CASE REPORT

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# Purpura Fulminans in *Plasmodium vivax* Malaria

*Shruti Arora*, Amit Aggarwal**, Sumita Saha Kanwar***, Prem Singh Nayyar*****

## Abstract

***Plasmodium vivax is the most common protozoan species affecting humans. It can have varied clinical manifestations in the human body. A 42-year-female presented to the emergency department with complaints of fever, skin rashes and drowsiness. She was diagnosed as severe malaria with hepatic failure, acute kidney injury, haemolysis, sepsis and purpura fulminans. The association of purpura fulminans with Plasmodium falciparum is strong in available medical literature; however, we came across this association in a case of Plasmodium vivax malaria.***

***Key words: Purpura fulminans; Plasmodium vivax; malaria.***

## Introduction

Malaria is an endemic protozoan infection prevalent throughout most of the tropical countries. According to the World Malaria Report, released in November 2017, there were 216 million cases of malaria in 2016, up from 211 million cases in 2015 with the estimated number of deaths standing at 4,45,000 in 2016[1]. Transmission of this acute febrile illness most commonly occurs through the bite of the female anopheles mosquito. The dominant species infecting humans is *Plasmodium vivax*. We report and discuss the case of a 42-year-old woman who presented to the emergency department with an acute febrile illness and large generalised ecchymotic skin rashes and was diagnosed to be having severe *Plasmodium vivax* malaria with purpura fulminans. Purpura fulminans is a very serious skin condition of sudden onset featuring widespread cutaneous haemorrhage and necrosis as a result of disseminated intravascular coagulation and dermal vascular thrombosis associated with high mortality and morbidity[2].

## Case summary

A 42-year-old woman presented to the emergency of our hospital with complaints of fever of 5 days duration along with multiple large purpuric skin lesions for preceding two days on various parts of the body including upper and lower extremities, chest, abdomen, back and gluteal region, which were asymmetrical in distribution. She was drowsy since one day before admission. There was no history of any convulsive episode. The patient was a known case of type 2 diabetes mellitus, on oral hypoglycaemic agents for last 12 years and a known hypothyroid, on thyroxine 50 micrograms supplementation daily. She had sought treatment for fever from a facility near her house and was prescribed anti-pyretics only.

On examination, she was pale, deeply icteric and stuporous; her heart rate was 110/minute, regular; blood pressure was 100/60 mmHg in both arms in supine position, temperature ( axillary) was 102.4° F; respiratory rate was - 40/minute and respiration was abdominothoracic, shallow and rapid, suggestive of Kussmaul's breathing. On auscultation, she had bilateral basal crepitations. Cardiovascular examination was unremarkable, except for tachycardia. Abdominal examination revealed mild splenomegaly. On central nervous system examination, she was stuporous with GCS - $E_2V_2M_4$ with bilateral normal sized, normally reacting pupils and no meningeal signs. Plantar response was bilaterally extensors. There was no obvious focal neurological deficit. On fundus examination she had bilateral flame shaped haemorrhages with central clearing. She also showed lesions of herpes labialis and was bleeding from oral mucosa. Skin lesions were described as multiple rounded purpuric rashes over trunk and extremities suggestive of purpura fulminans.

