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Case Report

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Systemic Lupus Erythematosus with Massive Splenomegaly: A Case Report

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ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disease that can affect any organ system in the body. It may also be complicated by other autoimmune diseases. This case report describes a patient who presented with massive splenomegaly on a background of clinical features of SLE. Splenomegaly in SLE however, is not common. The patient was evaluated further for haematological complications and liver involvement. She was diagnosed to have SLE-Autoimmune hepatitis overlap. SLE-AIH overlap syndrome is rare, but specific diagnosis is important because it influences the choice of immune-suppressants as well as long-term outcome. Liver biopsy helps clinch the diagnosis and should be encourage early in the diagnostic plan. It is also important to differentiate between the various causes of liver involvement in SLE.

Keywords: massive splenomegaly, systemic lupus erythematosus, autoimmune hepatitis, lupus hepatitis, lupoid hepatitis

INTRODUCTION

SLE (Systemic Lupus Erythematosus) may involve one or several organ systems at the outset, and manifestations may range from fatigue to kidney failure. Due to the underlying autoimmune process involving multiple systems SLE may mimic many other diseases. It has rightfully been called 'the great imitator (1). The co-occurrence of autoimmune hepatitis (AIH) and SLE is considered to be rare. The diagnosis of AIH is imperative in a case of SLE as it may influence the choice of immune-suppressants and long-term prognosis (2). It is also important to differentiate between SLE-AIH overlap and non-specific liver involvement seen in SLE.

Hematologic abnormalities are common in SLE, and include anaemia, leucopoenia and thrombocytopenia. Mechanisms for the cytopaenias in SLE involve immune and non-immune processes. Cytopaenias may also be due to splenic sequestration, as seen in patients with chronic liver disease (3). A chronic liver disease process, and portal hypertension, is, however, rarely seen in SLE alone. While, splenomegaly may occur in SLE, it is more likely a response to demand

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for stem cell resources rather than portal hypertension.

In this case report we describe a patient of SLE who presented with massive splenomegaly. She was diagnosed to have overlapping autoimmune hepatitis, which had progressed to fibrosis with portal hypertension.

CASE REPORT

A 35-years-old lady from Uttar Pradesh, farmer by profession, presented with the complaints of fever and pain in the abdomen for past 6 months. She did not have any co-morbid illness and was an oral tobacco user since approximately ten years. She had fever for past six months, which was undocumented, low-grade, not associated with chills or evening rise of temperature. She also complained of weight loss and decreased appetite, especially early satiety. Patient had pain in the abdomen for past six months, in the left upper quadrant, dull aching, continuous and non-radiating, associated with abdominal distension. There was no history of bleeding from any site, pica, passage of worms in stools. There was no history of tuberculosis in past. Patient was vegetarian by diet, and had normal and regular menstrual cycles.

On examination, she was alert, conscious, and cooperative. She was hemodynamically stable. On head-to-toe examination, she was found to have vitiligo and pallor. On per abdomen examination, spleen could be palpated 15 cm below left subcostal margin, tender to touch, firm in consistency, well defined borders with palpable splenic notch. Shifting dullness could also be elicited in the abdomen. Rest of the systemic examination was unremarkable.

Patient was worked-up for fever with anaemia and massive splenomegaly with ascites. A differential diagnosis of haemolytic anaemia and connective tissue disorder was kept.

On investigations, the patient had pancytopenia (haemoglobin - 3.3 g/dL, total leukocyte count – 2,130 cells/mm3, platelet count -27,000 cells/mm3. The peripheral smear showed macrocytosis. The reticulocyte count was 7.9%. Lactate dehydrogenase was 783 U/L and direct and indirect Coomb's test were negative. Stools also tested negative for occult blood loss. Vitamin B12 levels were found to be deficient. Bone marrow studies were normal but for presence of megaloblasts. Appropriate supplementation was added.

Her liver function tests showed mild serum transaminitis (AST – 139 U/L and ALT 64 U/L), and kidney function tests were normal. Viral markers

were normal. Infectious disease profile did not reveal any positive tests.

Ascitic fluid analysis was done. It was straw-coloured and showed 200 cells/mm3 (40% neutrophils and 50% lymphocytes). The protein level was 1.65g/dL, and serum-ascitic albumin gradient more than 1.2. The adenosine deaminase level was normal.

Work-up for autoimmune disorders is summarised in table 1 below.

Table 1. Work-up for connective tissue disorder done in our patient.

No.	Investigation	Result
1.	ANA by immunofluorescence	1:80 **positive**, speckled pattern
2.	Extended Nuclear Antigen profile	Anti PCNA - **3+**
3.	Auto-immune Hepatitis profile	Anti LKM 1 **positive**
4.	cANCA, pANCA	Negative
5.	IgG levels	2241.0 mg/dl (**high**)
6.	C3, C4	68.5mg/dl (**low**), 14.9 mg/dl (normal)
7.	Anti-Thyroid peroxidase	38.6 IU/ml (**positive**)
8.	Anti-Tissue transglutaminase	1.38 IU/ml (normal)

Ultrasound scan whole abdomen with Splenic-portal vein doppler showed a normal liver of size 14 cm. There was massive spleen of 18.6 cm with prominent splenic vein of 1 cm at hilum. There was

no evidence of extra-hepatic vein obstruction. Fibroscan was also done which showed a median stiffness of 10.5 kPa suggestive of fibrosis.

