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CASE REPORT

A Rare Case of Porto-Sinusoidal Vascular Disease Associated with Systemic Lupus Erythematosus and Antiphospholipid Syndrome.

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Abstract
Porto-sinusoidal vascular disease is a medical condition characterized by increased blood pressure in the portal vein in the absence of cirrhosis. This condition is considered poorly defined because its exact cause is unknown. It has been reported to be associated with several autoimmune diseases, including systemic lupus erythematosus and antiphospholipid syndrome. We report a case of 49-year-old Indian lady with a background history of systemic lupus erythematosus with secondary antiphospholipid syndrome who was found to have esophageal varices from an esophagogastroduodenoscopy performed for iron deficiency anemia. A follow-up ultrasound and computed tomography of the abdomen confirmed the absence of cirrhosis and excluded portal vein thrombosis as a potential etiology for portal hypertension leading to the diagnosis of porto-sinusoidal vascular disease. She started on propranolol as primary prophylaxis for variceal bleeding. The patient remained well during subsequent follow-ups with the absence of new or bleeding varices during annual esophagogastroduodenoscopy surveillance. This case contributes to the further understanding of PVSD in SLE and secondary antiphospholipid syndrome. Further research is needed to enhance our understanding of its pathophysiology and to help formulate comprehensive guidelines for the effective management of this condition.

Keywords: *Antiphospholipid syndrome, cirrhosis, esophageal varices, porto-sinusoidal vascular disease, systemic lupus erythematosus.*

Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with a wide array of clinical manifestations, including gastrointestinal and hepatobiliary involvement. Porto-sinusoidal vascular disease (PSVD) is a heterogeneous group of liver disorders characterized by signs of portal hypertension in the absence of cirrhosis [1]. The connection between SLE and PSVD underscores the systemic nature of autoimmune diseases, as they can impact different organ systems throughout the body, adding to the complexity of manifestations seen in individuals with SLE. While various causes can contribute to liver dysfunction in systemic lupus erythematosus, PSVD in the context of SLE remains relatively rare [2]. Here we report a case of SLE with secondary antiphospholipid syndrome (APS) who was noted to have PSVD during a diagnostic workup for iron deficiency anemia (IDA).

Case report

This is a 49-year-old lady who was diagnosed with SLE and secondary APS in 2010. She initially presented with oral ulcers, malar rash, joint pain, lupus nephritis, positive antinuclear antibodies (ANA), low complement levels, positive lupus anticoagulant and anticardiolipin antibody on two occasions tested 12 weeks apart. She had a history of four consecutive late fetal losses but had not experienced any thrombotic events prior. Her disease remains well controlled with prednisolone, azathioprine, hydroxychloroquine, and aspirin.

During a clinic review, she was noted to have IDA where her hemoglobin level was 8.9 g/dL with low serum iron and transferrin saturation. She had normal folate and vitamin B12 levels. She underwent esophagogastroduodenoscopy (OGDS) which revealed two columns of grade 1 esophageal varices with no evidence of fundal varices or portal gastropathy. A follow up ultrasound abdomen revealed evidence of hepatomegaly with no evidence of liver cirrhosis, splenomegaly or portal vein thrombosis. In addition, she also tested negative for hepatitis B, hepatitis C, human immunodeficiency virus, and liver autoantibodies.

A computed tomography (CT) of the abdomen revealed a homogenously enhanced liver with smooth margins and a dilated portal vein with no evidence of portal vein thrombosis, confirming the diagnosis of PSVD (Figure 1 and 2). A liver biopsy was not performed as the patient declined. A diagnosis of PSVD was made, and oral propranolol was initiated. She is monitored with annual ultrasounds of the hepatobiliary system and OGDS. Her most recent OGDS revealed one column of grade 1 esophageal varices with no red wale sign. She remains well on propranolol.

