Niger J Paediatr 2020; 47 (3):280 – 284

CASE REPORT

Katibi OS
Olorunshola BS
Akintade OO
Folayan OS

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

DOI:http://dx.doi.org/10.4314/njp.v47i3.15

Accepted: 17th April 2020

Akintade OO (✉)
Children Specialist Hospital,
Ilorin, Nigeria.
Email: yekintade@gmail.com

Katibi OS
Department of Paediatrics/ Child Health, University of Ilorin
Kwara State

Olorunshola BS
Scunthorpe General Hospital
Northern Linconshire an Goole Trust England

Folayan OS
Department of Paediatrics,
Federal Medical Centre, Bida
Kogi State

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 5thdigits and 3rd and 4thdigits 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 debilitating 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 10^9 cells/µl & platelet count of 112 x 10^9cells/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 5thdigits and 3rd and 4thdigits 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 x 10^9 cells/l, Platelet count71 X 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 48hours 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

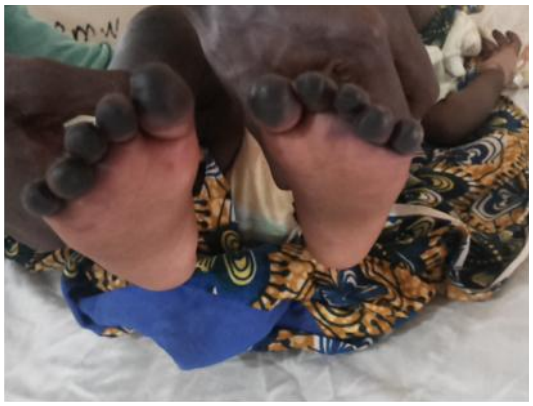
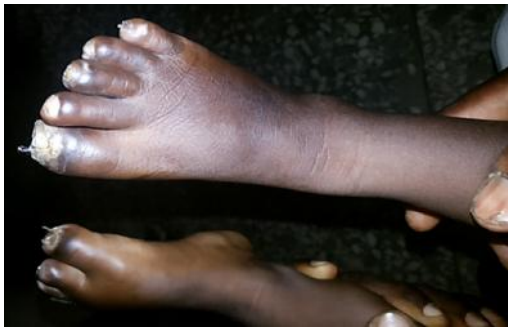


Fig 3: Autoamputation of the tips of the digits after two months

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.[7]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 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 interphallangeal 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(P*f*EMP1), increased cytoadherence and rosetting.[23] While sepsis causes upregulation 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.

Conflict of interest: None
Funding: None

References

1 Suarez-Amor O, Casado-arroyo R, Cabanillas M, Labandeira J, Toribio J. Symmetrical peripheral gangrene and disseminated intravascular coagulation associated with pneumococcal sepsis. *Actas Dermosifilor. 2009;100:329–43.*

2. Markelov A, DeFroda S, Baccaro L, Bastidas J. A unique case of unilateral lower extremity sparing systemic peripheral gangrene. *Case Rep Vasc Med* [Internet]. 2012 [cited 2016 Jan 8];2012(Figure 1):1–3. Available from: http://www.hindawi.com/journals/crivam/2012/750953/

3. Faraj O, Duncan M, Otieno W. Malaria complicated by gangrene: a case presentation and review. *Pan Afr Med J. 2011;8688:1–7.*

4. Adekanbi A, Egbuchulem I, Fawole A, Akinola A. Symmetric peripheral gangrene in a Nigerian woman : A rare complication of unsafe abortion. *Obs Gynecol Int J. 2015;0:9–11.*

5. Ejagwulu F, Ibrahim A. Symmetrical peripheral gangrene and extremity amputations. *Ann Niger Med.2014;8:98–102.*

6. Umar L Wasiu. Symmetric peripheral gangrene complicating sepsis and hypernatraemia in a 2 months old infant – a case report. In: 43rd Annual General Meeting and Scientific Conference of Paediatric Association of Nigeria (PANCONF), at Ile-Ife, Nigeria,. 2012. https://www.researchgate.net/profile/Lawal_Umar/publication/245024774_ Symmetric_Peripheral_Gangrene_Complicating_Sepsis_and_Hypernatraemia_in_a_2_months_old_Infant_-_A_Case_Report/links/540840890cf23d9765af319b/Symmetric-Peripheral-Gangrene-Complicating-Sepsis-and-Hypernatraemia-in-a-2-months-old-Infant-A-Case-Report.pdf

