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The Hyper-Reactive Malarial Splenomegaly- A Rare and Severe Form of Chronic Plasmodial Infection: About A Case

Keïta Kaly[1*], Sangaré Drissa[2], Berthé Brehima Boly[3], Tolo Nagou[4], Togo Mamadou[5], Dembélé Ibrahima Dembélé[1], Mallé Mamadou[1], Traoré Abdoulaye Mamadou[6,8], Dabo Garan[7,8], Sy Djibril[1,8], Traoré Djénébou[1,8], Traoré Abdel Kader[8], Soukho Assétou Kaya[1,8], Minta Daouda Kassim[6,8], Traoré Hamar Alassane[8]

[1]Department of Internal Medicine at the University Hospital Center of the Point G, Bamako, Mali
[2]Internal Medicine Unit, Department of Medicine and Medical Specialties, Fousseyni Daou Regional Hospital of Kayes, Kayes, Mali
[3]Infirmary of Bamako, Malian Army Health Service, Mali
[4]Department of Medicine at the Bocar Sidy Sall University Hospital Center of Kati, Koulikoro, Mali
[5]Department of Internal Medicine, Gabriel Touré University Hospital Center, Bamako, Mali
[6]Department of Infectious Diseases and tropical Medicine at the University Hospital Center of the Point G, Bamako, Mali
[7]Department of Medicine and Medical Specialties, at the Hospital of Mali, Bamako, Mali
[8]Faculty of Medicine and Odonto-stomatology (FMOS) - University of Sciences, Techniques and Technologies of Bamako (USTTB), Mali

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***Corresponding author:** Dr Keïta Kaly
Department of Internal Medicine at the University Hospital Center of the Point G, Bamako, Mali

Abstract **Case Report**

Introduction: Hyper-reactive malarial splenomegaly is a leading cause of large tropical splenomegaly in endemic zones. Here, we report a case diagnosed in a young woman living in Guinea, a malaria-endemic area. Clinical observation: A 32-year-old Guinean woman with a history of repetitive malaria infection episodes presented to the internal medicine outpatient clinic with 5-months history of voluminous mass of the left flank extending to the umbilical region, with no pain and progressive onset, and a sensation of early satiety accompanied by eructation and epigastralgia worsened with eating. Digestive examination revealed a large, firm, smooth-surfaced, painless splenomegaly with a splenic size 20 centimeters below the left costal margin on the mid-clavicular line and measuring 28 centimeters in its long axis. The initial complete blood count showed a normocytic normochromic anemia with lymphocytosis, neutropenia and thrombocytopenia. The erythrocyte sedimentation rate (ESR) was 65 mm at the first hour. Malaria rapid diagnostic test (RDT) was positive for Plasmodium. The thick blood smear had come back negative. Serum protein electrophoresis demonstrated a decrease in albumin to 36.5 g/l and an increase in gamma globulins to 19.1 g/l. Immunoelectrophoresis of serum proteins showed a polyclonal increase in IgG. Abdominal ultrasound revealed enormous homogeneous splenomegaly (180 millimeters). The diagnosis of Hyper-reactive malarial splenomegaly was made on the basis of diagnostic criteria established by Fakunle et al in 1981. Our patient presented with enlarged splenomegaly, negative thick smear, positive RDT for plasmodium, elevated erythrocyte sedimentation rate, lymphocytosis, pancytopenia, and a good therapeutic response. Atovaquone-proguanil 250mg/100 mg at a dose of 1000mg/400 mg, i.e. 4 tablets taken as a single dose over three days, was initiated, then relayed by alternance of doxycycline 100 mg (100 mg once daily) for 1 month and nivaquine 100 mg (100 mg once daily) for 1 month. The 2-month follow-up visit was marked by the disappearance of digestive signs, on 3 month follow-up visit by regression of splenomegaly with splenic size at 15.5 centimeters, and on 4-month follow-up visit it was at 9.5 centimeters. Conclusion: Hyper-reactive malarial splenomegaly, although a rare form of chronic plasmodial infection, should not be overlooked by physicians taking charge of this case, infectiologist, hematologist and internist.

