

A 16-year-old female presenting with Splenic Marginal Zone Lymphoma indistinguishable from Hyperactive Malaria Splenomegaly syndrome.

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Abstract:

Introduction: Splenomegaly is frequently observed among children and adolescents who reside in malaria endemic areas. Clinically, these are frequently complicated by hypersplenism, therefore defined as Hyperactive Malaria Splenomegaly (HMS). The underlying pathology of HMS is unknown, but is indistinguishable from splenic lymphomas such as splenic marginal zone lymphomas (SMZL). We present a case of SMZL in a Kenyan adolescent whose disease meets the clinical criteria of HMS.

Case Report: We present a case of a 16-year-old female who was referred to a tertiary teaching hospital in Kenya with massive splenomegaly, anaemia and peripheral blood lymphocytosis. Bone marrow studies showed infiltrative sinusoidal neoplastic atypical B lymphocytes. The eventual diagnosis on histology and clinical-pathological correlation is a Splenic marginal zone lymphoma. The patient received combination chemotherapy, antimalarial therapy with resolution of symptoms and splenomegaly.

Conclusion: This case suggests that SMZL could be the underlying lesion in HMS. Evaluation of SMZL should be performed in all suspected cases of HMS. Clinical – Pathological series should be performed to identify the underlying pathology of HMS.

Keywords: Splenic Marginal Zone Lymphoma, Hyperactive Malaria Syndrome.

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I. Introduction

Massive splenomegaly is common among African adolescents, children and young adults [1]. Most cases are managed as tropical splenomegaly syndrome, which is a diagnosis of exclusion because leishmaniasis is an important differential diagnosis [2]. These are indistinguishable from lymphoproliferative neoplasms of the spleen [3]. Some authors hypothesize that splenic mature B cell lymphomas are thought to arise from malaria induced B cell proliferative processes [4, 5].

In East Africa, myeloid and lymphoid neoplasms are the 6th most common malignancies among children and adolescents [6]. These mainly consist of high grade lymphomas, the majority being B cell lymphomas [6-8]. lymphoid neoplasms such as splenic marginal zone lymphoma, variant hairy cell leukaemia, B – Chronic lymphocytic leukaemia and the WHO category mature B cell lymphoma – Unclassifiable may present with splenomegaly [6].

We report a unique case of a mature B cell lymphoma in a 16-year-old Kenyan girl that presented as massive splenomegaly. These features were clinically indistinguishable from hyperactive malaria splenomegaly syndrome (tropical splenomegaly syndrome). Splenic marginal zone lymphoma was diagnosed on bone marrow biopsy, complemented by bone marrow studies.

II. Case presentation:

A 16-year-old girl was referred to Kenyatta National Hospital, a tertiary public referral hospital in Kenya. She presented with massive splenomegaly, easy fatigability and dizzy spells. She had received haematinics and recurrent blood transfusions. Repeated treatment for malaria did not provide relief. Clinical evaluation revealed anaemia, massive hepatosplenomegaly and hepatomegaly.

Laboratory findings at the tertiary hospital moderate anaemia (haemoglobin level of 70 g/L), peripheral blood leucocytosis and lymphocytosis (74.1% on differential counts). There was no evidence of peripheral blood eosinophilia or thrombocytopenia. Peripheral blood film showed abundant mature lymphocytes. Bone

marrow evaluation showed 45% of mature lymphocytes. A diagnosis of a mature lymphoproliferative neoplasm was made, and a bone marrow biopsy performed.

Bone marrow trephine biopsy showed atypical intra and peri sinusoidal lymphocytes. Immunohistochemistry confirmed mature pre germinal centre mature B cell phenotype. The pathological differential diagnoses of splenic marginal zone lymphoma and B cell lymphoma – unclassified were considered. These are presented in the figures below. The oncology team instituted rituximab based chemotherapy based on the diagnosis. Subsequent clinical evaluation confirms clinical improvement and resolution of splenomegaly. She has remained in complete resolution two years later with normal blood counts and no splenomegaly.

III. Discussion

In this case report, the young female patient presented with a massive splenomegaly and bone marrow involvement of an indolent B lymphoproliferative neoplasm (SMZL). Diagnosis of the splenic marginal zone lymphoma was based on the morphological and immunohistochemistry features on bone marrow biopsy [9]. Splenic marginal zone lymphoma is thought to arise from clonal proliferation of B lymphocytes due to persistent activation due to malaria [3].

Massive splenomegaly occurs in approximately 5% of children and adolescents living in Malaria endemic areas [2]. In these patients, there is increased malaria specific IgM and low grade persistent parasitemia [3, 5]. Hyperactive malaria splenomegaly (HMS), previously known as tropical splenomegaly syndrome, is invariably fatal if untreated [3-5]. While there are no concise reports of the morphology of hyperactive malaria splenomegaly, the clinical and pathological features are indistinguishable from splenic marginal zone lymphoma (SMZL)[3].

In developed countries, HMS resolves upon initiation of antimalarial therapy, resulting in a reduction of antimalarial IgM titers and resolution of splenomegaly [2]. This is not observed in malaria endemic areas in Africa and Asia [4]. In this case, lack of clinical response and the observation of peripheral blood atypical lymphocytosis which were demonstrated as indolent neoplastic intrasinusoidal lymphocytes suggest that SMZL is the pathological lesion in HMS [5]. There are no clinical trials that examine the efficacy of antimalarial therapy for the treatment of HMS [1].

While this case report is limited in its generalizability, it suggests that SMZL may be the underlying pathology of HMS. Marginal zone lymphoproliferative neoplasms are known to occur as a response to infectious diseases [10, 11]. *Helicobacter pylori* eradication results in resolution of gastric marginal zone lymphomas [9, 11]. We hypothesize that antimalarial therapy may be sufficient for the management of SMZL and subsequent resolution of HMS, however, clinical trials should be performed. Series that examine the pathology of HMS among children and adolescents in malaria endemic areas should be performed.

IV. Conclusion

The pathology of HMS is unknown. This is likely to be manifested by SMZL, which may resolve following antimalarial therapy. Patients in whom a diagnosis of HMS is established should undergo a diagnostic workup for SMZL.

Conflicts of Interest

The Authors declare no conflicts of interest

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