CASE REPORT

# Fatal Relapse Of Hyperreactive Malarial Splenomegaly (HMS) In A 10-Year Old Nigerian Female - A Case Report

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## ABSTRACT

***Background:*** *The Hyperreactive Malarial Splenomegaly Syndrome (HMS) originally called the tropical splenomegaly syndrome (TSS) or Big spleen disease refers to cases of splenomegaly in the tropics for which no cause was found despite thorough investigation. It is restricted to the malarial belt, yet there are few reports on HMS in Nigeria, probably due to a low index of suspicion and non-availability of laboratory facilities to determine titres of malarial antibodies. The objective of this paper is to highlight the features, management, risk of relapse and prognosis of HMS.*

***Method/Result:*** *We present a 10- year old female with recurrent massive splenomegaly with previous clinical response to antimalarials and evidence of hypersplenism.*

***Conclusion:*** *HMS should be suspected in any child with moderate to massive splenomegaly with evidence of hypersplenism and clinical response to antimalarials.*

**KEY WORDS:** *HMS; Massive splenomegaly; Antimalarials; Relapse; Hypersplenism.*

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## INTRODUCTION

A diagnosis of Hyperreactive Malarial Splenomegaly (HMS), originally called the tropical splenomegaly syndrome (TSS) or Big spleen disease is usually considered when there are cases of splenomegaly in the tropics for which no locally prevalent cause is found[1,2]. It occurs in long term residents in malaria endemic areas and is characterised by high levels of IgM and hepatic sinusoidal lymphocytosis[2]. Malarial parasitaemia is infrequent [3] and the spleen regresses slowly in response to antimalarial therapy[4]. HMS is thought to result from repeated malarial attacks which by a mechanism not exactly known, leads to the production of lymphocytotoxic antibodies specific for suppressor T lymphocytes which are themselves involved in the regulation of IgM production of B lymphocytes. The consequent overproduction of these antibodies leads to the formation of macromolecular immune complexes, the clearance of which leads to hypertrophy of the mono nuclear phagocytic system and massive hepato-splenomegaly[5,6].

HMS is restricted to the malarial belt, yet there are few reports on HMS in Nigeria probably due to a low index of suspicion and non-availability of laboratory facilities to determine titres of malarial antibodies. HMS is associated with a high mortality rate[2].

We present a 10-year old female with recurrent massive splenomegaly, previous clinical response to antimalarials and evidence of hypersplenism while recognising our limitation in laboratory diagnosis of HMS.

## CASE REPORT

O.C was a 10-year old female admitted into the Children Emergency Ward of the University of Port Harcourt Teaching Hospital (UPTH) with a one week history of fever, left sided abdominal pain and swelling and generalised weakness. She was taken to a private clinic at the onset of illness where she was transfused with two units of blood. She had been admitted 3 years ago in a hospital in another state with a similar history, where she was transfused with one unit of blood and placed on one tablet of proguanil daily for life. However after one year of treatment and complete regression of the left sided swelling, she stopped the drugs and was apparently well until this presentation. She was the first of five children, 4 alive (2 males and 2 females). Her immediate younger sibling died at 5 years from an unknown febrile illness.

Examination revealed an afebrile (36.7°C), severely pale girl in mild respiratory distress with no lymphadenopathy or pedal oedema. The abdomen was distended, moved with respiration with generalised tenderness but no guarding or rebound tenderness. The liver was enlarged by 9cm below the right coastal margin, smooth and tender. There was a huge spleen measuring 16cm with a firm, smooth and tender surface.

A diagnosis of a lymphoproliferative disorder to rule out hyperreactive malarial splenomegaly syndrome and haemoglobinopathy was made and the patient commenced on proguanil 200mg daily. Results of investigations done in the private hospital showed a pre-transfusion haemoglobin of 2.48g/dl, Genotype AA, Blood group O' Rhesus D positive. Other investigations done on admission in the Children emergency ward include an ultrasound

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scan which showed a massive splenomegaly with no focal masses, cysts or abscess cavity. Blood smear revealed the presence of *P falciparum spp*. Blood film showed severe hypochromia, anisocytosis, macrocytes and relatively reduced thrombocytes with marked lymphocytosis. Bone marrow aspirate showed reduced bone marrow cellularity with depressed erythropoesis, myelopoesis and lymphopoesis. She developed high grade fever and jaundice by day 3 and was commenced on ceftriaxone 1 gram daily. Periorbital and pedal swellings with reduced urinary output was noticed by Day 10. The blood pressure was normal. The nephrologists did not think child required a dialysis. She was transfused with sedimented cells 4 times during this admission because she was in anaemic heart failure and had an increasing splenic size. She however died on the 15th day of admission.

