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CASE REPORT

SYSTEMIC LUPUS ERYTHEMATOSUS COMPLICATED WITH HYPOPLASTIC MARROW AND HAEMOPHAGOCYTOSIS: A CASE REPORT

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ABSTRACT: Association of systemic lupus erythromatosus with hemophagocytic lymphohistiocytosis (HLH) has been reported by many authors[1,2,3,4] however association of systemic lupus erythromatosus with hemophagocytic lymphohistiocytosis and hypoplastic bone marrow is quite rare. Here we are reporting a case of HLH developing in a known case of SLE presenting with hypoplastic bone marrow in a 45 years old female, on low dose steroid therapy who presented with febrile pancytopenia, hepatosplenomegaly, hyperferritinemia with evidence of bone marrow hypoplasia and haemophagocytosis.

KEYWORDS: Systemic lupus erythematosus, hypoplastic marrow, haemophagocytosis.

INTRODUCTION: Hemophagocytic lymphohistiocytosis (HLH) is a rare disorder of the immune system. In Sweden, the incidence was estimated at 1.2 per million per year[5].It usually affects young children but may occur at any age. HLH is often referred to as either the primary form which is hereditary or the secondary form, associated with infections (may be viral), autoimmune diseases, and malignancies. The primary form, also known as familial hemophagocytic lymphohistiocytosis (FHLH) is inherited either as autosomal recessive or X linked forms. Five genes have been identified which correspond with five subtypes of autosomal recessive HLH. The genes encodes the protein normally involved in killing or eliminating abnormal immune cells or proteins which facilitate the delivery of perforin to the cells which are to be killed.

Primary form is usually seen in young children. Secondary HLH is often diagnosed in older patients with no positive family history of this disease. It may be associated with viral infections such as Epstein-Barr, cytomegalovirus (CMV) or herpes virus, autoimmune disorders and cancers. In both forms of the disease there is excessive activation of the macrophages and histiocytes producing haemophagocytosis in bone marrow and reticuloendothelial system. Patients usually present with fever (91%), hepatomegaly (90%), splenomegaly (84%), neurologic signs (47%), rash (43%) and lymphadenopathy (42%).[6]

Our case is a 45 years old female, known case of systemic lupus erythromatosus on corticosteroid therapy (Prednisolone 5mg per day) presented with complaints of prolonged fever, generalized weakness, malaise and rapidly increasing skin rashes for the past one month. Two weeks prior to admission, the dose of steroid was escalated to 20 mg three times daily on suspicion of progression of the basic disease. On examination the patient was febrile (temp. - 103^0F), anaemic, icteric mildly with mild hepatosplenomegaly and psoriasiform rashes all over the body. Other systemic examinations were unremarkable. The following tables show the laboratory findings of the patient.

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Parameters	Initial	Repeat
Haemoglobin (Hb)	8.5 gm/dl	7gm/dl
Total erythrocyte count	3.3 million/cu mm	
Packed cell volume (PCV)	25.8%	
Mean corpuscular volume (MCV)	78fl	
Mean corpuscular Hb (MCH)	25.7pg	
Mean corpuscular Hb Conc (MCHC)	32.9gm/dl	
RDW	16.6%	
Total leucocyte count (TLC)	3120 /cu mm	2580/cu mm
Total lymphocyte count	610/cu mm	390/cu mm
Total granulocyte count	2300/cu mm	1600/cu mm
Differential count (DLC)	P 74, L20, M5, E1	P 67, L 16, M 1, E 6
Platelet count	1.1 lac /cu mm	90000/cu mm
Reticulocyte count	0.3%	
ESR	46mm in first hour	136mm in first hour
Peripheral smear picture	Microcytic hypochromic red cells with thrombocytopenia with normal morphology. No haemoparasite and atypical cells seen	Microcytic hypochromic red cell with moderate anisocytosis

Table 1: Complete blood picture

Parameters	Values
Total bilirubin	1.2 mg
SGOT	80U/L
SGPT	76U/L
Gamma glutamyl transferase	52U/L
Alkaline phosphatase	85U/L
Total protein	6.8gm%
Albumin	3.5gm%,
Globulin	3.5gm%
A:G ratio	1:1.
Urea	27mg%
Creatinine	0.9mg %
Sodium	129meq/L
Potassium	4.1meq/L