Discussion

PSVD is a group of rare, heterogenous liver disorders characterized by intrahepatic portal hypertension in the absence of liver cirrhosis. The exact pathophysiology of PSVD remains unknown, but it has been associated with autoimmune disorders, chronic infections, exposure to medications or toxins, genetic disorders, and prothrombotic conditions [3].

Including our patient, a total of 26 patients with SLE-related PSVD have been reported in the literature [2,4,5]. The most common clinical manifestations of SLE in this cohort include malar rash (75%), arthritis (68.8%), lupus nephritis (56.3%) and hematological involvement (52.2%). Most patients tested positive for ANA (92%) followed by antidouble stranded DNA (anti-dsDNA) (76%) and anti-Sm (24%). Nine (36%) and six patients (24%) tested positive for anticardiolipin antibody and lupus anticoagulant respectively. The most common clinical manifestations of PSVD in this cohort were splenomegaly (76.5%), varices (44.5%), and ascites (29.4%). The most frequently reported liver histology was nodular regenerative hyperplasia (NRH) (61.5%). (Table 1)

A hypercoagulable state and vasculitis caused by deposition of immune complexes in the intrahepatic vessels has been reported to be

possible reasons why PSVD occurs in patients with SLE and APS [6]. Patients can be asymptomatic or present with ascites, variceal bleeding, splenomegaly, and hypersplenism with normal or slightly abnormal liver function tests. Rarely do they develop hepatic encephalopathy, hepatorenal and hepatopulmonary syndrome.

Besides assessing for liver cirrhosis, Dopplar ultrasound of abdomen remains essential to exclude portal vein thrombosis [5]. CT and magnetic resonance (MR) imaging of the abdomen can be useful in assessing vascular abnormalities, cirrhotic changes, and benign hypervascular nodules [7]. Liver biopsy remains the gold standard in the diagnosis of PVSD. Common pathological findings include hepatoportal sclerosis, periportal fibrosis, perisinusoidal fibrosis, and NRH.

Data on the management of PSVD remains scarce due to its rarity and lack of randomized controlled trials. Its management is mainly extrapolated from guidelines in cirrhotic patients with portal hypertension. Primary and secondary prevention of variceal bleeding in PSVD include the use of non-selective beta-blockers and endoscopic variceal ligation [8]. Trans-jugular intrahepatic portosystemic shunting can be a potential salvage therapy for patients who fail to respond to medical and endoscopic therapy. The evidence of corticosteroids is unclear but can potentially be beneficial [2,9]. The use of other immunosuppressants, such as cyclophosphamide or rituximab, should ideally be guided by the involvement of other organ systems in SLE [4]. Splenectomy remains a salvage therapy in refractory cases. Patients who have portal vein thrombosis should be treated with anticoagulation therapy [8].

The overall prognosis of PSVD appears favourable as most patients have preserved hepatic function [8]. Overall survival was reported at 100%, 78% and 56% at 1, 5 and 10 years respectively. The presence of ascites is a poor prognostic factor for these patients [10].

A high index of suspicion of PSVD should be maintained when SLE patients present with unexplained IDA, varices, ascites, thrombocytopenia, and splenomegaly. It is also more common among SLE patients with positive dsDNA and antiphospholipid antibodies. Although usually benign, its early detection remains essential as late complications, such as variceal bleed, hepatic encephalopathy, hepatorenal syndrome and acute liver failure may be potentially fatal.

Conclusion

PSVD is a rare condition, often overlooked both clinically and pathologically, particularly in patients with SLE who exhibit manifestations of portal hypertension in the absence of cirrhosis. Due to the lack of clinical studies, there are presently no evidence-based recommendations for the prevention, treatment, and follow-up of patients with SLE-associated PSVD. This highlights the need for further research to better understand the pathophysiology of SLE-associated PSVD and to establish comprehensive guidelines for managing this condition.

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WCY contributed to the writing of the manuscript while PSO supervised and edited the manuscript.

