Malarial Hematopathy

Dhanashree S Kelkar*, Mrinal M Patnaik**, Shashank R Joshi***

Malarial infection reported as early as 1570 BC from Egypt still at times poses a diagnostic and therapeutic challenge in this modern anti microbial era.¹ It is transmitted through 103 countries causing 1-3 million deaths per year, predominantly in tropical countries like India. Malaria today affects approximately 5% of the world’s population. Approximately 270 million people suffer every year from malaria, and there are between 1 and 3 million deaths annually.¹ India shares a large burden of this disease especially drug resistant malaria. With inadequate diagnostic facilities this tropical parasitic infection poses a challenge to physicians.

“The great malaria problem and its solution” was the subtitle of the autobiography of Sir Ronald Ross, published in 1923. Few if any would have then believed that this parasitic disease would still continue to be the scourge of most nations especially developing countries. The disease is far from solved and is expanding its pathogenic armour by the evolution of unique mechanisms of drug/insecticide resistance and pathogenicity.

Malaria is a multisystem infection but importantly the affection of renal, haematological, central nervous system adds to the mortality. The involvement of various systems is seen irrespective of the type of malarial infection though the degree of involvement may vary. Pernicious syndrome consisting of anemia, hypotension, hematological abnormalities and cerebral involvement is seen not only in P falciparum infection but also in P vivax infection though with less frequency.²

With the emergence of advanced laboratory and investigational aids, it has now become fairly clear that the malarial parasite produces a hematological dysfunction. The term Malarial Hematopathy attempts to describes the involvement of one or more hematopoietic cell lines and includes the endothelial dysfunction that can give rise to a thrombotic microangiopathy that may evolve into a consumptive coagulopathy. Malarial haematopathy has been studied over ages and will continue to be researched on till malaria is existent as essentially it is a blood borne parasite.

The pathogenesis of anemia in malaria is multifactorial. There is an obligatory destruction of red blood cells containing parasites, there is an accelerated destruction of non-parasitized red blood cell that parallels disease severity and then there is the bone marrow dyserythropoiesis. The cause of dyserythropoiesis is believed to be related to intramedullary cytokine production.³ Studies have documented the presence of severe malarial anemia in African children and associated it with the 238 TNF-α promoter polymorphism and low levels of the anti-inflammatory cytokine IL-10.³

Platelet abnormalities are both qualitative as well as quantitative. Thrombocytopenia is a common occurrence in acute malaria. It is attributed amongst other factors to excessive splenic platelet pooling and a shortened platelet life span. Most patients have appropriately raised concentration of thrombopoietin. Thrombocytopenia appears to be associated with elevated serum concentrations of both pro- and anti-inflammatory cytokines their exact role still being under investigation.⁴ Protein aggregates, red cell or white cell fragments are known to interfere with platelet counts in automated blood analyzers, both by aperture impedance and optical technologies, giving rise to falsely normal platelet counts.⁵,⁶ When a falsely normal level is suspected, interference by pseudo-platelet particles can be confirmed by systematic examination of stained blood films.

The ideal test however would be to carry out a phase contrast microscope platelet count. There is also a problem of pseudo-thrombocytopenia that arises in patients of malaria. A large number of small platelets are seen, mixed with a few giant platelets due to the cytokine interference of megakaryopoiesis. These small platelets tend to get clumped together in groups of 3 to 12 and are falsely counted as a single platelet by the auto analyzer. Apart from thrombocytopenia patients with malarial fever can have platelet function abnormalities.⁶

Thrombocytopenia has been identified as a key indicator for malaria in patients with acute febrile illnesses. Thrombocytopenia occurs in both infections due to plasmodium vivax as well as falciparum. Although the mean platelet counts tend to be lower in patients with falciparum malaria, thrombocytopenia per se cannot be used as a distinguishing feature in a particular case of malaria. It also must be remembered that very low platelet counts can be encountered in both vivax and falciparum malaria and that they may not necessarily have prognostic implications or merit platelet transfusions. Clinical bleeding in malaria due to thrombocytopenia per se is not common even with low platelet counts, unless a co existing coagulopathy is present.

Total leukocyte count is usually normal however leukocytosis can occur especially when associated with pernicious malaria and superadded bacterial infections.⁷
Kenyan studies leukocytosis was associated with both severity and mortality in children with falciparum malaria irrespective of bacteremia. Leucopenia has also been observed. Increase in the number of atypical lymphocytes has been reported in acute falciparum infection at times leading to false positive serological tests like the widal titres.

Plasmodium falciparum has unique properties of cytoadherence and endovascular sequestration resulting in rosette formation. The pfEMP1 (plasmodium falciparum erythrocyte membrane protein 1) antigen is mainly responsible for this effect and is coded by the var gene found in the parasitic genome. The pfEMP1 protein is then apposed to a sub membranous accretion of parasite derived histidine rich protein (HRP) via electrostatic forces. These accretions form knobs on the surface of the RBC, which form the site for binding to the vascular endothelium causing diffuse endothelial damage and an accelerated coagulopathy in severe cases.

In the current study by Jadhav et al it has been found that although thrombocytopenia is a common occurrence in malarial fever, its presence is not a distinguishing feature between the two types. Although lower platelet counts are more likely to be seen with falciparum malaria they can also occur in cases of vivax infections. The take home message is that malarial fever can affect almost all aspects of the hematopoetic system including the endothelium as an organ. Malarial Hematopathy describes the protean range and mechanisms of this hematopoetic dysfunction. Also amongst all the hematological parameters the platelets are predominantly and prominently affected. However the platelet count cannot help to differentiate between different forms of malaria or help prognosticate the severity of the disease.

REFERENCES