Table 2: Liver and Renal Function Tests

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Repeated Urine Culture	Sterile	
Blood culture	Sterile	
Quantitative buffy coat	Negative for malaria parasite	
ANA	1.2 (positive)	speckled
Anti-ds DNA	34	
Enterocheck	negative	
Mantoux test	5mm	
CXR PA View	Normal	
Echocardiography	Normal study, no vegetations was found	
Hb electrophoresis	Normal	
Serum ferritin	564ug/dl	
Ultrasound whole abdomen	mild hepatosplenomegaly	

Table 3: Other Laboratory tests

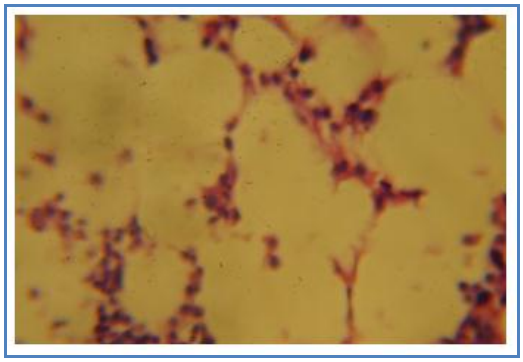

Fig. 1: Histopathological section of Bone marrow Biopsy showing hypocellular marrow. (Haematoxylin and Eosin stain, 400 x magnifications)

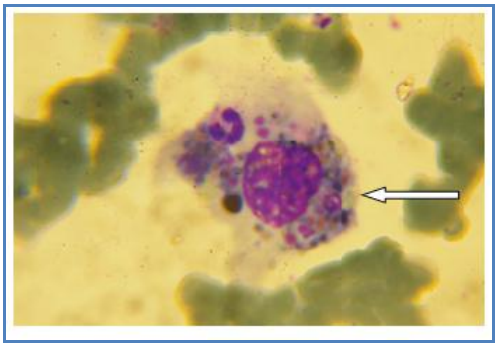

Fig. 2: Photomicrograph of bone marrow aspirate showing a macrophage with degenerated haemic cells in the cytoplasm (Leshmann Stain, 1000x magnification)

Patient continued to be febrile. Repeat blood & urine cultures showed no growth of organism (Both aerobic and anaerobic). A complete viral screen (EBV, Herpes virus, and parvo virus) was done

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and showed no sign of recent infection. Patient was subjected to bone marrow examination as part of investigation for pyrexia of unknown origin. Under aseptic conditions bone marrow biopsy & aspiration were performed on the right posterior iliac crest. Consistency was normal, Cellularity was reduced (Around 15%) with reduction of all cell lineages (Fig. 1). Erythropoiesis was predominantly normoblastic. Differential leucocyte count was within normal range.

Myeloid: Erythroid ratio was 3.5:1. Reduction of the number of megakaryocytes with normal morphology was seen. Bone marrow iron store was increased (Grade 4). Most striking feature was the presence of many macrophages engulfing haemic cells including leukocytes & red cells (Fig. 2). A diagnosis of Hypoplastic anaemia with haemophagocytosis in a patient of SLE was finally considered. However, the exact cause for prolonged intermittent fever was not found. High dose corticosteroid in the form of Methylprednisolone intravenous was given. Fever gradually subsided and the general condition of the patient improved subsequently.

DISCUSSION: HPS is a rare entity characterised by proliferation of nonneoplastic cells of histiocytic lineage along with evidence of haemophagocytosis. The course of the disease is usually aggressive and potentially fatal. It may be associated with the marrow hypoplasia seen may be due to therapy with Cyclophosphamide. Marrow toxicity is the most important toxic effect, depends on the total cumulative dose[7] (Bruce A. Chabner at el) or may be associated with autoimmune disorder like SLE[8] (Aplastic anaemia: acquired and inherited, George B. Segel and et al).

In our case, the levels of serum auto antibodies were just marginally raised; however the signs and symptoms could not be due to aggravating primary disease. Moreover the findings in our case satisfied the diagnostic criteria laid by Histiocyte Society (Histiocyte Society treatment protocol HLH-2004).[9] Increasing neutropenia with high ferritin level was noted. Findings in our case satisfied criteria for diagnosis of LHL according to Histiocyte society treatment protocol, HLH 2004.

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