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Conflicts of Interest
None.

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Table 1. Summary of clinical characteristics, treatment and outcome of patients with SLE-related PSVD

No	Age/ Sex	Interval between SLE and NCPH (yr)	SLE manifestations	Immunological Markers	Clinical Manifestations of NCPH	Hepatic dysfunction	Portal vein thrombosis	Liver histopathology	Treatment of SLE	Treatment of NCPH	Outcome
1 [2]	29/M	3	Malar rash, AIHA, lupus nephritis	ANA, CH50, dsDNA, Sm, RNP, Ro	Splenomegaly, esophageal varices, thrombocytopenia	Yes	No	PF	GCs, Aza	EVL, propranolol, splenectomy	Alive
2 [2]	43/F	N/A	Malar rash, lupus nephritis, fever	ANA, dsDNA, CH50, IgG	Ascites, hepatosplenomegaly	Yes	No	NRH	GCs	N/A	Alive
3 [2]	26/M	6	Malar rash, arthritis	ANA, dsDNA, CH50, aCL	Massive splenomegaly, eosphageal and gastric varices, thrombocytopenia	Yes	No	PF	GCs	GCs	Alive
1 [2]	19/F	8	Malar rash, arthritis, leucopenia, lupus nephritis, pulmonary hypertension	ANA, dsDNA, CH50	Hepatosplenomegaly, ascites, esophageal varices	No	No	PF	GCs, CTX	N/A	Alive
5 [2]	38/M	12	Lupus nephritis, fever	LA, aCL, dsDNA, CH50	Esophageal varices, massive splenomegaly, thrombocytopenia	Yes	No	PF	GCs	EVL, partial splenic embolization, splenectomy and devascularization around stomach	Alive
6 [2]	40/F	14	Malar rash, arthritis, serositis, lupus nephritis	ANA, dsDNA	Esophageal varices	No	No	NRH	GCs	Endoscopic injection sclerotherapy	Dead (Bacterial endocarditis)
7 [2]	39/F	8	Arthritis, malar rash, oral ulcers, lupus nephritis, pericarditis, bicytopenia, PAH	ANA, dsDNA, aCL, low C3/C4	Splenomegaly, esophageal varices, bicytopenia	No	No	NRH	GCs, CTX	N/A	N/A
8 [2]	37/F	3	Arthritis, serositis, PAH	ANA, dsDNA, Sm, RNP, SSA	Hepatosplenomegaly, esophageal varices	Yes	No	NRH	GCs	N/A	Alive
9 [2]	37/F	0	Malar rash, thrombocytopenia	ANA, dsDNA, aCL, SSA, low C3/C4	Hepatosplenomegaly, ascites	Yes	No	NRH	GCs	Propranolol	Alive
10 [2]	54/F	14	Malar rash, arthritis, lupus nephritis	ANA, dsDNA	Splenomegaly, ascities, esophageal	Yes	No	NRH	GCs, Aza	Endoscopic histoacryl injection, EVL	Alive