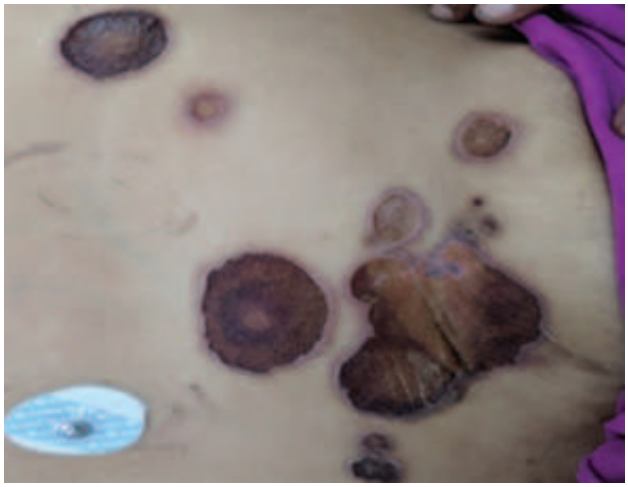
## Clinical investigations

Blood investigations were as follows: Arterial blood gas analysis showed a pH – 7.34, $pCO_2$ – 22 mmHg, $pO_2$ – 70 mmHg, $HCO_3$ – 11.5 mMol/l (acute partially compensated metabolic acidaemia). Her haemoglobin was 9.6 gm/dl with total leucocyte count of 26,000/cumm ( neutrophils – 78, lymphocyte – 12, eosinophil – 4, monocytes – 6) and platelet count nadir of 24,000/cumm. Peripheral blood smear showed *Plasmodium vivax* with ring shaped trophozoites

***Medical Officer, ***Specialist and Head, ****Medical Specialist and Medical Superintendent, Department of Medicine, Sanjay Gandhi Memorial Hospital, Delhi;***

*****Specialist, Department of Medicine, PGIMER and Dr Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, New Delhi - 110 001. Corresponding Author: Dr Amit Aggarwal, Specialist, Department of Medicine, PGIMER and Dr Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, New Delhi - 110 001. Phone: 9716112232, E-mail: amitaggarwal@doctor.com.***

and Schuffner's dots with normocytic normochromic red blood cells. Parasite index was 12%. Blood urea was 114 mg/dl, serum creatinine was 1.0 mg/dl; serum sodium was 130 meq/dl and serum potassium was 7.1 meq/dl; total bilirubin – 21.9 mg/dl, direct bilirubin – 7.2 mg/dl, indirect bilirubin – 14.7 mg/dl; SGOT – 125 U/L and SGPT – 70 U/L; blood lactate level was 4.2 mmol/l. Serum CPK was 155 U/L. Prothrombin time was 16.5 seconds with INR – 1.25, APTT was 27.3 seconds; HBsAg and Anti-HCV were negative. Dengue NS1 antigen was negative. Random blood sugar at the time of admission was 76 mg%. Her glycosylated haemoglobin was 11.5%. Serum LDH was 391 IU/l. A routine urine examination showed albumin 2+, epithelial cells – 1 - 2, pus cells – 8 - 10 per HPF and RBCs – 1 - 2 per HPF but no active sediments. ECG showed left bundle branch block with sinus tachycardia. An initial supine X-ray chest revealed prominent bilateral interstitial markings in lower zones. Her 2D-echocardiography was normal. Abdominal ultrasonography revealed mild splenomegaly with minimal ascites. NCCT head was done which was normal. Her TSH was 0.27 mIU/ml, FT3 was 1.23 pg/ml and FT4 was 0.82 ng/dl. Her G6PD level was 9.5 U/gmHb. Serum ANA was negative. Her blood cultures, urine culture, and fluid culture from skin lesions of purpura fulminans did not isolate any organisms. Skin biopsy of the lesions done on day 4 of admission showed features of vasculitis with subcorneal blistering, although no organisms were seen on appropriate staining. Protein-C, protein-S and antithrombin-III assays could not be done due to logistical reasons.



