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journal homepage: www.jpascasereports.comMalaria-associated peripheral gangrene[☆]Deborah B. Martins^b, Vanda Amado^a, Stella Langa^a, Joyce Ventura^a, Atanasio Taela^a, Daniel A. DeUgarte^{b,*}^a Central Hospital of Maputo, Mozambique^b Department of Surgery, UCLA, USA

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ABSTRACT

Malaria is a common parasitic disease endemic in tropical and subtropical areas, including Mozambique. Symmetrical peripheral gangrene is a rare complication of malaria. The purpose of this study was to review cases of malaria-associated peripheral gangrene that were evaluated by the pediatric surgical service at Hospital Central. Four patients ranging in age from 11 months to 7 years with documented *Plasmodium falciparum* infection and peripheral gangrene were identified. Amputation was required in cases of wet-gangrene. The majority of cases were allowed to self-demarcate, and one was allowed to auto-amputate.

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Malaria is the leading cause of childhood mortality in Mozambique, reportedly killing about 27,612 children in 2010 with the disease accounting for a large proportion of out-patient consultations and in-patients in pediatric wards [1]. Symmetrical peripheral gangrene is a rare and severe complication of malaria in which there is distal ischemic damage without the presence of a vascular occlusive disease in two or more extremities [2]. We describe four cases with documented *Plasmodium falciparum* infection and peripheral gangrene that presented to the pediatric general surgical ward at the Hospital Central–Maputo.

1. Case 1

An 11-month-old boy presented with sepsis and required vasopressor support (dopamine/noradrenaline) to maintain blood pressure. On examination, he was noted to have peripheral gangrene in all extremities. Wound care was initiated to prevent

infection. The extremities were observed and allowed to self-demarcate and auto-amputate (Fig. 1).

2. Case 2

A 3-year-old boy was evaluated for lower extremity pain a couple of weeks following initiation of treatment for malaria. On examination, he was found to have gangrene of the right foot and the 3rd, 4th, and 5th digits of the left foot (Fig. 2). The patient was lost to follow up.

3. Case 3

A 6-year-old boy was transferred with malaria complicated by sepsis, hepatitis, and acute renal failure. On examination, he was noted to have bullae of the anteromedial aspect of the right lower leg and gangrene of the ankle and foot. In addition, he was noted to have patchy gangrene of the left foot. He ultimately underwent a right trans-metatarsal amputation and subsequent skin grafting (Fig. 3).

4. Case 4

A 7-year-old girl was admitted with cerebral malaria, hepatitis, and sepsis. On examination, the patient was noted to have left hand gangrene and a contracture. In addition, the patient developed

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Fig. 1. Case 1. A. Peripheral gangrene in all extremities. B. Follow up after self-demarcation and auto-amputation.

patchy gangrene in the left arm following subcutaneous infiltration of an IV infusion. The patient developed wet gangrene and underwent amputation at the level of the wrist (Fig. 4).

5. Discussion

Symmetrical peripheral gangrene is an extremely rare complication of malaria, reported in adults more often than in children [3]. To our knowledge, this is the first reported series of malaria-associated peripheral gangrene in young African children. In addition, we report a case of malaria-associated peripheral gangrene that was not symmetrical in that it involved only one extremity. As in other reported cases, *Plasmodium falciparum* was the responsible parasite. The reported mortality rate for malaria complicated by

peripheral gangrene may be as high as 35%, with an amputation rate of 70–90% [4].

Several theories have been postulated to explain the pathophysiology of malaria-associated peripheral gangrene. One theory is that parasitemia results in activation of the intrinsic coagulation pathway or complement system [5]. Parasite-infected erythrocytes interact with endothelial receptors, leading to adhesion and sequestration of the erythrocytes and consequently obstruction of small vessels [6]. This is the most likely mechanism of intravascular thrombosis leading to peripheral gangrene in malaria infections. Another theory is that parasitized erythrocytes, which are less deformable, experience mechanical ‘sludging’ in the microvasculature as is believed to occur in cerebral malaria [7]. Microvascular occlusion may propagate proximally and result in distal ischemia and necrosis. Microthrombi found in amputated specimens further corroborates this as a possible mechanism [7].

