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Symmetrical peripheral gangrene in a child following severe malaria with concomitant sepsis

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Abstract: Symmetrical peripheral gangrene (SPG) is a well-documented but rare clinical syndrome characterized by symmetrical distal ischemic damage leading to gangrene of two or more sites in the absence of large vessel obstruction or vasculitis. The aetiological factors responsible for SPG are vast and it could follow many common diseases such as malaria. This is a report of a 9month old child who developed symmetric peripheral gangrene following severe malaria (severe anaemia) and sepsis. Gangrene involved the 2nd to the 5th digits

and 3rd and 4th digits of the left and right hands and all the toes. Autoamputation of the affected digits followed several weeks after discharge and was limited to the distal interphalangeal joints. There is the need for a high index of suspicion, early detection and prompt management of patients with disorders associated with SPG in order to limit the risk of permanent disability in otherwise treatable diseases.

Key words: peripheral, gangrene, malaria, child

Introduction

Symmetrical peripheral gangrene (SPG) is a rare but well documented clinical syndrome first described by Hutchinson in 1891.¹ It is characterized by symmetrical distal ischemic damage and gangrene of two or more sites in the absence of large vessel obstruction or vasculitis.² Commonly involved sites include the extremities, genitalia, ear and nose.

Symmetrical peripheral gangrene has been described in association with several infectious and non-infectious factors.¹⁻³ It is commonly found in conditions complicated by disseminated intravascular coagulopathy (DIC), and in 85% of cases, DIC was an associated factor.¹ Sepsis and very rarely, severe plasmodium falciparum malaria are the two leading infectious conditions linked with symmetrical peripheral gangrene.¹⁻⁶ Only a few published reports have highlighted the occurrence of SPG in children with severe malaria.^{5,7}

Malaria remains a common disease in tropical parts of the world and children below 5 years of age are the most affected, it is also one of the leading causes of mortality among them.⁸ In regions of high malaria transmission, children are more susceptible to the severe and life-threatening forms, the commonest parasitic agent being *Plasmodium falciparum*.⁹ The association of SPG with severe malaria may result in a highly disabling and de-

bilitating outcome of an otherwise treatable condition. Our patient, a 9month old male infant, developed SPG following severe malaria and sepsis with marked physical, psychological and financial consequences.

Case Summary

A 9month old infant presented to the Emergency Paediatric Unit with a two day history of high grade, intermittent fever and one day history of paleness of the palms and soles. There was no bleeding from any part of the body, jaundice nor passage of dark coloured urine. On examination, he was lethargic, severely pale, febrile (temperature of 38 C), in severe respiratory distress with grunting. He had tachycardia with a pulse rate of 160 beats per minute while the blood pressure was 70/40mmHg. He was also tachypneic (respiratory rate of 40 breaths per minute) and had hepatosplenomegaly. Urgent Packed cell volume done was 9% and rapid diagnostic test for malaria was positive. Full blood count (FBC) done at initial presentation revealed a white blood count (WBC) of 79 x 10⁹ cells/μl & platelet count of 112 x 10⁹ cells/μl. Blood culture done did not yield any growth. He was managed for severe malaria (with severe anaemia in heart failure) and sepsis. He was promptly transfused with packed cells and commenced on artesunate injection. Other initial treatment given included parenteral antibiotics (Augmentin and Ceftazidime) and intravenous fluids.

Twenty-four hours into admission, he developed dark discolouration over the digits of the left hand and the

toes of both feet (Figures 1, 2), which progressively became gangrenous involving the tips of the 2nd to the 5th digits and 3rd and 4th digits of the left and right hands respectively. All the toes were also involved with progression to the distal interphalangeal joints. There was associated swelling of the dorsa of both feet. Further investigations were done including clotting profile (normal), Antinuclear antibody – negative, doppler studies of the limb vasculatures were normal., Subsequent FBC showed WBC 20×10^9 cells/l, Platelet count 71×10^9 cells/l. Adequate hydration was ensured, sodium bicarbonate and IV hydrocortisone were added to the medications. There was no further progression of the gangrene after 48 hours on conservative management.

Patient was co-managed with the orthopaedic surgeons who recommended a continuation of the conservative management until a definite level of the gangrene was delineated. He was subsequently discharged but defaulted outpatient appointment. He presented 2 months later with autoamputation of the gangrenous digits. (Fig 3)

Fig 1 : Onset of gangrene with dark colouration of the tips of the digits



Fig 2: Gangrene involving all the toes



Fig 3: Autoamputation of the tips of the digits after two months



Fig 4: Autoamputation of the tips of the toes after two months



Discussion

Symmetrical peripheral gangrene (SPG) is a very rare clinical condition usually associated with varying degrees of ischaemic damage to the limbs. Many reported cases resulted in different forms of disabling outcomes, with many requiring differing degrees of amputation.^{3,5,6} It is usually unexpected and comes up suddenly with significant psychological impact on the family. Many of the cases of SPG reported are due to several different systemic illnesses,¹⁰⁻¹² with fewer cases resulting from malaria.^{7,13-15}

The exact incidence of SPG is not known, however, it can involve any age-group. Umar et al documented a 2 month old with sepsis and hypernatremia with SPG.⁶ The gender predilection is also similar. Davis et al reported a slight male preponderance for the disease (7 out of 12 patients)¹¹ while Gosh et al documented a female preponderance.¹⁶ Mortality rates with SPG are high with at least a third of affected patients dying.¹⁷

