

A case report of plasmodium vivax malaria presenting as hemophagocytic syndrome

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Abstract

Malaria is a protozoal disease caused by Plasmodium species and transmitted by the bite of anopheles mosquitoes. It is still a treat in the tropical countries causing more than 1 million deaths every year. P. falciparum is responsible for most of the complicated cases. P.vivax infection presents with febrile illness, but complicated malaria can occur. Here we present a case report of Plasmodium vivax malarial fever presenting as hemophagocytic syndrome.

Keywords: Malaria, plasmodium vivax, hemophagocytic syndrome

Case Report

A 28 year old male patient presented with complaints of high grade fever intermittent type for 15 days associated with fatigue, headache and vomiting. No history of cough, decreased urine output, joint pain or hematuria. No history of previous co morbidities. On examination patient was conscious, oriented, febrile- T-101.4 F, pallor (+), icterus (+), lymphadenopathy or edema. Pulse- 96/min, BP- 80/50 mmHg, cardiac and respiratory examination was

normal; per abdomen was soft with hepatosplenomegaly and nervous system intact.

The patient was admitted in intensive care and investigated. His investigations revealed pancytopenia with hemoglobin – 8.2 gm/dl; total leukocyte count - 3000 cells/cu.mm; Differential count– P-27%, L-61% and platelets- 24,000/ cu.mm. His blood sugar was 112 mg/dl and RFT deranged with urea – 55 mg/dl and creatinine – 1.5 mg/dl. Patient also had dyselectrolytemia with sodium – 126 meq/l, potassium – 4 meq/l and chloride – 86 meq/l. His liver function tests were deranged with total bilirubin- 6.2 mg/dl, direct bilirubin- 5.8mg/dl, AST- 630 IU/L, ALT- 710 IU/L, ALP and serum protein were normal. Patient was admitted with the diagnosis of fever with pancytopenia in septic shock and was evaluated.

Dengue serology, scrub typhus IgM antibody test and leptospirosis antibody test were negative. IgM Monospot test for EBV and viral markers– negative. Blood and urine cultures revealed no growth. Malarial antigen test (rapid method) was positive for P.vivax and peripheral blood smear showed normocytic normochroic anemia with lymphocyte predominance and thrombocytopenia with

gametocytes and schizonts of *P.vivax*. Patient was treated with iv fluids, antipyretics, antimalarials (inj.Artesunate 120 mg iv 0, 12, 24 and 48 hours followed by T. primaquine 15 mg OD for 15 days) and the patient improved symptomatically.

Since patient was diagnosed as *P.vivax* malaria with pancytopenia we had a suspicion of Hemophagocytic syndrome and investigated further. Serum triglyceride was elevated **564 mg/dl**, elevated serum ferritin - **1135.4 ng/dl** and serum fibrinogen was normal. Bone marrow aspiration showed scanty macrophages with phagocytised red blood cells. The final diagnosis of the patient was **Complicated plasmodium vivax malaria with pancytopenia secondary to hemophagocytic syndrome.**

Patient improved symptomatically and was discharged after 10 days of treatment and his complete haemogram, peripheral smear, renal and liver function tests were normal at the time of discharge.

Discussion

Hemophagocytic syndrome (HPS) also called hemophagocytic lymphohistiocytosis (HLH) is a highly fatal condition due to hyperactive immune response. It is a reactive disorder of the mononuclear phagocytic system, characterized by benign, generalized histiocytic proliferation, with marked hemophagocytosis in bone marrow. The pathophysiology is the failure of the negative feedback mechanism in downregulating the immune response after the antigenic stimuli is removed. As a result it leads to inappropriate or excessive immunological response of T-cells. There is activation and elaboration of cytokines like IL-1, IL-2, IL-6 and TNF- α by T-helper cells which promote activation of macrophages resulting in phagocytosis of the blood cells. These cytokines cause sequestration and rapid destruction of the formed blood cells. It also depresses the proliferation of progenitor cells which aggravates the

pancytopenia. HPS may be primary (a familial disorder) or secondary to infections.^{1,2}

The familial HLH is an autosomal recessive condition presenting early in life most commonly associated with perforin deficiency. The other conditions include HLH with partial albinism and X-Linked proliferative syndrome. Most of these conditions require active immunosuppression.^{1,2} The secondary causes include connective tissue disorders, malignancies commonly lymphomas and infections. The most commonly encountered infectious diseases with HPS are viral (Epstein barr virus, cytomegalovirus and varicella); bacterial (Gram-negative rods, Pneumococci and Mycoplasma); fungal (e.g. *Candida albicans*, *Cryptococcus neoformans* and *Histoplasma capsulatum*) and parasitic (e.g. *Babesia microti*, *Plasmodium falciparum*, *Strongyloides stercoralis*). Diagnosis is based on molecular diagnosis with pathologic mutations in the genes associated with HPS or fulfilment of five out of the eight criteria given below.