Computed tomography of the abdomen showed a normal liver of size 14 cm, marked splenomegaly (22 mm) with prominent spleno-portal venous axis.

Liver biopsy was done which showed partial effacement of the liver architecture, with the formation of incomplete nodules. Hepatocytes show presence of focal steatosis along with the dilatation of sinusoids. Mild focal interface hepatitis and focal emperiopolesis was seen. The portal tract shows presence of ductular proliferation, periportal fibrosis and periportal inflammation predominantly comprising of lymphocytes. Modified hepatic activity index (HAI) grading: necro-inflammatory score of 3/18. Modified staging: architectural changes, fibrosis cirrhosis score was 3 (fibrous expansion of most portal areas with occasional porto-portal bridging).

The patient was diagnosed to have systemic lupus erythematosus by the EULAR criteria. She was also diagnosed to have autoimmune hepatitis by the International Autoimmune Hepatitis group scoring for AIH. She thus had SLE-autoimmune hepatitis overlap syndrome which had progressed to cirrhosis with portal hypertension and resultant massive splenomegaly.

While evaluating for other autoimmune disorders, the patient had four autoimmune pathologies – vitiligo, autoimmune thyroiditis, autoimmune hepatitis and SLE, and thus could be labelled as Type 3 autoimmune polyendocrine syndrome (APS-3).

DISCUSSION

Massive splenomegaly is defined as spleen that extends greater than 8 cm below the left costal margin and/ or weighs more than 1000 gram. Massive splenomegaly in SLE has previously been seen in association with non-Hodgkin's lymphoma (NHL) (4). It has been suggested that NHL be searched for in cases of SLE with prominent lymphadenopathy and massive splenomegaly. Colmegna et al. reported a case of massive splenomegaly is SLE secondary to nodular regenerative hyperplasia of the liver (5).

Table 2 – Difference between non-specific liver disease in SLE (Lupus hepatitis) and AIH (Lupoid hepatitis)

S. No	Distinguishing Point	Lupus Hepatitis	Lupoid Hepatitis
1.	Incidence	Seen in 8 to 23% of patients of SLE	Coexistence of AIH and SLE as an overlap syndrome is seen in 1%–2.6% of the AIH cases
2.	Auto-antibody	Anti-ds-DNA, anti-ribosomal P antibody	Antibodies to soluble liver antigen (SLA),Liver-pancreas, smooth-muscle antibody (SMA) with specificity for F-actin and microsomal autoantigens, such as anti-liver kidney antibodies (anti-LKM antibody)
3.	Histology	Miscellaneous and non-specific - The inflammation is usually lobular and occasionally periportal with a paucity of lymphoid infiltrates	Interface hepatitis with dense lympho-plasma cell infiltrates and rosette formation, showing moderate or severe activity with periportal piecemeal necrosis.

Harris et al. studied splenic volume in patients with SLE. They highlighted that splenomegaly in SLE occurs as a result of lymphoid hyperplasia. It tends to be mild and is associated with disease activity in SLE patients (6). Gemery et al. also suggested that the spleen enlargement in SLE is a secondary to an increased demand for stem cell resources in response to granulocyte-colony stimulating factor (7).

In autoimmune hepatitis massive splenomegaly has been reported by Ahmed et al. in a case of AIH with overlap of primary sclerosing cholangitis.8

To the best of our knowledge, ours is the first reported case of massive splenomegaly seen in a patient with SLE-AIH overlap syndrome.

Liver involvement is seen in up to 60% of SLE patients.9 The aetiology of liver involvement in SLE may be categorised as –

1) Immune-mediated10
    a. Non-specific liver dysfunction aka Lupus hepatitis
    b. SLE-AIH overlap syndrome aka Lupoid hepatitis
2) Vascular
    a. Anti-phospholipid antibodies causing Budd-Chiari syndrome
3) Non-immune-mediated
    a. Infections
    b. Non-alcoholic fatty liver disease due to use of steroids.

Lupus hepatitis and SLE-AIH overlap syndrome have similar clinical manifestations but are associated with different autoantibodies and histopathological features. The SLE-AIH overlap syndrome is rare, and only few cases have been reported.9 Here, we attempt to distinguish between non-specific liver involvement in SLE from AIH overlap (Table 2) (11, 12, 13).

Our patient fulfilled the EULAR criteria for SLE and International Autoimmune Hepatitis group scoring for AIH. Liver biopsy clinched the diagnosis of SLE-AIH overlap to explain the liver involvement with resultant massive splenomegaly.

CONCLUSION

In conclusion, massive splenomegaly in SLE is a rare occurrence and mandates an extensive work-up. Apart from haematological disorders and other disease processes, it is vital to look for autoimmune hepatitis overlap in these patients. This influences the choice and degree of immunosuppression as well as long-term outcome. Liver biopsy is mandatory to make a specific diagnosis in patients of SLE who present with liver function derangement or splenomegaly.

Author declaration

Authors' contributions:
Study concept and design: P.S., A.P., and H.S.; Acquisition of data, analysis, and interpretation of data: A.P., S.M.S., and H.S.; Drafting of the manuscript: P.S., and P.B.; Study supervision: P.B.

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The authors declare that there is no financial or non-financial conflict of interest.

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Informed written was obtained from the patient for the publication of case details.

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