Tropical Splenomegaly Syndrome in a pregnant woman: A good response and prognosis to splenectomy

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Abstract

The tropical splenomegaly syndrome (TSS) is characterized by massive splenomegaly with hypersplenism, moderate hepatomegaly, and lymphocytic infiltration of the hepatic sinusoids. TSS is restricted to native residents of and visitors to the "malaria belt," which roughly encompasses equatorial regions of South America, Africa, the Middle East, South Asia, and Southeast Asia. A 24 years old female patient gravida II and para I with gestational age 24 weeks from south west of Eritrea (Shelallo) Gash Barka presented with dizziness, general body weakness, and abdominal discomfort for 3 weeks and left upper quadrant swelling of three years duration. Other associate symptoms were palpitation and dyspnea. She had history of repeated malaria attack. Physical examination revealed massive hepatosplenomegaly and pallor. Hematological studies revealed that severe anemia Hgb 3.8 g/dL, WBC 2.2× 10^3/mm^3, MCV 97.6fl. Platelet 30×10^3/mm^3, and reticulocyte count was 7%. Peripheral smear examination revealed normocytic normochromic red blood cells. Bone marrow examination revealed marked erythroid hyperplasia without sign of malignancy and left shift. The patient received 11 units of blood preoperative but, no improvement Hb remaining 3.7g/dl. Elective splenectomy was done. Intra-operatively and postoperatively she received an additional 5 units of blood. There was no postoperative complication. The patient was discharged with Hb of 6.0g/dl with slight improvement. The response to splenectomy was good. Four months postoperative and 40 days post delivery Hbg 16.3g/dl and platelet 254,000/mm and WBC 5000/ mm^3. The outcome and prognosis of splenectomy in this patient was satisfactory.

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 [1-3]. It is seen among residents of endemic areas of malaria and it is not species specific. It occurs mainly in tropical Africa, but also in parts of South America, the Middle East, South Asia, and Southeast Asia [2]. Tropical Splenomegaly Syndrome is characterised by massive splenomegaly, hepatomegaly, marked elevations in levels of serum Ig M and malaria antibody [3]. Hepatic sinusoidal lymphocytosis is also seen. The interaction of repeated malarial infection and unknown host factors result in the production of cytotoxic Ig M suppressor lymphocyte (CD8+) antibodies. This causes inhibition of suppressor T cells, which normally regulate IgM production. This leads to uninhibited B cell production of IgM and the formation of cryoglobulins. The need to clear these macromolecular aggregates stimulates the reticuloendothelial system, resulting in hyperplasia. This causes the progressive and massive enlargement of the spleen and hepatomegaly [4, 5, 6].

Most patients present during adult life. Patients present with dragging pain in the upper abdomen, or sometimes may even complain of a palpable mass. Some may experience recurrent sharp pains in the upper abdomen, probably due to perisplenitis or splenic infarcts. Some patients may have weight loss and cachexia. On examination, there is massive splenomegaly and hepatomegaly.

The peripheral smear shows normocytic normochromic anemia with increased reticulocyte count. Leukopenia and thrombocytopenia may also be seen due to hypersplenism. Malarial parasites are not found in the peripheral blood. There is increase in the serum levels of polyclonal IgM with cryoglobulinemia, reduced C3 and the rheumatoid factor may be positive [2, 7].

Medical management with antimalarial drugs for prolonged period of time is the gold standard therapy for tropical splenomegaly syndrome. Previous studies showed that treatment with chloroquine had the upper hand and good outcomes [8]. A recent study did not support splenectomy for the management of TSS as it has poor prognosis and patients die due to the over whelming infections.[2] We are presenting a 24 year old pregnant woman with severe anemia and hepatosplenomegaly: a treatment challenge.

Case report

A 24 years old female patient gravida II and para I from south west of Eritrea (Shelallo) Gash Barka presented with dizziness, general body weakness, and abdominal discomfort for 3 weeks and left upper quadrant swelling of three years duration. Other associate symptoms were palpitation and dyspnea. She had history of repeated malaria attacks. On general physical examination she looked her stated age, acutely sick looking with mild respiratory distress.

She had mildly icteric sclera with very pale conjunctiva and bucal mucosa. Vital signs on admission were blood pressure of 80/60 mmHg, temperature 37°C, respiratory rate of 28 breaths /min, and pulse rate of 120/min. She was tachycardic with functional systolic II murmur on apex without any radiation. Abdominal examination revealed grossly distended asymmetric abdomen more bulged on the left side with no visible scar or collateral veins, gravida uterus, fundal height measured 22 cm. The liver was palpable 4 cm below the right costal margin, and was soft, rubbery in consistency, non tender, regular with sharp edges. The spleen was enlarged 16 cm below the left costal margin, firm and regular, slightly tender. Examination of other systems revealed normal findings.

