Doi: 10.32677/IJCR.2016.v02.i03.004 Case Report

A complicated case of Plasmodium falciparum malaria with symmetrical peripheral gangrene with a review of literature

Rohan S Sequeira, Manju B Wadikhaye, Sham P Kamble, Ashwini M Ronghe, Amol R Bhore, Parag H Rahatekar, Sandeep Kumar

From, Department of Medicine, Grant Government Medical College, Mumbai, Maharashtra, India

Correspondence to: Dr Ashwini Ronghe, *Department of Medicine, Grant Government Medical College, Mumbai, Maharashtra, India, Email:* ashuronghe@gmail.com.

Received: 01 July 2016 Initial Review: 10 July 2016 Accepted: 01 August 2016 Published Online: 11 August 2016

ABSTRACT

Malaria causes nearly one million deaths each year and with its recent re-emergence, several fatal complications are seen such as cerebral malaria, hypotension or shock, renal failure, pulmonary oedema/adult respiratory distress syndrome, and hypoglycaemia. Symmetric peripheral gangrene (SPG) is a severe but extremely rare complication of malaria. It has a rapid and sudden onset leading to necrosis which cannot be reversed. A 26 year old male was admitted and treated for complicated malaria and developed SPG. He was given intravenous artesunate, doxycyline, clopidogrel and acetyl salicyclic acid for the gangrene; however, he went into multiple organ dysfunction syndrome and septic shock and thus could not be resuscitated. We report this case to highlight that physicians treating malaria should always look for these signs for timely correction and to improve the patient outcome.

Keywords: *Complicated malaria, Gangrene, Plasmodium falciparum, Peripheral gangrene*

Malaria is a disease caused by protozoa transmitted by the bite of infected Anopheles mosquito. Malaria is one of the major causes of mortality worldwide and was responsible for 627,000 globally in 2012. According to the World Malaria Report 2013, about 97 countries had on-going malaria transmission. It was found that there were 1,067,824 confirmed cases of malaria in India; out of which, 524,370 were attributed to Plasmodium falciparum [1].

If treated appropriately and in time, it has a mortality rate of 0.1% only. However, if total proportion of erythrocytes infected increases to >2% or if there is vital organ dysfunction, mortality risk rises steeply [2]. Symmetric peripheral gangrene (SPG) is a rare complication, with a high mortality (up to 40%) which leads to ischemic gangrene of two or more sites in the absence of large vessel obstruction or vasculitis [1-3]. Its exact pathophysiology is not understood well and several factors such as parasitemia, adhesion molecules etc. have been considered over the period of years [1].

CASE REPORT

A 26 year old male presented to our hospital with complaints of fever and chills for 5 days. There was no history of rashes, trauma to limb, exposure to cold, diabetes or hypertension, drug intake, burning micturition, cough or drowsiness. On admission, the pulse was 80/min, respiratory rate was 18/min, blood pressure was 120/80 mm Hg and SpO_2 was 98% on room air. Other systemic examinations were within normal limits.