7 Fowotade A, Oladokun RE, Bello OE, Aigbovo EO. Purpura fulminans with peripheral gangrene in severe falciparum malaria : A Case Series. *J Case Reports 2018; 8: 27–32.*

8 World Health Organization. Malaria. Chapter 7. 2016[cited 2019 Oct 29] Available from https://www.who.int/ith/ITH_chapter_7.pdf

9 World Health Organization. Guidelines on the treatment of malaria.3rd ed ; [Cited on 2019 Oct 31] Available at htttps://www.who.int › malaria› publications › atoz

10 Ahmadu BU, Emmanuel P, Kurna BM. Case report digital gangrene an unusual feature of tuberculosis : a case report of a toddler from a low health resource country. *J Paediatr Infect*2013; 8: 93–96.

11 Davis MDP, Dy KM, Nelson S. Presentation and outcome of purpura fulminans associated with peripheral gangrene in 12 patients at Mayo Clinic.*J Am Acad Dermatol* 2007;57:6:944-56. [cited on 2019 Oct 31] Available at https://wwwncbi.nlm.nih.gov› pubmed/17719676 doi:10.1016/j.jaad.2007.07.039.

12 Semeraro N, Ammollo CT, Semeraro F, Colucci M. Sepsis-associated disseminated intravascular coagulation and thromboembolic disease. *Medit J Hemat Infect DIs [Internet]*. 2010 Jan [cited 2015 Oct 16];2 (3):e2010024. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3033145&tool= pmcentrez&rendertype=abstract

13 Kakati S, Doley B, Barman B, Devi A. Symmetric peripheral gangrene and falciparum malaria. *JAPI 2004; 52: 2004–2005.*

14 Kumar P, Tansir G, Gupta H, Dixit J. Symmetrical peripheral gangrene in severe plasmodium vivax malaria. *Indian J Crit Care Med 2017; 21: 245–6.*

15 Alkizim FO, Matheka D, Mwanda OW. Malaria complicated by gangrene: a case presentation and review. *Pan African Med J 2011;8688: 1–7.*

16 Gosh S, Bandyopadhyay D, Gosh A. Symmetric peripheral gangrene: a prospective study of 14 consecutive cases in a tertiary-care hospital in Eastern India. *J Eur Acad Dermatology Venereol 2010;24: 214–8.*

17 Parmar M. Symmetrical peripheral gangrene : a rare but dreadful complication of sepsis. *Can Med Assoc J 2014; : 28–30.*

18 Passi GR, Singsit J, Singh M. A 12 year old boy with fever and blue Ears. *Indian Paediatr 1997; 34: 343–344.*

19. Ahluwalia J, Naseem S, Singh S, Suri D, Das R, Sachdeva MUS *et al.* Prothrombotic profile in children with peripheral gangrene : A single center experience. *Clin Appl Thromb 2011; : 497–501.*

20. Ahmed, KK. Bilateral peripheral gangrene following malaria parasitaemia at the University Teaching Hospital of Butare. *Rwanda Med J 2016; 73: 26–28.*

21. Bhattacharyya P, Agarwal J, Sharma M. Symmetrical peripheral gangrene of lower limbs in a case of complicated Falciparum Malaria. *Southeast Asian J Trop Med Public Health. 2008 Jul;39 (4):589-92.*[Cited on] Available athttps://www.researchgate.net/publication/23625691_Symmetric_peripheral_ gangrene_of_the_lower_limbs_in_a_case_of_complicated_falciparum _malaria

22. Shih-Tsung H, Yu-Yun L, Ming-Fei L. Symmetrical peripheral gangrene of sudden onset-a paraneoplastic syndrome. *Dematol Sin1996; 14: 82–88.*

23 Dondorp AM. Pathophysiology, Clinical presentation and treatment of cerebral malaria. *Neurol Asiaeurology Asia* [on Internet].2005 [cited on 2019 Nov 2]; 10: 67–77. Available from: http://www.neurology-asia.org/articles/20052_067.pdf