

Severe Thrombocytopenia And Epistaxis Secondary To Plasmodium Vivax Infection

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Citation

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Abstract

As implied by its older, descriptive name, "benign tertian malaria," infection due to *Plasmodium vivax* is generally not fatal. While severe thrombocytopenia is one of the well-recognized complications of malaria due to *P. falciparum*, it has been documented only rarely in association with *P. vivax*. We report the case of a Mexican immigrant who presented to a rural Georgia hospital following the clinical onset of malaria due to *P. vivax* and whose course was marked by profound thrombocytopenia and spontaneous epistaxis initially unresponsive to platelet transfusions. Physicians everywhere must be aware of the both the common and uncommon manifestations of malaria, as early diagnosis and prompt treatment are key elements in minimizing morbidity and mortality.

INTRODUCTION

Malaria remains a global health problem with an estimated three to five hundred million new cases occurring each year. Although infection due to *Plasmodium falciparum* is responsible for the greatest overall morbidity and mortality, *P. vivax* contributes seventy to eighty million new cases to the annual worldwide burden of disease, especially in temperate regions (1). Autochthonous infections in the United States are uncommon and most domestic cases are diagnosed in immigrants or in travelers returning from endemic areas.

As implied by its older, descriptive name, "benign tertian malaria," infection due to *P. vivax* is generally not fatal. While severe thrombocytopenia is one of the well-recognized complications of malaria due to *P. falciparum*, it has been documented only rarely in association with *P. vivax*. We report the case of a Mexican immigrant who presented to a rural Georgia hospital following the clinical onset of malaria due to *P. vivax* and whose course was marked by epistaxis and profound thrombocytopenia initially unresponsive to platelet transfusions.

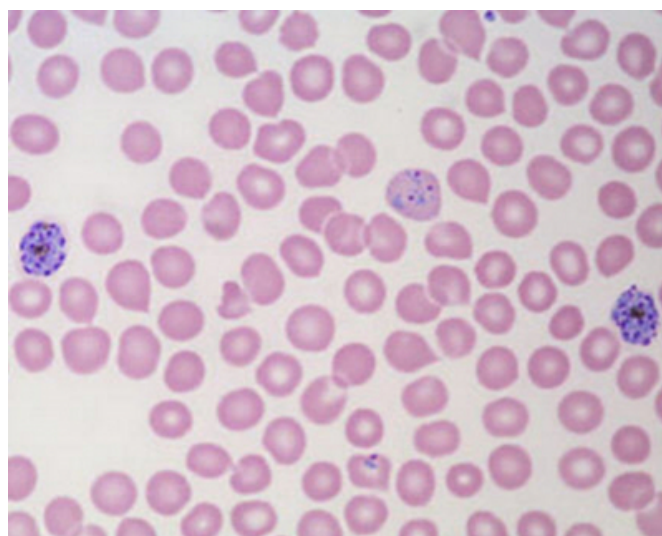
CASE REPORT

A 30 year old man presented with a one week history of intermittent severe headaches, fever and chills. Previously he had been in good health and took no medications. He was a native of Mexico; he worked as a farm laborer and had been

in Georgia for one year. He was febrile with a temperature of 103°F. The remainder of the physical exam was normal. Initial laboratory studies were remarkable for thrombocytopenia with a platelet count of 19,000/ul. Many parasitized red blood cells (Figure 1) were found in the peripheral smear.

Figure 1

Figure 1: A ring form, an early ameboid trophozoite with co-existing Schuffner stippling and a mature schizont can be seen in one field. Note that the red blood cells hosting the trophozoite and the schizont are larger than the surrounding non-parasitized red blood cells. (Wright stain, X1000)