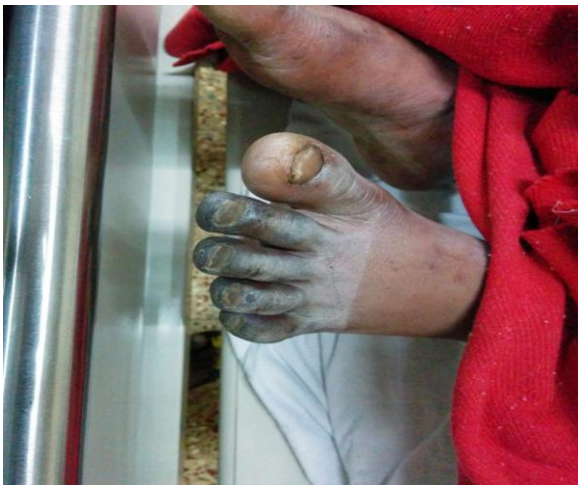

Figure 1 – Onset of gangrene on bilateral extremities

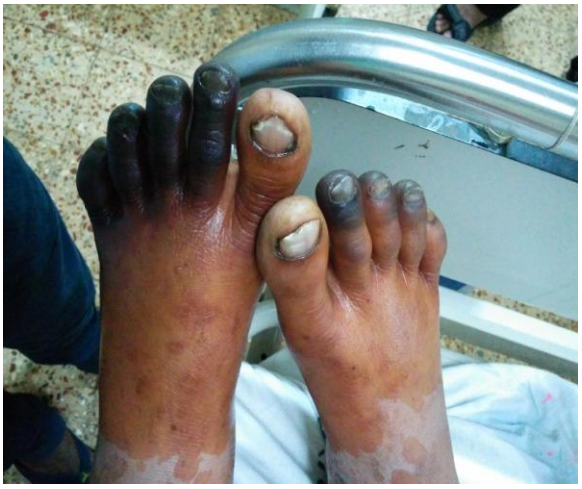

Figure 2 - Symmetrical gangrene on bilateral extremities

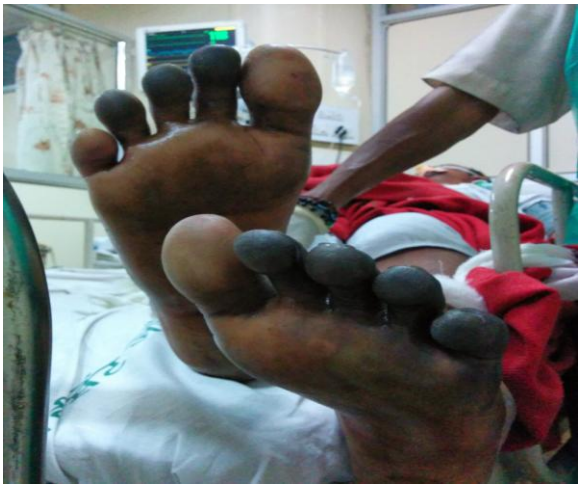

Figure 3 - Symmetrical gangrene on bilateral extremities

Blood investigations showed a decreased platelet count of 50,000/mm^3 with normal leukocyte counts. Serum electrolytes were normal (K^+=5.3 Meq/l and Na^+=153Meq/l). SGOT was 720U/l and SGPT was 200U/l and total bilirubin was 6.8g/dl. Serum creatinine was 1.4g/dl. Tests for HBV, HCV, HIV, Leptospirosis and syphilis were negative. Blood gas analysis showed pH of 7.26 with pCo2 of 31.3 mmHg and pO2 of 163mmHg.

The next day the patient developed a petechial rash all over his body. The patient complained of pain and numbness of lower extremities which on examination showed bluish darkening of the toes and fingers of his lower limbs (Fig.1). The skin was cold and dry. Dorsalis pedis pulses were absent. There was a clear line of demarcation between the live and the dead tissue (Fig. 2 and 3). Tests for DIC panel showed D dimer 5.4 mcg/ml, PT at 15.8 seconds, INR of 1.8 and LDH of 1791U/l. A Doppler examination was done to see the arterial circulation and to rule out other causes of gangrene. Management in the form clopidogrel and acetylsalicylic acid was started.

Over the period of next two days, the condition worsened and the patient required ventilatory support. Despite intensive care support, the patient developed MODS and went into cardiac arrest after one day and despite extensive efforts could not be resuscitated.

DISCUSSION

Plasmodium falciparum causes 95% of all the cases of complicated malaria, which is defined by World Health Organisation as those with an impaired level of consciousness (Glasgow Coma Scale score ≤7), severe anaemia, hypoglycaemia, acidosis, hyperlactatemia, hyperparasitemia (of more than 5%), and renal impairment [4]. SPG which leads to ischemic gangrene of two or more sites in the absence of large vessel obstruction or vasculitis was first described in 1891 by Hutchinson [5]. However, a common aetiology has not been established yet and following aetiologies have been proposed:

Heavy parasitemia activates the complement system and triggers the coagulation pathway causing alteration in lipid distribution across the infected erythrocytes. These erythrocytes get sequestrated by interacting with endothelial receptors, chiefly intercellular adhesion molecule (ICAM-I), Vascular adhesion molecule (VCAM-

I), endothelial leukocyte adhesion molecule-1 (ELAM-1), thrombospondin, and histidine-rich protein. Rosetting of uninfected erythrocytes around the parasitized ones also adds to the vascular obstruction. This thus initiates a microcirculatory obstruction in malaria similar to the process in cerebral malaria [4].

Another theory states that an adhesion protein family in Plasmodium falciparum named erythrocyte membrane protein 1 (PfEMP1), encoded by var genes, is responsible for both antigenic variation and cell to cell adhesion of infected red blood cells at microcirculation sites throughout the body [6-7]. This PfEMp1 interacts with endothelial receptor protein C receptor (EPCR), which mediates protective effects of activated protein C [7-8]. During haemolysis, which occurs in infected cells, negatively charged phosphatidylserines are exposed promoting the formation of prothrombinase. Furthermore, inflammatory cytokines, especially TNF-α and interleukin-6, increase tissue factor expression on mononuclear cells, leading to thrombus formation [4].

