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Case Report

A RARE PRESENTATION OF UNDIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSUS AS HEMOPHAGOCYTIC SYNDROME – A CASE REPORT

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease in which organs and cells undergo damage initially mediated by tissue-binding auto antibodies and immune complexes (Longo *et al.,* 2004). It manifests with involvement of multiple system and has various complications.

The haemophagocytic syndrome (HS) also known as hemophagocytic lymphohistiocytosis, is a potentially lethal, rare, clinical, and pathological condition (Rahal *et al.,* 2015). It is characterized by a massive production of proinflammatory cytokines, which causes clinical manifestations and result in multiple organs failure (Rahal *et al.,* 2015). This can occur as a familial primary form or secondary to disrupt immune homeostasis, like infections, medications, neoplasms, and rheumatologic diseases (Arnez *et al.,* 2012). Its etiology is essentially unknown but is thought to result from uncontrolled T lymphocyte activation that leads to macrophage activation and an increment of cytokines like tumor necrosis factor-α, interleukin-1 (IL-1), IL-6, IL-18, and interferon-γ (Sharmeen and Hussain, 2016). Clinical presentation of hemophagocytic syndrome is with prolonged fever, Hepatosplenomegaly, pancytopenia, liver function abnormalities, coagulopathy, hypertriglyceredemia and high ferritin levels (Rahal *et al.,* 2015; Arnez *et al.,* 2012; Sharmeen and Hussain, 2016). Occurrence of hemophagocytic syndrome in evidence of systemic lupus erythematosus has been reported. We present one such rare case of hemophagocytic syndrome in a patient of systemic lupus erythematosus.

CASES

A 35 year old female, presented to us with chief complaints of generalized swelling over the body since 1 month, dyspnea since 1 month, oral ulcer since 20 days, fever since 7 days. Fever was high grade intermittent type associated with chills. She also gave history of polyarthritis in the form of multiple painful swollen joint with morning stiffness. There was no history from bleeding from natural orifices except for mouth. No history of high colored urine

She denied any history of travel or animal exposure. Her relatives denied any history of seizure or acute mental confusion.

On examination patients vitals were, temp- 102^{o} Fahrenheit, pulse was 112/min regular, Blood pressure – 100/60, respiratory rate of 28 cycles/min. She also had bilateral pitting oedema, JVP was not raised. Oral cavity examination showed ulcers with active bleed, ecchymotic patches were seen on b/l arms, thighs, trunk and abdomen. On systemic examination – per abdomen was distended, shifting dullness was present, both liver and spleen were palpable. Respiratory auscultation revealed fine crepts in b/l lung fields. Cardiovascular and neurological examination revealed no abnormality.

On laboratory investigations – complete blood count showed pancytopenia with hemoglobin levels of 5.4 gm%, WBC count of 2700 mm^3 and platelet count of 9000mm^3, liver enzymes were AST – 445 I.U./L AND ALT – 648 I.U./L, renal function test was normal. On routine biochemical urine examination proteinuria was ++ and there was proteinuria of 1280 mg in 24 hour protein collection and RBC casts were present on urine microscopy.

Erythrocyte sedimentation rate was 110mm in first hour. She tested strongly positive for anti – double stranded DNA and ANA. Moreover, her triglyceride level was 348 mg/dl and sr. ferritin level was 628 ng/ml, Lactate dehydrogenase was 1228. I.U./L, Direct coombs test was positive.

The blood culture, urine culture, all the viral markers and other Infectious work up was negative. 2d echocardiography showed no regional wall motion abnormality with left ventricular ejection fraction of 65%. Chest x-ray showed no obvious abnormality.