**Table I. The Results Of Other Investigations**

| Dates | Day 1 | Day4 | Day 6 | Day 14 |
|---|---|---|---|---|
| Parameters | | | | |
| Hb g/dl | 4 | 4 | 4 | 3.3 |
| PCV % | 12 | 12 | 12 | 10 |
| Genotype | AA | | | |
| HIV I&11 | NEG | | | |
| WBC $10^9$/L | 3 | | 2.6 | |
| Neutrophils % | 56 | | 20 | |
| Lymphocytes% | 47 | | 80 | |
| Eosinophils% | 0 | | 0 | |
| Monocytes% | 0 | | 0 | |
| Basophils% | 0 | | 0 | |
| Blasts | 0 | | 0 | |
| ESR mm/hr | 132 | | 150 | |
| Platelets | | | Reduced | |
| Urine analysis microscopy/ culture | Normal | | | Protein +++, blood ++, bil++, pH 5 Protein/ heavy growth of klebsiella spp |
| E/U/Creatinine, Uric acid | Normal | | | Na 122,K 5.2, $HCO_3$ 13,Urea 29.4, Creatinine 155, Uric acid 931µmol/l |
| Serum protein, albumin, cholesterol | ND | ND | | 41g/l, 30g/l, 4.2µmol/l |
| Widal test | NEG | | | |
| HBsAg | NEG | | | |
| IgM | ND | | | |

ND-not done

## DISCUSSION

HMS is most frequently observed in the young and middle aged adults, although the process probably commences during childhood. Though uncommon in children less than 8 years, it has been reported in a 6-year old patient[7]. Our patient was 7 years old when she was first diagnosed. HMS is commoner in females[2].

This syndrome may be relatively asymptomatic[8] but abdominal swelling and pain are noted in 64% and 52% of patients respectively[2]. Our patient presented with both abdominal swelling and pain. Patients adapt physiologically to the chronic anaemia and are symptomatic only when severe[9].

The patient was transfused 4 times during this admission because she was in anaemic heart failure. Though susceptibility to infection is usually slightly increased[2], patients are usually afebrile at presentation and the presence of fever may indicate overwhelming septicaemia. Non-specific symptoms include cough, dyspnoea, epistaxis and headache. Pressure on the abdominal contents may lead to hernia and leg swelling; however because of the concurrent periorbital swelling in this patient, a renal pathology probably explains the oedema. Moderate to massive splenomegaly is the hallmark of HMS. The spleen is firm and in 93% of patients, as in this case, have accompanying hepatomegaly. Lymphadenopathy is absent but bilateral parotid swellings have been noted though neither was present in our patient. Ascites is uncommon[2] and was absent in our patient.

Certain criteria must be fulfilled to make a definitive diagnosis of HMS[9] (Box 1).

**Box 1. Diagnostic Criteria For Hyperreactive Malarial Splenomegaly[9]**

**Major Diagnostic Criteria:** always present

1. Gross splenomegaly of at least 10cm below the costal margin.
2. Immunity to malaria -high antibody levels for *P. falciparum*
3. Elevated serum (polyclonal) IgM of at least 2 standard deviations above the local mean
4. Clinical and immunological response to long term appropriate antimalarial therapy, but no reduction in spleen size may be apparent for the first three months.

**Minor Diagnostic Criteria:** frequently or nearly always present

1. Hepatic sinusoidal lymphocytosis is a diagnostic histologic finding, occurring in over 80% of cases (only seen in Felty's syndrome, non-tropical idiopathic splenomegaly or Dacie's syndrome and some rare cases of chronic lymphocytic leukaemia)
2. Normal cellular and humoral immune responses to antigenic challenge, (except to malarial antigens, where enhanced lymphocyte proliferation has been shown
3. Normal response to phytohemagglutination (PHA)
4. Hypersplenism
5. Lymphocyte proliferation (in some populations)
6. Occurrence within families, tribes

O.C had two of the major (massive spleen and previous clinical response to antimalarials) and two minor (haematological evidence of hypersplenism and lymphocyte proliferation) criteria. Other criteria could not be assessed because of lack of further laboratory diagnosis in our centre. Hypersplenism, the typical haematological manifestation of HMS as seen in our patient, presents with anaemia (which is always present), leucopaenia associated with lymphocytosis and mild thrombocytopaenia. Both neutropaenia and thrombocytopaenia are due to splenic pooling[2] and together with anaemia give the blood picture of aplastic anaemia. Though peripheral smear does not reveal the presence of malarial parasite in most cases, trophozoites of *P falciparum* were seen in this case. Ultrasonography is helpful in documenting and monitoring the sizes of the hepato-splenomegaly. Liver biopsy is rarely indicated but a hepatic sinusoidal lymphocytosis exists[2]. The mainstay of therapy is antimalarials which are effective in decreasing spleen size. Chloroquine and proguanil are found to be equally effective. The huge splenomegaly regressed completely when our patient took proquanil for one year, three years earlier. It has been reported that premature discontinuation of treatment may lead to relapse[2]. Poor response to antimalarials by our patient may have been due to the overwhelming septicaemia. Our patient's genotype was AA and relative protection is observed with sickle cell trait as is with malaria[2].

HMS is associated with high mortality rate. Overwhelming infections are the leading cause of death. A 5- year mortality rate of 50% has been reported in Uganda[4].

Splenectomy plays no role in HMS and fatality is very high following splenectomy, because of fulminant and overwhelming infections[10]. The role of lifelong prophylaxis for individuals residing in endemic is not clear; however because of the risk of relapse, we advocate lifelong treatment for all patients.

We wish to, through this report, highlight the presenting features, management and prognosis of HMS which, though rarely reported, may be missed because of lack of appropriate investigation. The high relapse and the fatality rate have also prompted this report.

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