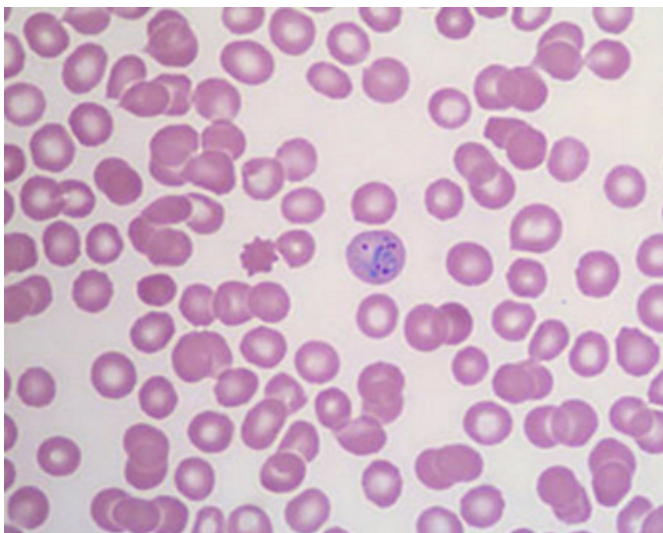
A presumptive diagnosis of malaria was made. The patient

was begun on quinine sulfate and doxycycline. Three hours later, his platelet count was 6,000/uL. He received ten units of random donor platelets, but his platelet count rose to only 24,000/uL. Eighteen hours later he experienced spontaneous epistaxis and received ten units of random donor platelets. His platelet count rose to 64,000/uL and the bleeding stopped. His platelet count remained in the 50-60,000/uL range for three days and then became normal.

Peripheral blood smear examination revealed that approximately two percent of red blood cells harbored parasites. The parasites ranged from ring forms to more mature trophozoites with Schuffner stippling (Figure 2).

Figure 2

Figure 2: Maturing trophozoite with Schuffner stippling. (Wright stain, X1000)



Many mature schizonts containing malaria pigment and gametocytes were also present (Figures 3 and 4). Parasitized red blood cells appeared larger than non-parasitized cells. Occasional red blood cells were noted to contain more than one ring form. The schizonts consistently possessed in excess of twelve nuclei. The white blood cells appeared normal qualitatively and quantitatively; no malaria pigment was seen in neutrophils.

Figure 3

Figure 3: A mature schizont possessing in excess of 16 merozoites. (Wright stain, X1000)

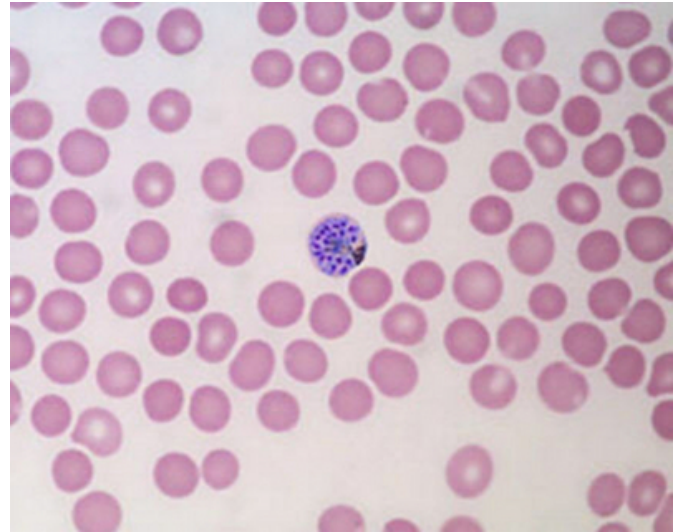
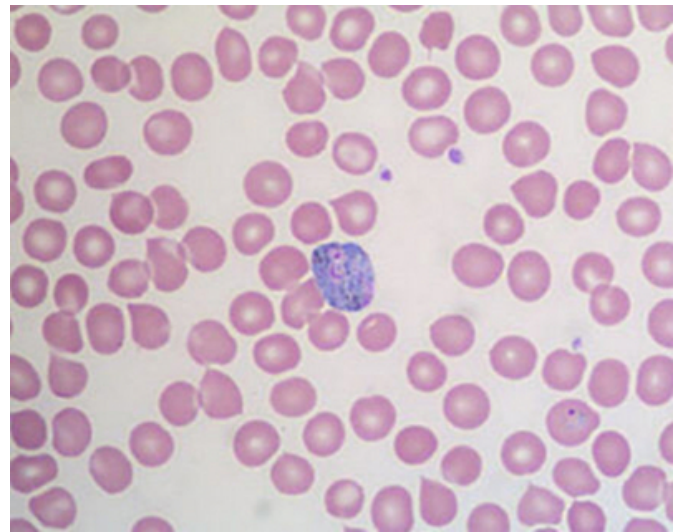


