

Hyper-reactive malarial splenomegaly and splenic infarct in a caucasian toddler

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Abstract

A 4-year-old boy from the United States had been staying in Indonesia for five months when he presented with fever, severe lethargy, progressive weight loss, and abdominal distension. He was first diagnosed with *Plasmodium vivax* infection in Indonesia and received treatment with chloroquine. However, his condition continued to deteriorate and he required erythrocyte transfusion for severe anemia. Three weeks into his illness, he was found to have low parasitemia with *Plasmodium falciparum* with massive hepatosplenomegaly in Singapore. A splenic infarct was also documented on computed tomography. Treatment with atovaquone-proguanil resulted in stabilization of the hemoglobin level and rapid reduction in splenic size, with clearance of malarial parasites from the bloodstream. Although reported typically in adult tropical residents, hyper-reactive malarial splenomegaly may occasionally be found in the pediatric traveler. Clinicians receiving children returning from the tropical regions should be aware of this potentially life-threatening complication of partially treated malaria.

Introduction

The spleen plays an important role of clearing infected erythrocytes in malarial infection.¹

Complications involving the spleen have been reported with infarction,² abscess,³ subcapsular hematoma,⁴ rupture,⁵ and hyper-reactive malarial splenomegaly (HMS) or tropical splenomegaly syndrome.⁶

The latter is commonly understood as an immunological reaction from the infected host and may be confused with lymphoproliferative syndromes. HMS is usually described in tropical residents as a result of chronic malarial infection, and is mostly recognized in young and middle-aged adults.⁶

A unique case of HMS complicated by splenic infarct affecting a Caucasian child is reported.

Case Report

A 4-year 11-month-old boy from the United States was staying with his family in a tribal region in Indonesia in the preceding five months. He had recurrent febrile illnesses during this period and had been given chloroquine intermittently as prophylaxis, but his general health started to deteriorate about a month before admission. The child complained of epigastric pains. He was noted to be febrile, increasingly tired, and losing weight. He was first admitted to a local hospital and was diagnosed to have *Plasmodium vivax* infection. He was treated with chloroquine (the exact treatment could not be verified) but the condition did not improve. He was also found to have increasing splenomegaly and severe anemia (lowest hemoglobin recorded, 3.6 g/dL). Red cell transfusion was carried out twice before he was evacuated to Singapore for further management.

The child's condition was stable on admission. Pallor was mild and there was no jaundice. The liver and spleen were grossly enlarged at 6 cm and 8 cm below the costal margins, respectively. The first full blood counts showed hemoglobin 9.8 g/dL, white cells $5.48 \times 10^9/L$, platelet $123 \times 10^9/L$. The red cells were anisopoikilocytic with prominent polychromasia and occasional nucleated forms. Immature trophozoites and gametocytes characteristic of *Plasmodium falciparum* were also seen (Figure 1), with a parasite load of 0.1%. Treatment with atovaquone 500 mg-proguanil 200 mg for three days was commenced.

Computed tomography revealed enlarged liver and spleen with no signs of thrombosis in the portal venous system. The liver parenchyma was normal. An area of infarction was found in the anterior aspect of the lower pole of the spleen (Figure 2).

Two days later, his hemoglobin dropped to 8.3 g/dL and another red cell transfusion was given. Tests for glucose-6-phosphate dehydrogenase deficiency, direct Coombs test, and occult blood in stool were negative. Serum ferritin (664 mg/mL), bilirubin (15 $\mu\text{mol/L}$), aspartate transferase (37 U/L), and alanine transferase (14 U/L) were normal. Serologic tests for hepatitis B, hepatitis C, human immunodeficiency virus, and Parvovirus B19 were negative. Serum IgA (0.81 g/L), and IgG (10.4 g/L) were normal. Serum IgM was raised (2.97 g/L, normal 0.51-2.14). Lymphocyte subsets showed a mild increase in B cells (663/ μL , normal 65-620) only.

A week after completion of the anti-malarial treatment, the child became more cheerful and had regained his premorbid body weight. The liver was no longer palpable and the spleen was 4 cm below the costal margin. Repeat

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hemoglobin was 11.7 g/dL, identical to the post-transfusion measurement. Parasite load was less than 0.01%, and no more parasites were seen on the blood film a week later.

Discussion

Hyper-reactive malarial splenomegaly is believed to be an immunological complication of malarial infection.⁷ Defective function of suppressive T cells leads to dysregulation of B cells and over-production of IgM. The deposition of immune complexes in the reticuloendothelial system results in the enlargement of the liver and spleen even in the absence of significant parasitemia as illustrated in this case. Clinico-

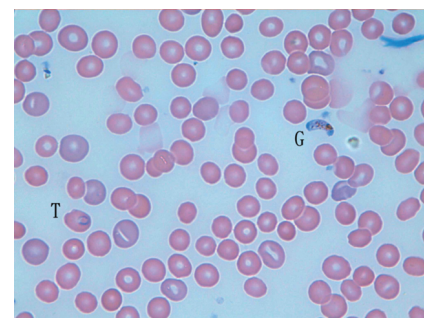


Figure 1. Photomicrograph of the peripheral blood film with Giemsa stain ($\times 100$) showing an immature trophozoite (T) and a gametocyte (G) characteristic of *Plasmodium falciparum* infection.

laboratory diagnostic criteria have been described.⁸ Differentiation from chronic lymphoproliferative disorders is important in the adult patient, but this is usually not an issue in childhood, though the condition has rarely been reported in pediatric ages.^{9,10} However, diagnostic confusion may happen as HMS may be mistaken as other febrile illnesses in the young child,⁹ or when the child presents late after

returning from an endemic area.¹⁰

Splenic infarct is an unusual complication from malarial infection, but it is often innocuous and no treatment is required.² Splenic infarct has to be distinguished from abscess which has also been noted after malarial infection.³ Spontaneous rupture is a recognized risk in patients with grossly enlarged spleens with an estimated risk of 2% in those affected by malaria.⁵

Clinicians evaluating patients returning from the tropics should be aware that diagnostic and therapeutic details from remote health-care facilities may be difficult to verify. Failure to eradicate the parasite may be encountered because of inaccurate parasite identification, re-infection, inadequate drug dosing, drug resistance, or omission of the treatment for the hepatic stage of infection. It is not clear if the malaria parasite had been misidentified or a co-infection with two malarial species had not been found at the initial stage in the reported case. Nevertheless, severe splenic complications following malaria should be looked out for in any child returning from the tropics, and they should be followed up for radical cure.



Figure 2. Axial and coronal contrast-enhanced computed tomography showing an infarct in the anterior aspect of the lower pole in the enlarged spleen.

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