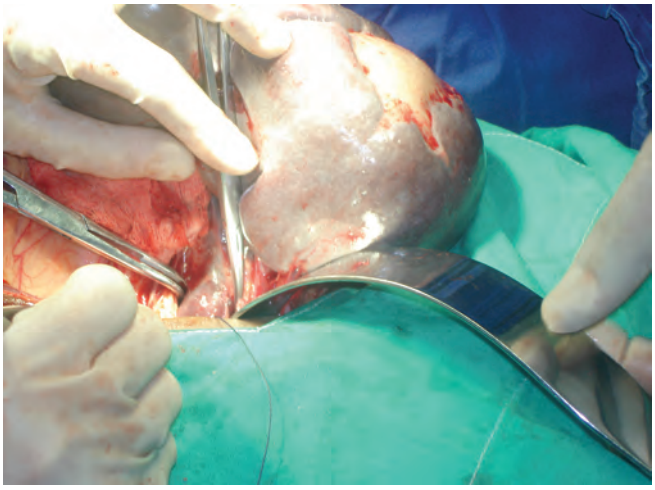
The patient was investigated for the severe anemia and organomegaly. CBC revealed Hgb 3.8 g/dL, WBC 2.2 $\times 10^3/mm^3$, MCV 97.6fl and platelet 30 $\times 10^3/mm^3$. Peripheral smear examination revealed normocytic normochromic red blood cells. Reticulocyte count was7%.

Liver function tests showed a mild elevated ALT 98 U/L (reference range 0-31 U/L), total and indirect bilirubin 1.4 mg/dl and 1.3 mg/dl respectively. Alkaline phosphatase was within the normal limit, 73 IU/L (ref. range 39 –117), albumin was as low as 3.2g/dl (ref. range 3.4-4.8). Blood smear was negative for malarial parasites. Stool and urine examination were negative for ova or parasite. Serological tests, which included Widal test, ELISA, Coomb's test, and surface antigen for hepatitis B and C, were negative. Bone examination indicated a mild myeloid dyspoiesis, erythroid maturation markedly left-shifted with numerous normoblasts. Myeloid to erythroid ratio slightly increased. Megakaryocitic maturation was small and hypolobated. Leishman-Donovan bodies, abnormal dysplastic and myeloplastic cells were negative.

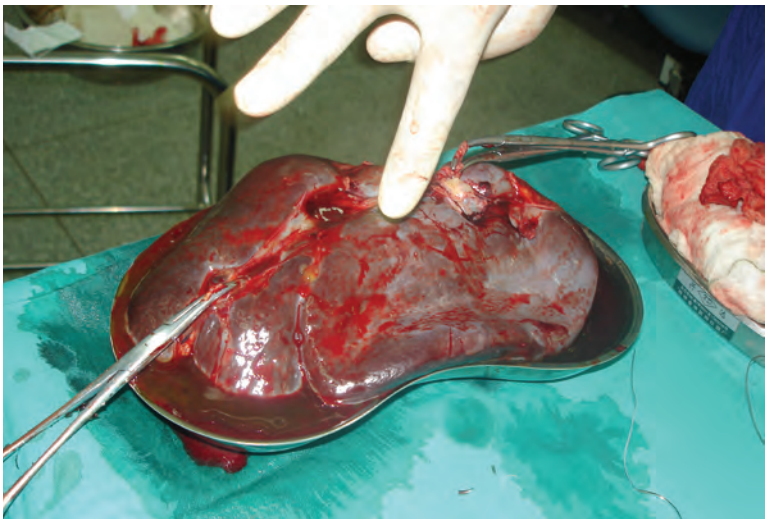
The patient was diagnosed as a case of tropical splenomegaly syndrome or hyperreactive malarial splenomegaly through exclusion criteria.

Before the woman got pregnant she was given a course of chloroquine. Patient was given supportive treatment: normal saline IV fluid, vitamin B12, iron and folate. On admission she was given two units of whole blood, one week later she received three units of blood, on a course of one month a total of ten units of whole blood was given. Lasix 40 mg twice daily was given in respective blood transfusion to avoid fluid overload. But there was no improvement, Hgb level was 3.7g/dl. After she was assessed by the obstetrician and the surgeon, elective splenectomy was done. Intraoperative finding showed a huge spleen with infarction areas.

Figure 1: Intra-operative and postoperative appearance of the spleen.