Cyanosis and pallor of the distal parts of the extremities are typically the first signs of the disease, and is usually symmetric involving either the upper or lower extremities or both as seen in our report. Other areas of affectation are the tip of the nose, ears, scalp and genitalia.¹⁸ Frank gangrene subsequently ensues and is usually dry with mummification which progresses proximally from the distal digits and may involve the whole extremity if aggressive management is not instituted. This has resulted in amputations of part or whole limbs in some reports.^{5,11,19}

Autoamputation is a very common complication, seen in as high as 80% of survivors. Features of purpuric fulminans (purpuric patches with necrosis of the skin) and shock are common however, this was not seen in this child. There are a myriad of causes of SPG including cardiovascular problems like heart failure, hypovolemic shock, sickle cell disease, malignancies, drugs (like adrenaline, noradrenaline, dopamine) and infections. Infectious causes appear to be the most common and include bacterial, viral and parasitic disorders. Sepsis, particularly from bacterial infections is the leading cause of SPG.^{4,11}

Malaria remains endemic in this part of the world with *Plasmodium falciparum* being the causative agent of most cases of severe malaria.⁹ Most of the cases of SPG arising as complications of malaria isolated *Plasmodium falciparum* in the peripheral blood. Faraj et al in India reported a case of SPG involving the hands and feet in a 54 year old man with severe malaria.¹⁵ A similar presentation was reported in 30 year old Ethiopian woman with severe *Plasmodium falciparum* malaria (cerebral malaria).²⁰ Kumar et al also reported a case of a 62 year old Indian woman who developed gangrene of the extremities following *Plasmodium vivax* malaria.¹⁴

SPG is a rare complication of malaria in children. However, there have been few reports of digital gangrene complicating severe malaria in children. In Nigeria, Ejagwulu reported a 5 year old child with auto amputation of distal third of both legs and amputation stumps on the 2nd to 4th digits following complicated malaria with DIC (thrombocytopenia, prolonged bleeding and clotting time) and shock.⁵ Fowotade *et al* in Ibadan reported the occurrence of purpura fulminans in two infants, both of whom had associated features of DIC in settings of severe *Plasmodium falciparum* hyperparasitaemia.¹⁷ Purpura fulminans is a close differential of SPG which is characterised by DIC, shock, purpuric lesions and gangrene whereas SPG is basically characterised by tissue necrosis in distal limbs which ascends proximally and is symmetrical.

In the management of SPG, a good history and thorough examination regarding systemic illnesses and symptoms, drug ingestion, surgical procedures are important as these can lead to identification of predisposing factors to SPG. Investigations like complete blood count, blood cultures and peripheral blood film for malaria parasite are useful to diagnose infections. Screening for DIC can be done with peripheral blood film showing the presence of schistocytes, deranged clotting profile, elevated fibrinogen degradation products and D-dimer. Doppler ultrasound shows sparing of the large peripheral arteries which is consistent with SPG. Histopathology of the lesions will help to rule out vasculitides, as the features as mostly non-specific in SPG.

No specific treatment has been found to consistently halt the disease. Various modalities used include aggressive management of underlying cause by giving antibiotics, antimalarials if necessary, use of anticoagulants like heparin, aspirin, replacement of coagulation factors, fluid therapy, plasmapheresis and intravenous immunoglobulin with varying success. Amputation is delayed until a clear line of demarcation is seen, following which skin grafting can then be done.

The case we report involved an infant who had a fever

and severe anaemia and thrombocytopenia with no evidence of bleeding or DIC. Digital extremity gangrene was sudden in onset and progressed only as far as the distal interphalangeal joints of the affected digits. Doppler flow studies of the vasculature was normal, none the less, there was a resultant auto-amputation of the affected digits after several weeks.

Though the aetiology of SPG is not yet fully explained, association with DIC and low flow states has been documented as possible risk factors.¹ As a result, many systemic conditions such as severe malaria, sepsis, tumour, septic abortion and drugs have been linked with its occurrence.^{4,5,21,22} The convergence of sepsis and severe malaria, two of the most common predisposing factors, may explain the development of this rare condition in our patient. Both sepsis and severe malaria can independently predispose to SPG through microvascular obstruction and development of DIC. Severe malaria results in microvasculature thrombosis and obstruction through the expression of *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1), increased cytoadherence and rosetting.²³ While sepsis causes up-regulation of pro-coagulant molecules, suppression of fibrinolysis and endothelial dysfunction which result in diffuse intravascular thrombosis with varying degree of microvascular obstruction.¹²

We attribute the halt in the progression of gangrene in this patient to early detection and prompt use of appropriate antimalarial and antimicrobials as well as adequate hydration. The high financial, physical and psychological burden of managing patients with SPG, and the resulting disability, underscores the need to raise awareness among clinicians in order to promote early detection and anticipatory management.

Conclusion

Symmetrical peripheral gangrene is a rare but highly disabling complication of many common clinical conditions that may result in varying degree of permanent disability. There is the need for early detection and prompt commencement of appropriate treatment in order to limit the risk of permanent disability in otherwise treatable diseases.

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