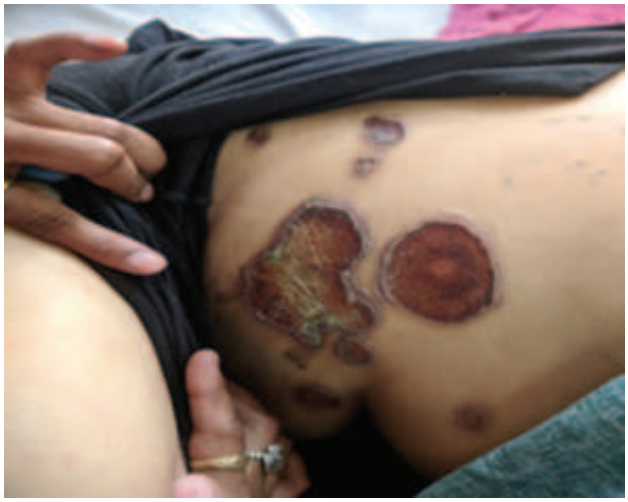


***Fig. 1 and 2:*** *Lesions of purpura fulminans from our patient (trunk and groin).*

## Course in the hospital

She was managed with intravenous artesunate, clindamycin, meropenem, 25% dextrose with insulin drip and calcium gluconate for hyperkalaemia, paracetamol, pantoprazole, bowel wash, oral lactulose, platelet rich plasma, platelet concentrates, supplemental oxygen and IV fluids. Foley's catheterisation and Ryle's tube insertion were done. On day 2 of admission, her respiration became irregular, and she became hypoxic even on supplemental oxygen by mask, thus she was intubated and put on mechanical ventilation. ABG showed type-I respiratory failure with metabolic acidosis. Chest X-ray showed features of ARDS. She remained on mechanical ventilation for two days, during which her acidosis was corrected and the above medications continued along with Ryle's tube feeding and dextrose insulin infusions. Gradually, she started improving and was extubated on day 4 of admission. Her biochemical parameters showed gradual recovery with near – normalisation, on the 7th day with the given treatment.

## Discussion

*Plasmodium vivax,* that was previously associated with milder clinical manifestations of malarial infection running a benign course, is now seen to be associated with much more fulminant and severe clinical disease resembling *Plasmodium falciparum* infection[3]. Features like severe anaemia[4], thrombocytopenia[5], disseminated intravascular coagulation, hepatic[6] and renal dysfunction[7], cerebral malaria[8], ARDS[8] and MODS[9] usually associated with *P. falciparum* are now also seen with *P. vivax* infection.

Severe disseminated infections due to organisms like *Neisseria meningitides, Streptococcus pneumoniae, group A and B Streptococci, Haemophilus influenzae, Staphylococcus aureus, Rickettsia sp.* and *Plasmodium falciparum* are known to cause purpura fulminans with disseminated intravascular coagulation, apart from hereditary causes[2,10].

The initial manifestation of purpura fulminans is a well-defined erythematous macule that progresses to an irregular lesion of blue-black haemorrhagic necrosis. These

may become dark and raised, as a result of haemorrhage into the dermis, occasionally also exhibiting vesicle formation as was seen in this case. Histologically, there may be congestion with red blood cells and subcorneal blistering, while deeper lesions may involve the dermis with occlusion of small vessels by microthrombi, dilatation of capillaries and extravasation of blood inside dermis[2]. The lesions in this patient were seen on anterior chest wall, axilla, upper arms, back and gluteal region; however, the head and neck region and the lower limbs were spared. The first signs of healing started appearing after seven days of treatment, and the lesions showed gradual improvement subsequently. In patients with purpura fulminans, the laboratory parameters reflect underlying DIC, viz., increased plasma clotting time, thrombocytopenia, a decrease in plasma fibrinogen concentration, increase in plasma fibrin-degradation products and occasionally, microangiopathic haemolysis. Although these are not characteristic of purpura fulminans and can be found in any DIC related disease. The normally flexible biconcave disc of an erythrocyte becomes spherical and rigid with *Plasmodium falciparum* infection. The infected RBCs are less filterable than the uninfected cells and thus escape splenic filteration leading to sequestration causing microvascular obstruction[10].

Management involves the treatment of the underlying infection by appropriate antimicrobial agents. Many other modalities like intravenous immunoglobulins, Activate Protein C concentrates and hyperbaric oxygen therapy have been attempted with no proven consistent benefits. Also, as patients of DIC are at increased risk for either acute thrombosis or haemorrhage and it is tough to predict the occurrence of either in a particular patient, prophylactic anticoagulation is not presently indicated in the management of acute infectious purpura fulminans[11]. Our patient recovered fully with artesunate, clindamycin and broad spectrum antibiotic cover.

## Conclusion

The aim of this article is to highlight the association of a very rare clinical manifestation of purpura fulminans in a very common clinical entity of *Plasmodium vivax* malaria and the challenges involved in the management of such a presentation. Properly structured studies, are required to ascertain the reasons behind the recently seen severe and often fatal clinical manifestations of an earlier benign *Plasmodium vivax* malarial infection.

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