Keywords: Hyper-reactive malarial splenomegaly, hypersplenism, malaria, internal medicine, Mali.

INTRODUCTION

Hyper-reactive malarial splenomegaly is the chronic stage of a long-term stimulation of the immune system secondary to plasmodial infections, more frequently in genetically predisposed patients [1]. It is a leading cause of large tropical splenomegaly in endemic zones [2, 3]. Here, we report a case diagnosed in a young woman living in Guinea, a malaria-endemic area.

CLINICAL OBSERVATIONS

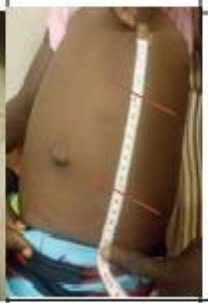
A 32-year-old Guinean woman with a history of repetitive malaria infection episodes presented to the internal medicine outpatient clinic with 5-months history of voluminous mass of the left flank extending to the umbilical region, with no pain and progressive onset, and a sensation of early satiety accompanied by eructation and epigastralgia worsened with eating. On physical examination, the blood pressure was 100/60 mmHg, the heart rate was 94 beats per minute, the respiratory rate 22 cycles per minute, the temperature was 37.3°C and the Body Mass Index (BMI) was 18.08 kilogram per square meter. Digestive examination revealed a large, firm, smooth-surfaced, painless splenomegaly with a splenic size 20 centimeters below the left costal margin on the mid-clavicular line and measuring 28 centimeters in its long axis (see table below).

The initial complete blood count showed a normocytic normochromic anemia (the hemoglobin level was 9.3 g per deciliter, the mean corpuscular volume was 82.9 femtoliter, and the mean corpuscular hemoglobin concentration was 26.1 picograms) with lymphocytosis (lymphocytes, 7, 590 cells per cubic millimeter), neutropenia (neutrophils, 1,720 cells per cubic millimeter) and thrombocytopenia (platelet count, 120 000 cells per millimeter). The inflammatory workup showed that the erythrocyte sedimentation rate (ESR) was 65 millimeters at the first hour (normal range, 0 to 29 millimeters) and the blood C-reactive protein level was 5 mg per liter (normal value, < to 6 mg per liters). Malaria rapid diagnostic test (RDT) was positive for Plasmodium. The thick blood smear had come back negative. Serum protein electrophoresis demonstrated a decrease in albumin to 36.5 g per liter and an increase in gamma globulins to 19.1 g per liter. Immunoelectrophoresis of serum proteins showed a polyclonal increase in IgG. Abdominal ultrasound revealed enormous homogeneous splenomegaly (180 millimeters). Liver biopsy was not performed.

The diagnosis of Hyper-reactive malarial splenomegaly was made on the basis of diagnostic criteria established by Fakunle et al in 1981 [4]. Our patient presented with enlarged splenomegaly, negative thick smear, positive RDT for plasmodium, elevated erythrocyte sedimentation rate, lymphocytosis, pancytopenia, and a good therapeutic response.

Atovaquone-proguanil 250mg/100 mg at a dose of 1000mg/400 mg, i.e. 4 tablets taken as a single dose over three days, was initiated, then relayed by alternance of doxycycline 100 mg (100 mg once daily) for 1 month and nivaquine 100 mg (100 mg once daily) for 1 month (see table below). The 2-month follow-up visit was marked by the disappearance of digestive signs, on 3 month follow-up visit by regression of splenomegaly with splenic arrow at 15.5 centimeters, and on 4-month follow-up visit it was at 9.5 centimeters (see table below).