- 1) Fever $> 38.5^{\circ}\text{C}$
- 2) Splenomegaly
- 3) Cytopenia (atleast two lineages)
- 4) Hypertriglyceridemia ($> 265 \text{ mg/dl}$) and/or hypofibrinogenemia
- 5) Documented hemophagocytosis in bone marrow, spleen or lymph node
- 6) Low or absent natural killer cell activity
- 7) Increased serum ferritin $> 500 \text{ mg/dl}$
- 8) Soluble CD 25 $> 2400 \text{ U/ml}$.³

Our patient fulfilled 6 criteria out of the eight for the diagnosis of hemophagocytic syndrome. Treatment of secondary HPS is identifying the cause and treating it. Prolonged HPS is associated with hyperbilirubinemia, acute renal failure, encephalopathy, seizures and coagulation abnormalities.

Malaria one of the important disease affecting the tropical countries is still a major burden of health related conditions in India. The majority of the patients are affected by Plasmodium falciparum and P.vivax species. Most of the complicated disease with multiorgan involvement and mortality in malaria is caused by P. falciparum infection. The complications of malaria are ARDS, severe anemia, thrombocytopenia, seizures & coma, acute renal failure, hepatitis and rarely myocarditis.⁴

As discussed above there are plenty of reports of HPS associated with falciparum malaria. Recently several case reports and studies are coming with complications in vivax malaria. There is recent change of vivax from a more benign behavior to a malignant behavior. Our patient had p. vivax malaria infection presenting with hemophagocytic syndrome. There are few reports of vivax malaria presenting as HPS. A recent report from J.Comm med revealed that pancytopenia is a completely atypical manifestation of plasmodium vivax which occurs in only 0.9 %.^{5,6}

Some researches are suggesting a change in the virulence of P. vivax and is believed that it capable to cause cytoadherence and microvascular sequestration leading to organ dysfunction. The other explanation is the ability to activate proinflammatory cells (especially TNF & IFN). Also IL-10 a down regulator of inflammation is reduced in complicated vivax malaria. Age, malnutrition and parasite burden are associated with severe disease.^{7,8}

To conclude P.vivax malaria is having a trend towards more malignant behavior and further studies and researches are needed to understand the pathophysiology and identifying predictors of severe disease to reduce the morbidity and mortality.

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List of Figure

Figure 1:

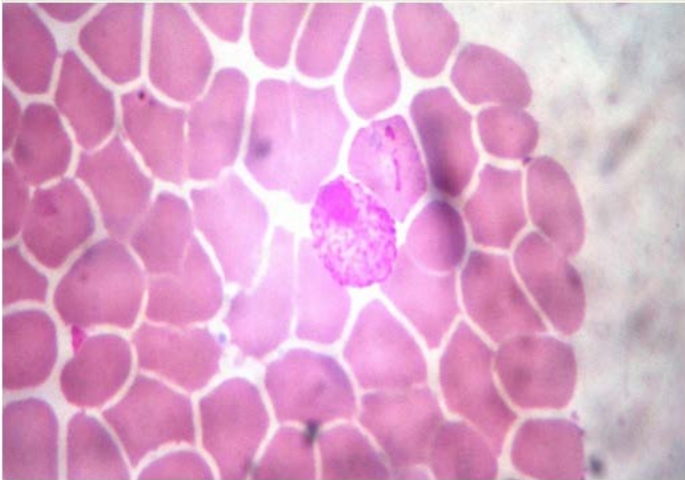


Figure 2:

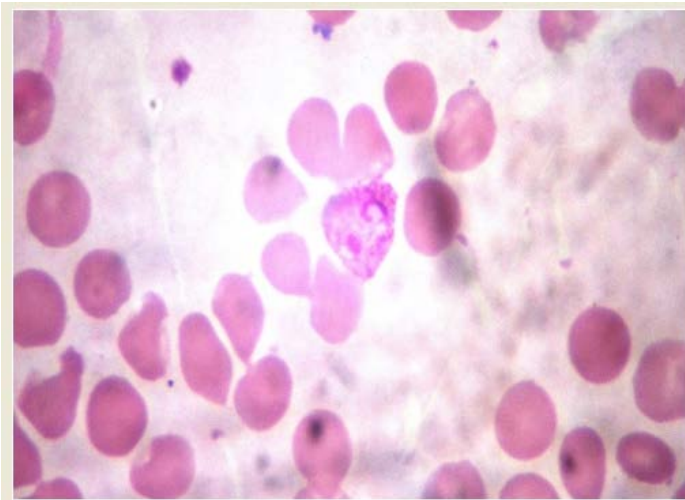


Figure 3:

