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Hyper-Reactive Malarial Splenomegaly Syndrome (HMS): Management Challenges in a Rural Community in Southwest Nigeria – Case Report

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ABSTRACT

Hyper-reactive malarial Splenomegaly Syndrome (HMS) is a condition with multifaceted etiopathogenesis. Some authorities believe it is linked to reticuloendothelial hyperplasia from repeated bombardments by malaria IgM complexes.

Here we present a 14-year old boy found with a massive spleen during a community malaria survey. He had no formal education and lived in a swampy area with his grandmother. He was pale, icteric, and undernourished. He was administered acute antimalarial therapy, malaria prophylaxis and followed up for 18 months. He showed remarkable improvement with his massive spleen receding and was enrolled into school, but compliance with medication, schooling, and relocating from a swampy home was challenging.

Keywords: Hyper-Reactive Malarial Splenomegaly Syndrome, Malaria, Community Outreach, Environmental Sanitation, Nigeria

INTRODUCTION

Hyper-reactive Malarial Syndrome (HMS) is also known as Tropical Splenomegaly Syndrome (TSS) [1]. It is associated with chronic exposure to malaria, characterized by gross splenomegaly of at least 10cm below the costal margin, for which no other cause is identified, elevated serum immunoglobulin M (IgM) levels, high antibody levels of Plasmodium species, and clinical and immunologic responses to antimalarial drugs such as Proguanil [1,2]. The afore-listed are the major diagnostic criteria for HMS as proposed by Fakunle in 1981 [1,2]. The minor diagnostic criteria include hepatic sinusoidal lymphocytosis, hypersplenism, especially anemia, normal immune responses to antigens and occurrence within families [1,2]. Affected individuals are prone to infections, splenic rupture and death if untreated [3]. HMS is treated with antimalarial drugs; most commonly used include weekly Chloroquine or daily Proguanil [1,3]. The duration of treatment in endemic countries may vary from one month to lifelong [3]. Therapeutic splenectomy is not routinely done because of the high perioperative mortality rate. It is usually reserved for patients with disabling splenomegaly and those who do not respond to drugs [3].

Several authors have reported a global reduction in malaria over the last decade, especially

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since the adoption of malaria intervention programs, including the use of artemisinin-based combination therapies (ACTs), insecticide-treated nets (ITNs) and indoor residual spraying (IRS) [4–7]. Consequently, it is expected that manifestations of chronic malaria such as TSS should become extinct. In Nigeria, children younger than 5 years are the main focus of these interventions [8,9], while older children living in malaria-endemic areas are expected to have acquired some herd immunity [7,10,11]. On the contrary, there have been reports of frequent malaria infection among this group of older children despite the general decline of malaria infection in recent times [11,12]. We report a case of HMS in an adolescent met during a malaria surveillance activity in a rural community in Southwest Nigeria, highlighting its management challenges in a resource-poor setting.

CONSENT: The adolescent and his caregiver gave their assent and written consent respectively, for this case report to be published.

CASE PRESENTATION: A.S., a 14-year-old boy encountered during a community survey on malaria among children aged 1–15 years, at Ire-Ekiti, Southwest Nigeria, in April 2019 with an enlarged spleen. He had been abandoned in his widowed paternal grandmother's care since his then-teenage 14-year-old mother delivered him. His mother was a petty trader and his father was a subsistence farmer; both had secondary school levels of education.

He lived in a household of 9 people in a crowded one room and a parlor apartment in a water-logged environment. He never slept under a mosquito net as he did not have one, but his grandmother routinely gave him paracetamol and local herbs each time he had a fever. He had never been transfused.

Physical examination revealed that he was pale, icteric, afebrile, undernourished with a weight of 24.9kg (below the 3rd percentile for age and sex), stunted with a height of 1.26m (below the 3rd percentile for age and sex). He had a low BMI of 15.7kg/m2 which corresponded to the 3rd percentile of the expected BMI for his age and sex. His spleen measured 17.5cm, taken from the left subcostal margin to the tip of the spleen, but his