Electrocardiogram showed sinus tachycardia. Ultrasonoraphy of abdomen showed moderated ascites with hepatoslpeenomegaly. The bone marrow aspiration examination was reported with the presence of abundant hemosiderophages with focal hemophagocytosis

On basis of examination a diagnosis of SLE with HS with multiorgan failure was made. She was immediately started with IV methylprednisolone 1 gm IV OD, iv cytoxan was also started, prophylactic antibiotic coverage was given, blood transfusions and platelet transfusions were also given. On 3rd day of intensive care hospitalization patient developed sudden onset altered sensorium in the form of drowsiness responding only to deep painful stimuli. There was profuse bleeding from her oral ulcers. Her condition rapidly deteriorated and shortly she was comatosed and was intubated electively. An urgent Computed tomography of brain showed massive intraparenchymal bleed with midline shift with intraventricular extension. Patient eventually succumbed on the same evening.

DISCUSSION

Hemophagocytic syndrome, a rare and potentially fatal condition has been found in case with SLE. Our case was once such rare presentation. SLE was diagnosed on the basis of systemic lupus International Collaborating Clinic Criteria for Classification of Systemic Lupus Erythematosus and criteria of American College of Rheumatology for SLE (Longo *et al.,* 2004).

Lambotte *et al.,* (2006) studied 8 cases where SLE was diagnosed along with HS pancytopenia which was characterized by high ferritin level, uncommon in SLE, which is highly suggestive of HS. Parodi *et al.,* (2009) in his study, proposed preliminary diagnostic criteria for macrophage activation syndrome as a complication of juvenile SLE. This diagnostic criteria had a sensitivity and specificity of 92.1% and 90.9%, respectively, and a confidence interval between 21.9 and 621.6 at 95% confidence (Parodi *et al.,* 2009).

Several triggering factors have been given but the infectious processes are most important starting elements for this complication (9.10). Epstein-Barr virus, HIV, cytomegalovirus, and are among the reported viral causes of HS (McClain *et al.,* 1988; Chen *et al.,* 2003).

Clinically, hemophagocytic syndrome presents with prolonged fever, Hepatosplenomegaly, pancytopenia, liver function abnormalities, coagulopathy, hypertriglyceredemia and high ferritin levels (Rahal *et al.,* 2015; Arnez *et al.,* 2012; Sharmeen and Hussain, 2016). Few studies attribute the clinical manifestations of hemophagocytic syndrome to overproduction of pro-inflammatory cytokines (interleukin 1, tumoral necrosis factor, gamma-interferon, among others) (Silva *et al.,* 2004; Rosa *et al.,* 2007).

Many authors believe that the presence hiperferritinemia is a highly suggestive sign of reactive macrophage disease and this factor associated with the bone marrow aspirate has defined HS clinical features (Favara *et al.,* 1997).

The diagnosis of HS secondary to SLE is extremely complicated as they have some features in common however, HS is characterized by hyperferritinemia, hypofibrinogenemia, and hypertriglyceridemia which diefferentiates HS from SLE (Rahal *et al.,* 2015).

As per the hemophagocytic lymphohistiocytosis, another name for HS, (HLH)-2008 diagnostic criteria, the diagnosis of HS is made by either molecular identification of an HLH-associated gene mutation or by fulfilling five of eight diagnostic criteria (Jordan and Filipovich, 2008).

Of the diagnostic criteria for HLH – 2008 guidelines, our patient fulfilled 5/8 criteria on the basis of which she was diagnosed as a case of hemophagocytic syndrome.

The mainstay of diagnosis of HS depends on the cytological findings of hemophagocytosis. Ideally, both Bone Marrow biopsy and aspiration should be performed when HS is suspected (Henter *et al.,* 2002).

Patients have shown a good response to the pulse methylprednisolone and cyclophosphamide therapies following the cyclosporine treatment (Kumakura *et al.,* 2004). A standard Treatment of primary HLH is based on the HLH-2004 protocol using cyclosporine, etoposide, and dexamethasone with or without

intrathecal methotrexate which should be, ideally, later on followed by hematopoietic stem cell transplantation (Henter *et al.*, 2006). In cases of HS due to SLE, it has been reported that corticosteroids and immunosuppressive agents have been used including cyclosporine, cyclophosphamide, intravenous immunoglobulin, and etoposide with variable success (Strout *et al.*, 2010).

Conflict of Interest

The authors declare no conflict of interest whatsoever arising out of the publication of this manuscript.

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