Host factors like hypotension, an inflammatory response, and the development of disseminated intravascular coagulation (DIC) may also play a role in the pathophysiology of peripheral gangrene [8]. DIC can be seen in critically-ill patients, and it is characterized by widespread activation of the clotting cascade, occasionally consumptive coagulopathy, microvascular thrombosis, and often multi-organ failure [4] [9]. DIC can be challenging to diagnose especially in low-resource settings with limited laboratory testing. DIC may have contributed to three of the four patients with sepsis. The utilization of pressors was only documented in one of these patients, and it may have also contributed to distal ischemia.

Prompt diagnosis of peripheral gangrene is necessary to minimize proximal progression of the disease. Most patients present with signs of fever and other constitutional symptoms, as well as pain and edema in the affected extremities [4]. Malaria treatment should be initiated immediately. Patients should be adequately resuscitated to minimize hypovolemia and improve perfusion of the extremities. Vasopressors should be avoided when possible. Care should be taken to avoid trauma to the affected limbs. Skin injury or infection caused by IV infiltration and the rupture of bullae may have contributed to the development of wet gangrene in two of the cases we report. There is no reported benefit to routine administration of anticoagulants or thrombolytics.

Surgical debridement or amputation is frequently required for the management of peripheral gangrene especially in the presence of infection (i.e. wet gangrene). A staged amputation may be helpful in these cases to control the infection and minimize tissue



Fig. 2. Case 2.

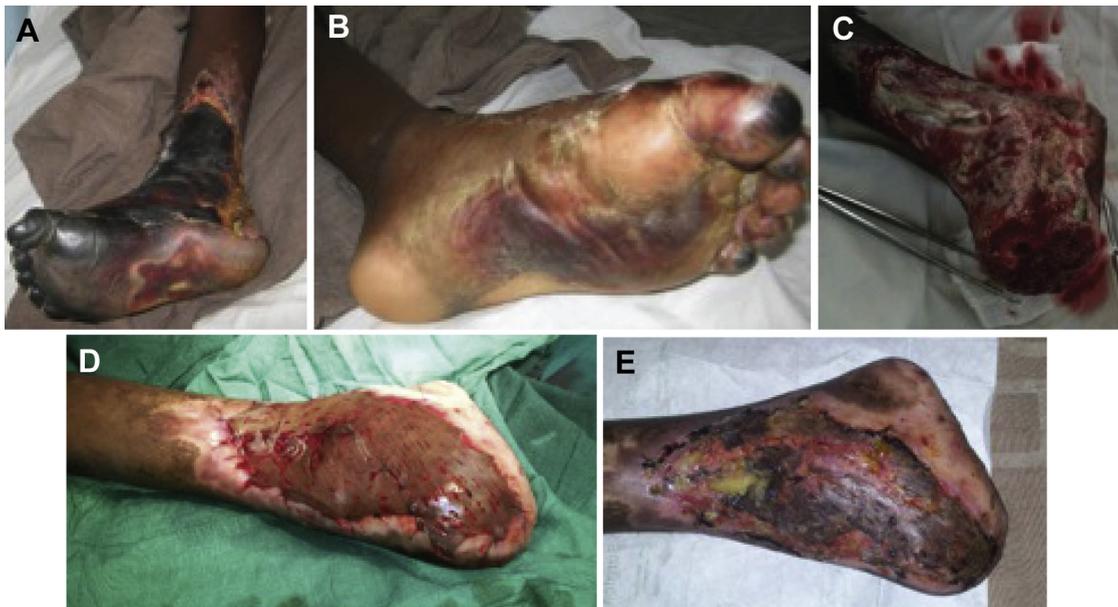


Fig. 3. Case 3. A, B. Gangrene of right foot/ankle and left foot. C. Transmetatarsal amputation. D. Skin graft. E. Post-operative photo.

loss. In addition, amputations should be performed with the goal of optimizing function taking into account the local context and availability of prosthetics. In the second case, a staged amputation with a definitive Symes amputation might have prevented the need for skin grafting without compromising functional results.

In cases where there is no associated infection, peripheral gangrene should ideally be allowed to self-demarcate. In some cases, auto-amputation may occur and help to minimize tissue loss

and preserve function as was seen in the first case. In summary, peripheral gangrene should be managed much like frost bite or pressor-foot [4]; wet gangrene requires immediate amputation and dry gangrene can be allowed to self-demarcate before considering amputation.

Conflict of interest

The authors declare that they have no conflict of interest.



Fig. 4. Case 4. Unilateral gangrene and IV infiltration of the left arm.

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