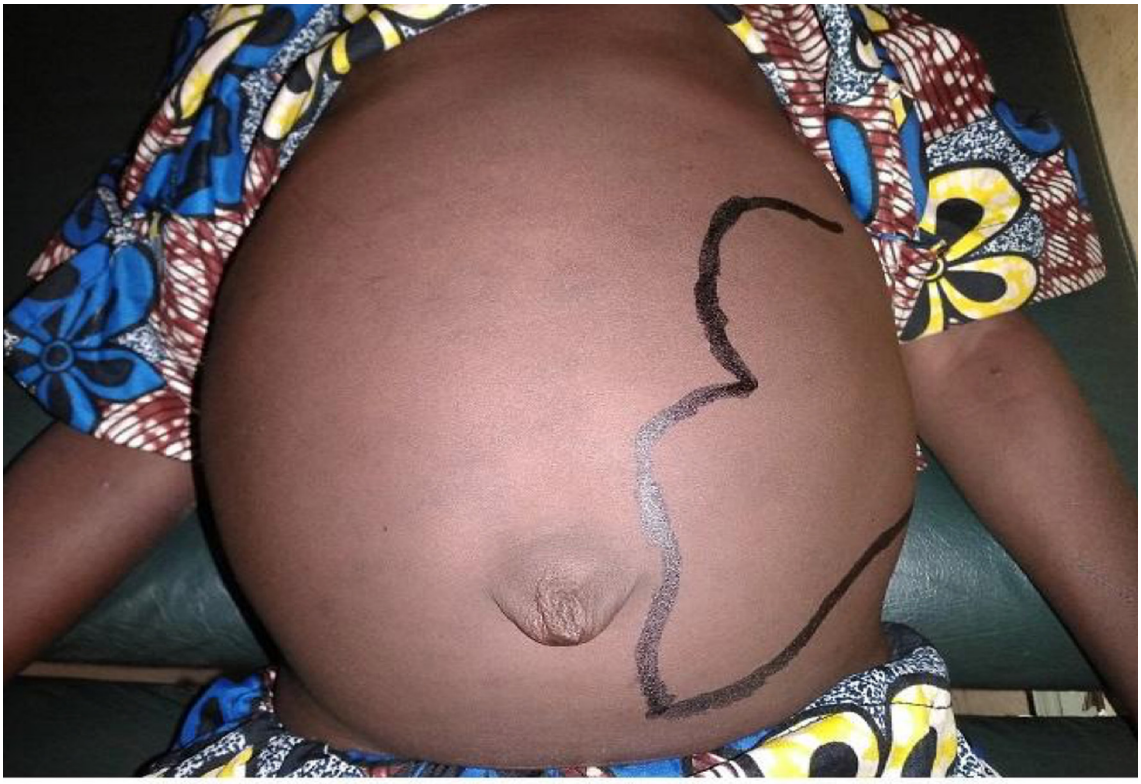


Figure 1: Splenomegaly outlined with a black marker

liver was not enlarged with a normal liver span of 6cm. Figure 1 shows his abdomen with his large spleen outlined in black. He did not have any significant lymph node enlargement. Although he was tachypneic with a respiratory rate of 24 cycles/min, he had a normal pulse rate of 96 beats/min and a normal temperature of 36.6oC.

He was severely anemic with a hemoglobin concentration of 5.0g/dL and a low red blood cell count of 2.03 cells x 1012/L. Still, he had a normal leukocyte count of 6.3 cells x 109/L with normal differentials and a normal platelet count of 228 cells x 109/L. He had a low MCV of 72 fL and a high RDW of 21.7%. His genotype was AA. His blood film showed infection with Plasmodium falciparum with a low parasite density of 88 parasites/µL of cells, microcytosis and hypochromia. There were no blasts seen. His Sputum AAFB by gene Xpert was negative for Mycobacterium tuberculosis. HIV screening was negative and his stool microscopy was negative for ova of parasites. There was, however, no facility for IgM malaria assay or malaria antibodies.

According to the WHO recommendation, he was treated for malaria with Artemether/Lumefantrine III oral tablets twice daily for 3 days; thereafter, he was commenced on malaria prophylaxis of Proguanil 200mg oral tablets daily and followed up for 18 months. He was given an insecticide-treated net under which he now sleeps and also enrolled in an elementary school. He initially had poor compliance with Proguanil, which improved after frequent persuasions at home visits. He, however, had a repeat dose of the ACT and was also given tabs Albendazole 400mg twice at a 12-month interval because of his risk for hookworm infestation, as he often accompanied his grandmother to the farm. His grandmother declined blood transfusion for reasons she preferred not to disclose.