Panel A: Intra-operative spleen with sign of necrosis



Panel B: Spleen in kidney dish

Intra and postoperatively five units of whole blood were transfused. One week post operative Hgb started to increase doubling to 6.2g/dl. The patient was discharged with two week follow up appointment and advices not live in malarious areas and to seek medical help whenever she get febrile. Patient was followed for a period of three years and still in follow up. She was not given any immunoprophylaxis against pneumococcus, meningococcus and H-influenza as well as antibiotic prophylaxis post splenectomy. Four months postopertative and 40 days post partum, hematogram results were WBC 5000/mm^3, Hbg 16.3g/dl and platelet 254,000/mm^3. Still she is living in the malarious area and she gave a second birth.

Discussion

The patient is a resident of malarious hyperendemic area. She had repeated malaria attack in her life time and chronic massive splenomegaly. People living in malaria endemic area are prone to develop tropical splenomegaly syndrome / hyper-reactive malarial splenomegaly. The most common presentations of TSS are dragging sensation, abdominal swelling,

anemia, and hepatomegaly. Anemia is {normochromic normocytic} almost always present and associated with pancytopenia (hypersplenism); and there is increased susceptibility to bacterial infections. Peripheral blood picture for malarial parasite is usually negative. Weakness, dyspnea, and functional murmur reflect the degree of anemia. All these findings were manifested by the woman [7, 9].

The exact assessment for TSS (HMS) is difficult and the condition should be differentiated from other causes of splenomegaly in the tropics- Kala-Azar, schistosomiasis, post-necrotic cirrhosis, thalassemia, leukemia, lymphoma, myelofibrosis, non-tropical idiopathic splenomegaly, Felty's syndrome [2]. Certain criteria are set to diagnose patients with HMS. These criteria includes, residence in malaria endemic area, gross splenomegaly 10 cm or more, elevated serum IgM level two standard deviations or more, hypersplenism, clinical and immunologic responses to antimalarial therapy, hepatic sinusoidal lymphocytosis [9].

The first four criteria were documented in our patient. If we strictly follow these criteria half of patients with HMS will not have the diagnosis, so exclusion criteria are preferable as we did in our case. Genetic factors, pregnancy, and malnutrition are documented as predisposing factors of HMS [2, 10]. Although the exact mechanism is uncertain, evidence suggests that exposure to malaria elicits exaggerated stimulation of polyclonal B lymphocytes, leading to excessive and partially uncontrolled production of immunoglobulin M (IgM) as the initiating event. IgM is polyclonal and is not specific for any particular malarial species T-cell infiltration of the hepatic and splenic sinusoids accompanies this process. Serum cryoglobulin and autoantibody levels increase, as does the presence of high molecular weight immune complexes. The result is anemia, deposition of large immune complexes in Kupffer cells in the liver and spleen, reticuloendothelial cell hyperplasia, and hepatosplenomegaly. [2, 5, 6]

Medical management with antimalarial drugs for prolonged period is the mainstay of therapy. Response to therapy is guided by the splenic size and symptomatic improvement. Specific choice of drug is dictated by the pattern and prevalence of drug resistance in that geographic area. Chloroquine and Proguanil appear to be equally effective. But Chloroquine and Proguanil are not recommended during pregnancy [7]. Quinine is the antimalaria drug of choice for pregnant women. So far there is no data that suggest quinine as treatment TSS/ HMS. To avoid the grave consequence of anemia in pregnancy such low infant birth weight, intrauterine growth retardation, still birth, and maternal death anemia should be corrected as fast as possible. Transfusion of blood could not be a solution in chronic anemia the underlying problem should be treated[11].

The role of splenectomy for various hematological disorders has definitely earned a place as a therapeutic measure especially in disorders like idiopathic thrombocytopenic purpura and hereditary spherocytosis, lymphoma, and leukemia. There are common practice guidelines that advocate immunoprophylaxis against pneumococcus, meningococcus and H-influenza as well as antibiotic prophylaxis for the patients undergoing total splenectomy to avoid the overwhelming infection, although the efficiency of these measures has not been proven in randomized trial [12, 13, 14]. Splenectomy plays no role in the treatment of hyperreactive malarial syndrome (HMS). The mortality rate after splenectomy is high because of fulminant and overwhelming infections. There is limited data splenectomy as choice of treatment for tropical splenomegaly syndrome/ hyperreactive malarial syndrome [2]. There are reported cases of TSS with splenectomy, the response and outcome is not satisfactory[14] and there are with good outcome [13]. There are, as yet, no convincing data which show that splenectomy in the tropics causes a significant diminution of immunity to malaria (or other diseases) and it does not, therefore, predispose to the development of cerebral malaria[15]. The outcome and prognosis of in this woman is excellent. Finally the author suggests that the role of splenectomy in patients with tropical splenomegaly syndrome/ hyperreactive malarial syndrome should be examined in individuals.

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