Table 1: showing the evolution of splenomegaly under antimalarial therapy

	On baseline visit (M1)	*On two month follow-up visit (M2)*	*On three month follow-up visit (M3)*	*On four month follow-up visit (M4)*
Splenic size in centimeter below the left costal margin on the mid-clavicular line	20 centimeters	19 centimeters	15.5 centimeters	09.5 centimeters
Images taken during the measurement			-	
Treatment	Atovaquone-proguanil 250/100 mg over 3 days then doxycycline 100 mg for 1 month	Nivaquine 100 mg for 1 month	Doxycycline 100 mg for 1 month	Nivaquine 100 mg for 1 month

DISCUSSION

Hyper-reactive malarial splenomegaly represents one of the leading causes of massive splenomegaly in malaria-endemic countries [3]. It is caused by an aberrant immune response to a chronic antigenic stimulation in subjects long exposed to malaria parasites [2]. In tropical areas, cases have been described most frequently in South Africa, Uganda, Nigeria, Zambia, Ghana, Kenya and, most notably, Papua New Guinea [1]. The prevalence of the condition is difficult to pinpoint, but figures of 1-2% have been reported in Nigeria [5]. We describe a case diagnosed in a young woman of Guinean origin, revealed by a large splenomegaly and a dyspeptic syndrome. Overall, the range of the spleen size reported to define splenomegaly was extremely variable, from 3 to 30 centimeters below the costal margin [6, 7, 8]. It was 20 centimeters in our patient on the baseline visit.

The syndrome is characterized by macroglobulinaemia with overproduction of immunoglobulin, especially of the IgM class, which aggregate into high molecular immune complexes and cause persistent splenomegaly be- cause of prolonged clearance from the reticuloendothelial tissue [9]. Indeed, the diagnostic criterion for Hyper-reactive malarial splenomegaly was proposed by Fakunle in 1981 [4], one of the major criteria is an elevated IgM titer. However, cases of hyperimmune malarial splenomegaly have been reported with a normal IgM titer and also with simultaneous elevation of IgM and IgG titers [8, 10]. We report a case with elevated IgG and normal IgM titers.

The main differential diagnoses of Hyper-reactive malarial splenomegaly include evolving visceral malaria, splenic lymphoma, cirrhosis post chronic viral hepatitis splenic hydatidosis. Evolving visceral malaria occurs in children who are unprotected, or who live in endemic areas, or Europeans in regions where chloroquine-resistant strains exist. In evolving visceral malaria, splenomegaly is a constant in children, thick blood smears are intermittently positive with low parasitaemia, antimalarial serology shows a high titre, and immunoelectrophoresis of serum proteins shows high level of IgM [11].

Our young adult patient presented with splenomegaly, anti-malarial serology showing a high titer, but the thick blood smear was negative. According to Bedu-Addo and Bates [3], in endemic areas and in the absence of molecular biology, suggest differentiating Hyper-reactive malarial splenomegaly from lymphoma on the basis of age (less than 40 years) and total circulating lymphocyte count (less than 10 G/l). Our patient was 30 years old and had a high lymphocyte count, but inferior to 10,000 cells per cubic militer.

Treatment is not well codified and is most frequently based on chloroquine, proguanil, primaquine and mefloquine, pyrimethamine, and sulphadoxine/pyrimethamine. The duration of antimalarial treatment is guided by the evolution of splenic volume; generally, the duration of therapy ranged from a minimum of one month to a life-long treatment [1, 8]. With administration of Atovaquone-proguanil 250mg/100 mg followed by alternance of doxycycline 100 mg (100 mg once daily) for 1 month and nivaquine 100 mg (100 mg once daily) for 1 month, evolution on 4 months follow-up visit was marked by regression of splenomegaly and disappearance of digestive signs related to the compression of the voluminous splenomegaly.

CONCLUSION

Hyper-reactive malarial splenomegaly, although a rare form of chronic plasmodial infection, should not be overlooked by physicians taking charge of this case, infectiologist, hematologist and internist.

Conflicts of interest

The authors declare that they do not have any conflict of interest for this article.

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