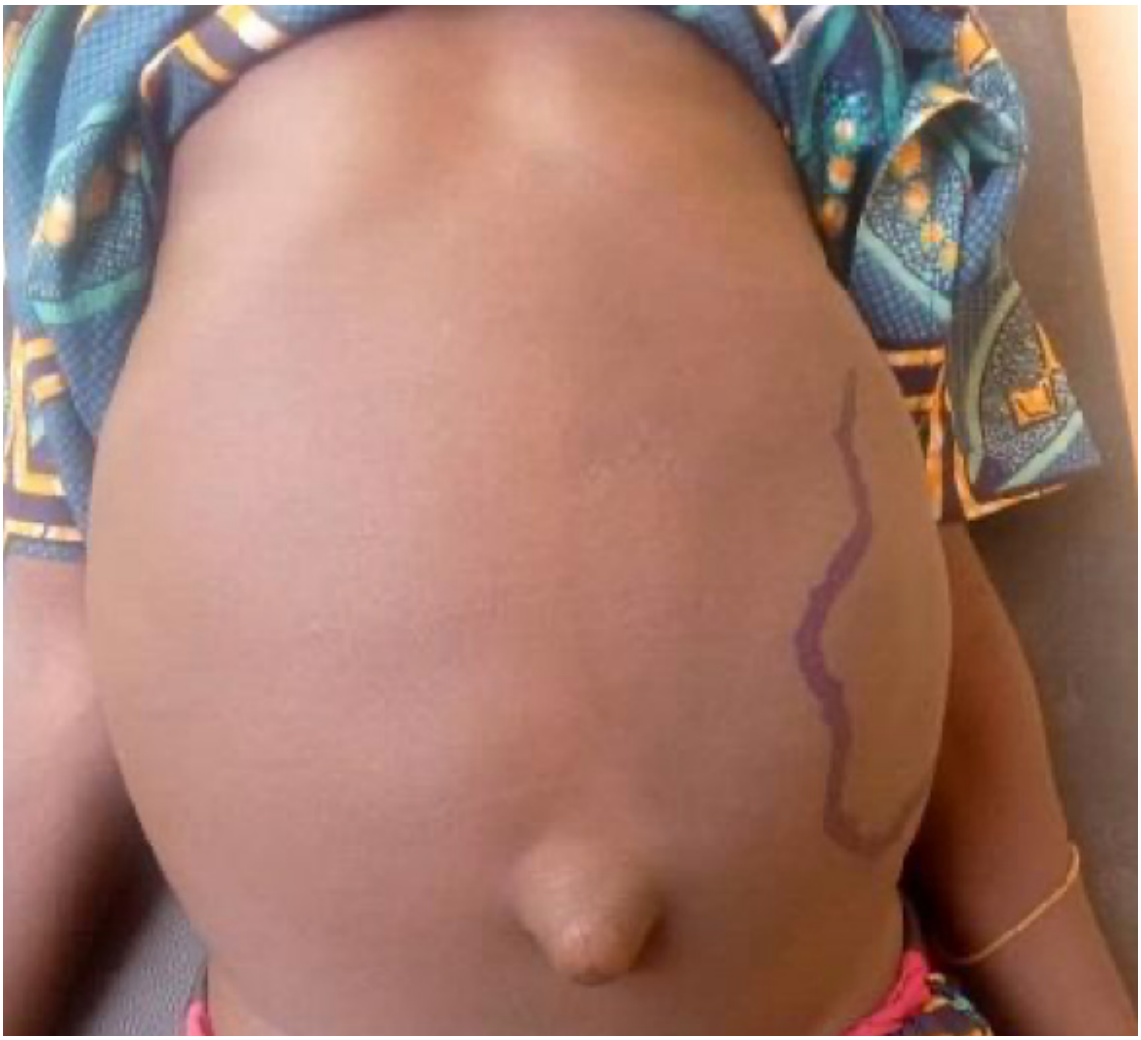
During the follow-up period, he was no longer icteric or tachypneic and his height had slightly increased to 1.30m, although his weight remained static. However, his schooling was transiently interrupted for about eight months by the government-imposed restrictions to curb the spread of COVID-19; hence his school performance could not be assessed. The movement restrictions also transiently interrupted home visits to ensure drug compliance.

His spleen size significantly reduced to 13.0cm (about 26% spleen size reduction), shown in Figure 2, his Hb concentration improved minimally to 5.6g/dL and his red blood cell count increased to 4.01 cells x 1012/L. Repeat microscopy after 18 months of encounter revealed intermediate malaria parasite density of 1,432 parasites/µL of cells. He also had a low serum iron of 58.2µg/dl and high serum ferritin of 847.7ng/ml, but there were no ova or parasites isolated from his stool. He was again treated with ACTs and thereafter recommenced on Proguanil and iron supplements. His grandmother was counselled on possibly relocating from the swamp to curb repeated exposure to malaria infection.