There is also a recent interest in deficiency of ADAMTS13, (a von Willebrand factor cleaving protease) activity in severe malaria causes accumulation of prothrombogenic, unusually large VWF multimers in plasma [9]. The presence of reduced ADAMTS13 activity may contribute to microvascular obstruction. However till now, there is no direct link between ADAMTS13 activity and the occurrence of SPG [9].

Finally, the life cycle of the Plasmodium has been shown to have an effect on the membrane of infected erythrocytes. As merozoites mature to trophozoites and schizonts, the erythrocyte membrane composition changes which leads to the appearance of knobs on their surfaces [2]. This alteration changes both their adherence to endothelial cells as well as non-infected and other infected red blood cells. This results in sequestered erythrocytes within the microcirculation, and ultimately vascular obstruction [4]. Thus, obstruction and endothelial activation play a major role in the pathogenesis of SPG.

This condition did not respond to artisunate and literature of review also did not mention role of antimalarial drugs in preventing SPG. SPG usually occurs within the first 3 days of effective antimalarial therapy, at which time parasitemia is often very significantly reduced which may be misleading [9]. Treatment of SPG is largely empirical with treatment of the underlying cause. There is no evidence that blood exchange transfusions or fresh frozen plasma administration could be effective treatment options for patients with DIC and SPG. Heparin or streptokinase is not indicated unless SPG is associated with DIC. Surgery and use of vasopressors should be delayed when the delimitation of dry necrotic areas is evident [9-10].

Other treatments can be intravenous nitropruside, phentolamine and prostaglandin (epoprostenol) which are vasodilators or sympathetic ganglion blockade can be done. Papaverine, dextran and hyperbaric oxygen therapy have not been shown to be beneficial [10].

CONCLUSION

The exact pathogenesis of SPG is still not known and the immediate onset of the ischemia followed by rapidly progressing complications like necrosis makes prevention and management of the gangrene difficult as anticoagulants are not routinely in the treatment regime of common malaria. The physician should thus be on the lookout for these signs while managing a malaria case.

REFERENCES

1. World Health Organisation *Factsheet on the World Malaria Report 2013*, viewed on 10th January 2016, http://www.who.int/malaria/media/world_malaria_report_2013/en/. [Last accessed on June 12, 2016].
2. Rana A, Singh DP, Kaur G, Verma SK, Mahur H. Symmetrical peripheral gangrene: A rare complication of plasmodium falciparum malaria. Trop Parasitol. 2015;5:130-2.
3. Gupta A, Dwivedi Y, Saxena AK, Joshi K. Symmetrical peripheral gangrene with Plasmodium falciparum malaria. J Nat Sc Biol Med. 2013;4:262-264.
4. Alkizim FO, Matheka D, Mwanda OW. Malaria complicated by gangrene: a case presentation and review. Pan Afr Med J. 2011;10:46.
5. Hutchinson J. Notes of uncommon cases. Br Med J. 1891;2:8–9.
6. Sriboonvorakul N, Leepipatpiboon N, Dondorp AM, Pouplin T, White NJ, Tarning J, et al. Liquid chromatographic–mass spectrometric method for simultaneous determination of small organic acids potentially contributing to acidosis in severe malaria. J Chromatogr B Analyt Technol Biomed Life Sci. 2013;941 (100):116-122.

7. Kraemer SM, Smith JD. A family affair: var genes, PfEMP1 binding, and malaria disease. Curr Opin Microbiol. 2006;9:374–380.
8. Turner L, Lavstsen T, Berger SS, Wang SS, Petersen JE, Avril M, et al. Severe malaria is associated with parasite binding to endothelial protein C receptor. Nature. 2013;498 (7455):502-505.
9. Masse E, Hantson P. Plasmodium falciparum Malaria Complicated by Symmetrical Peripheral Gangrene, Bowel Ischemia, Repeated Candidemia, and Bacteraemia. Case Reports in Medicine. 2014;Article ID 696725:4 pages.
10. Abdali N, Malik AM, Kamal A, Ahmad M. Symmetrical peripheral gangrene due to Plasmodium falciparum malaria. BMJ Case Rep. 2014. pii:bcr2014204268.

How to cite this article: Sequeira RS, Wadikhaye MB, Kamble SP, Ronghe AM, Bhore AR, Rahatekar PH, Kumar S. A complicated case of Plasmodium falciparum malaria with symmetrical peripheral gangrene with review of literature. Indian J Case Reports. 2016; 2(3): 58-61.
Conflict of interest: None stated, Funding: Nil