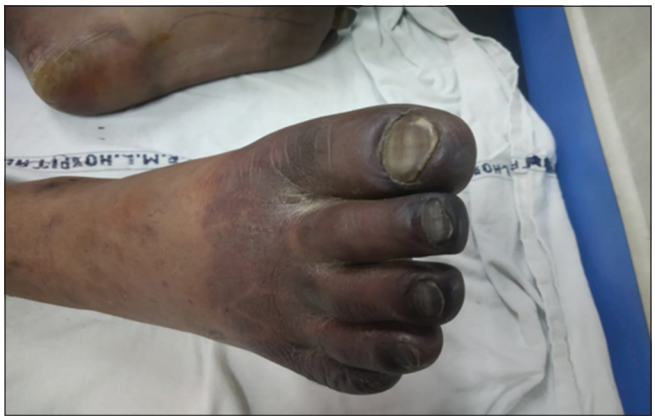

Figure 1: Blackish discoloration of both forefeet i.e. gangrenous changes (Day 5 of admission).

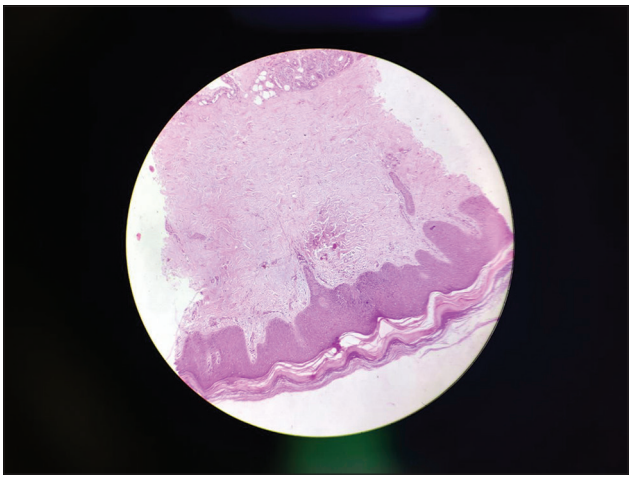

Figure 2: Skin biopsy showing epidermal acanthosis and parakeratosis. Edematous dermis with perivascular mixed inflammation. No definite evidence of vasculitis.

Figure 3: Mummification of toes and forefeet (Day 15 of admission).

3.1, d dimer was 5000, and Fibrinogen was 216. He tested reactive for antibodies against human immunodeficiency virus (HIV)-II. Hepatitis B surface antigen, anti-hepatitis C virus antibody, antinuclear antibody (ANA), antineutrophilic cytoplasmic antibodies, antiphospholipid antibodies, 2-D echocardiography, electrocardiogram, blood culture, rheumatoid factor test, Venereal Disease Research Laboratory test, and Coombs test were negative. Skin biopsy revealed epidermal hyperkeratosis and dermal edema with perivascular mixed inflammation [Figure 2]. There was no evidence of vasculitis. Direct immunofluorescence was negative for immunoglobulin (Ig)A, IgG, or C3 deposits. He was treated for HIV with complicated falciparum malaria-associated SPG. The patient had symptomatic relief with a resolution of acute kidney injury and coagulopathy but blackish discoloration was persistent with the mummification of the toes [Figure 3]. He started complaining of hemoptysis after 20 days of hospital admission. Contrast-enhanced computed tomography of the thorax revealed pulmonary tuberculosis to which he unfortunately succumbed eventually.

DISCUSSION

This case was an atypical case of malaria as the patient did not present with fever but rather with renal failure. His presentation impelled us to consider atypical hemolytic uremic syndrome for which he underwent dialysis. HRP-2 antigen testing was also done considering the endemicity of malaria in India and evidence of hemolysis.

P. falciparum is notorious for causing cytoadherence, that is, attachment of infected red blood cells to endothelium and rosetting of the uninfected erythrocytes leading to microvascular occlusion[6] The adhesive surface proteins upregulated over the erythrocyte membrane attach to the vascular endothelium. Some of these endothelial receptors are a cluster of differentiation 36, intercellular adhesion molecule 1, thrombospondin, vascular cell adhesion molecule-1, endothelial leukocyte adhesion molecule-1, and HRP.[7]

Another plausible mechanism for SPG in Falciparum malaria is DIC. The parasitized erythrocytes activate the intrinsic coagulation pathway and the complement system. This results in the procoagulant phase of DIC followed by the phase of consumptive coagulopathy which leads to thrombocytopenia and depletion in fibrinogen, and other coagulation proteins with bleeding manifestations.[8]

DIC was the probable mechanism of SPG in our case confirmed with thrombocytopenia, raised d dimer, PT, aPTT, and INR. Literature supporting an association between falciparum malaria and SPG includes Kumbhalkar *et al.*[8] and Anuradha *et al.*[9]

HIV is also among the causes of SPG.[2] Gangrene in HIV may occur secondary to arterial occlusion or vasculitis.[10] Even though the patient tested positive for Human immunodeficiency virus, the skin biopsy did not reveal any evidence of vasculitis thus, ruling it out as a source of SPG.

All other causes of SPG both infective and non-infective, were ruled out. Thus, it is inferred that this patient suffered SPG because of *P. falciparum* malaria.

SPG heralds a high amputation rate and fatality.[3] Therefore, it must be recognized promptly and the underlying cause should be diagnosed for swift and effective management. The treatment of SPG in malaria comprises antimalarials and supportive care.

CONCLUSION

SPG is a tragic complication of numerous diseases as it may cost a person his limb or life. A comprehensive clinical history and examination with appropriate investigations are pertinent in determining its cause. Malaria is one such common cause of this uncommon entity. Therefore, in an endemic country, malaria must be suspected strongly in a patient with SPG.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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