DISCUSSION

The diagnosis and management of HMS in resource-poor settings are quite cumbersome. Similar to the experience documented by Emodi and Ikefuna [13] in Enugu, Nigeria, we did not have the laboratory facilities to fulfil the other diagnostic criteria for TSS, such as elevated IgM and high levels of antibody to malaria as postulated by Fakunle in 1981 [2]. However, the clinical response to Proguanil in this case report and an absence of any other common cause of massive splenomegaly make the diagnosis highly suggestive of HMS. As submitted by Leoni et al. [3] in a systematic review of literature, diagnosing HMS based on clinical suspicion, in the absence of the aforementioned investigations, is acceptable for prompt treatment to prevent mortality as was done in this case because the boy was already symptomatic (anemic and tachypnoeic) as at the time of our first contact with him. Moreover, there were no other causes of splenomegaly, particularly lymphoproliferative disorders.

Aside from challenges with laboratory investigations, there were other challenges in managing HMS in this rural community. These included poor housing conditions and the water-logged home environment. Even though we provided a mosquito net for this adolescent to sleep under, the water-logged home environment of the adolescent encourages the breeding of mosquitoes [11,14]. Good environmental sanitation with an effective drainage system will further curb incessant malaria infection in the boy. Ideally, the adolescent and his caregiver need to relocate from their water-logged residence, but this is a daunting task that we are yet to achieve. However, we suggest a scale-up of malaria intervention programs, especially the free



distribution of mosquito nets, to incorporate older children, especially in rural communities. This will help achieve malaria control on a larger scale.

The resurgence of malaria parasitemia observed in this case further led credence to the previous report that malaria parasitemia may become more pronounced after initiation of Proguanil in patients with HMS because Proguanil reduces the spleen's hyperactive mopping of parasitized cells [13]. Therefore, it is necessary to follow up on malaria parasitaemia of patients with HMS to promptly and effectively treat acute malaria infections with ACTs as recommended by the WHO [15]. Hence, the active malaria parasitemia surveillance was done for him and his subsequent treatment with ACTs, as ACTs are currently the first-line treatment for malaria in Nigeria [15,16].

That the adolescent's schooling was adversely affected could reflect his social standing and or, as a consequence of his medical condition (HMS). Nevertheless, he probably would not have had optimal school performance given that he had chronic anemia, a known cause of poor cognition [17] and a cardinal feature of HMS. We, however, expect good school performance with time courtesy of the interventions he is having currently. Besides HMS, another cause of anemia identified in this case was iron deficiency. This is not surprising given the high prevalence of iron deficiency anemia in the tropics [18]. Also, his general bio-physiologic needs as an adolescent, coupled with his poor social standing, predispose him to develop an iron deficiency, for which he was managed. The interruption of school activities in Nigeria for seven

months during the COVID-19 pandemic [19,20] did not allow an evaluation of the impact of his anemia correction (iron deficiency and or HMS induced) on his school performance. We suggest that the school health program, especially the health services aspect, be strengthened to identify children with health challenges, especially anemia and TSS, among other conditions, so that prompt intervention can be instituted where feasible.

Although splenic reduction fell short of the 40% target [13], the shrinkage of his spleen following treatment with Proguanil and application of other malarial prevention strategies strongly suggest that the patient has HMS [3]. The lower spleen reduction rate observed with him could be due to the frequent disruption of his treatment, as noted above.

Also, the absence of features like lymph node enlargement, recurrent fever, easy bruising/bleeding tendencies, bone pains, and gastrointestinal or nervous system symptoms could suggest other differentials of HMS like Kala-azar lymphoproliferative disorder, disseminated/ abdominal tuberculosis and sickle cell disease points to HMS. Furthermore, we were able to exclude these differentials through some laboratory investigations: Hb electrophoresis (Sickle Cell Disease), hemogram (Lymphoproliferative disorder), and Sputum AAFB by gene Xpert (Tuberculosis).

Nevertheless, we were unable to carry out some complex investigations like ELISA, Direct agglutination test (DAT) complement fixation test (CFT), Counter-immune electrophoresis (CIEP) and bone marrow smear or splenic puncture for Leishmanaia Donovani bodies (LD bodies) to diagnose Kala-azar and exclude it. Moreover, the diagnosis of Kala-azar is usually made clinically in most resource-poor settings due to its being clinically distinguishable from HMS by its usually more florid symptoms, which are generally lacking in TSS as observed in this case [21]. Other treatment modalities for HMS, such as shunt operation or splenectomy, were not offered in this case as these treatments are used for very severe and complicated HMS [21].

CONCLUSION

HMS is a known cause of massive splenomegaly in malaria-endemic regions. The unavailability of laboratory facilities for diagnosing HMS in resource-poor settings should not delay intervention where other clinical criteria have been fulfilled. There is a need to complement the use of malaria drugs with other interventions such as the use of mosquito nets and environmental sanitation in the management of HMS to prevent repeated malaria infections.

This case report highlights the value of community outreaches in malaria surveillance, identifying rare cases that would not have sought for healthcare in competent facilities.

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