Figure 4

Figure 4: A ring form and a gametocyte are present in this field. (Wright stain, X 1000)



The findings supported a diagnosis of malaria due to *P. vivax*. The treatment was changed to chloroquine through the remainder of his hospitalization. Four days later, the patient was discharged to receive primaquine as an outpatient to treat any residual hepatic forms of the organism.

DISCUSSION

Mild reduction in circulating platelets is observed relatively frequently in cases of malaria due to *P. vivax* but cases of severe thrombocytopenia are quite rare.⁽²⁾ A recent review of 101 symptomatic patients revealed that 85% had platelet

counts less than 150,000/uL; less than five percent, however, had counts under 40,000/uL, and none were reported to be as severely thrombocytopenic as our patient.⁽³⁾ In 1999, Kakar et al. reported a patient whose platelet count was 5,000/ul at presentation.⁽⁴⁾ Most recently, Makkar et al. reported a patient who presented after two days of spontaneous gingival bleeding with a platelet count of 8,000/ul.⁽⁵⁾ In both instances the patients were adults. The last case and our own are the only two reported incidences of spontaneous mucosal hemorrhage associated with *P.vivax* infection.

The pathogenesis of thrombocytopenia in malaria is unclear, although increased platelet destruction rather than decreased production appears to be responsible. Bone marrow studies have revealed adequate or increased numbers of megakaryocytes and analyses of plasma thrombopoietin levels have ruled out reduction of this cytokine as the cause of thrombocytopenia.⁽⁶⁾ Platelet consumption by disseminated intravascular coagulation (DIC) has also been suggested; DIC, however, is seldom seen in even the most severe cases of malaria.⁽⁴⁾

The spleen has been implicated as a site of excess sequestration. Splenomegaly alone, however, cannot be the mechanism as most patients who develop thrombocytopenia do so early in the course of the infection before splenic enlargement has developed. An immune mechanism that would lead to opsonization of platelets with phagocytosis by fixed macrophages has been proposed.^(5,7) Studies showing the inverse relationship between titers of serum platelet-associated IgG and the platelet count in *P. vivax* infections support that hypothesis.⁽⁸⁾ Studies in experimental animals suggest an activation of caspases and subsequent apoptosis may be involved in the development of malaria-associated thrombocytopenia.⁽⁶⁾

Another possible cause of thrombocytopenia would be co-infection with *P. falciparum*. Our patient, however, had been in the United States for more than a year. It is unlikely that he would have presented so long after initial infection if he had been harboring *P. falciparum*. *P. vivax*, on the other hand, is characterized by a hypnozoitic stage which allows it to remain dormant in hepatocytes for extended time periods. Our patient could have been infected with *P. vivax* prior to his leaving Mexico and remained asymptomatic for months. Moreover, no pathognomonic gametocytes of *P. falciparum* were found in our patient's peripheral blood despite extensive evaluation of thick and thin smears.

Microscopic identification is still the "gold standard" of

malaria diagnosis. Non-morphologic diagnostic techniques for malaria have been developed and are most helpful when malaria is suspected, but parasites cannot readily be found or an experienced observer is not available.⁽⁹⁾ These procedures were not performed on our patient's blood because of the heavy parasite burden and ease in finding characteristic schizont forms.

CONCLUSION

Our case illustrates that, in an era of frequent travel and widespread immigration, malaria can be seen in areas far from endemic regions, and that clinical disease can be temporally remote from last exposure. This axiom is reinforced by a recent study that found one third of malaria-infected travelers developed illness more than two months after their return and that late-onset illness was not prevented by the commonly used schizonticides.⁽¹⁰⁾ In addition, a historically "benign" form of malaria can be associated with life-threatening complications, as seen in this case of severe thrombocytopenia.

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