					varices, pancytopenia						
11 [2]	56/F	18	Malar rash, arthritis, thrombocytopenia	ANA, dsDNA	Esophageal varcies	No	No	NRH	GCs	endoscopic injection sclerotherapy, endoscopic histoacryl injection	Alive
12 [2]	56/F	5	Cutaneous rash, arthritis, pericardial effusion, AIHA	ANA, dsDNA	Splenomegaly, thrombocytopenia, esophageal varices	Yes	No	NRH	GCs, Aza	N/A	Alive
13 [2]	37/F	N/A	N/A	N/A	Esophageal varices, thrombocytopenia, portal hypertensive colopathy.	Yes	No	NRH	GCs, Aza	Banding, betablockers, side-to-side portocaval shunt	Alive
14 [2]	N/A	N/A	N/A	ANA, dsDNA, SSA, IgG	N/A	Yes	No	NRH	MTX	N/A	N/A
15 [2]	N/A	N/A	N/A	ANA, aCL, ASMA	N/A	No	No	NRH	Aza	N/A	N/A
16 [2]	N/A	N/A	N/A	ANA, dsDNA, RNP, IgG	N/A	No	No	NRH	CTX	N/A	N/A
17 [2]	N/A	N/A	ILD	Sm, RNP, IgG	N/A	Yes	No	NRH	CTX	N/A	N/A
18 [2]	N/A	N/A	PAH	ANA, Sm, LKMI	N/A	No	No	NRH	CTX	N/A	N/A
19 [2]	35/F	2	Pancytopenia	ANA	N/A	No	No	NRH, PF	GCs, CsA	N/A	N/A
20 [2]	41/F	6	Pancytopenia	ANA, dsDNA	N/A	No	No	NRH	GCs, MTX	N/A	N/A
21 [2]	25/F	9.5	Pancytopenia	ANA, aCL	N/A	No	No	N/A	GCs, MTX	N/A	N/A
22 [2]	25/F	10	Pancytopenia	ANA, dsDNA, aCL	N/A	Yes	No	N/A	GCs, MTX	N/A	N/A
23 [2]	48/F	2	Arthritis, pancytopenia, lupus nephritis	ANA, Sm, dsDNA, SSA	Splenomegaly, pancytopenia	No	No	N/A	GCs	Metoprolol	Alive
24 [4]	43/F	5	Pancytopenia, alopecia, photosensitivity, retinal vasculitis, lupus panniculitis	ANA, dsDNA, low C3/C4	Splenomegaly, esophageal varices, ascites	No	Yes	Normal	GCs, CTX, diuretics, Belimumab + anticoagulation	N/A	Alive
25 [5]	43/F	22	Discoid lupus, arthritis, lupus nephritis	ANA, dsDNA, RNP, Sm, SSA, SSB, APS -ve	Gastroesophageal varices, splenomegaly	No	No	Normal	GCs, RTX	N/A	Dead (Breast carcinoma)

GCs = Glucocorticoids, CTX = Cyclophosphamide, CsA =. Ciclosporin, MTX = methotrexate, Aza = Azathioprine, ANA = Antinuclear antibody, aCL = anticardiolipin antibody, LA = lupus anticoagulant, ILD = interstitial lung disease, PAH = pulmonary arterial hypertension, AIHA = autoimmune hemolytic

anemia, NRH = Nodular regenerative hyperplasia, PF = Periportal fibrosis, EVL = Endoscopic variceal ligation

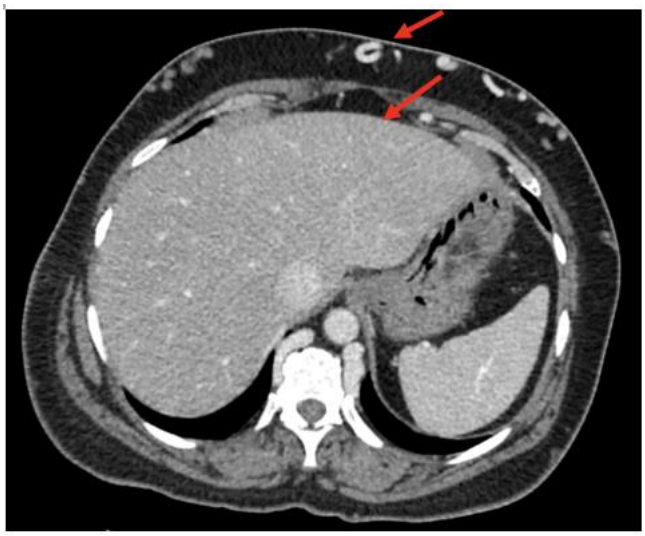

Figure 1. Smooth liver edge and dilated superficial veins (red arrows) with no evidence of liver cirrhosis

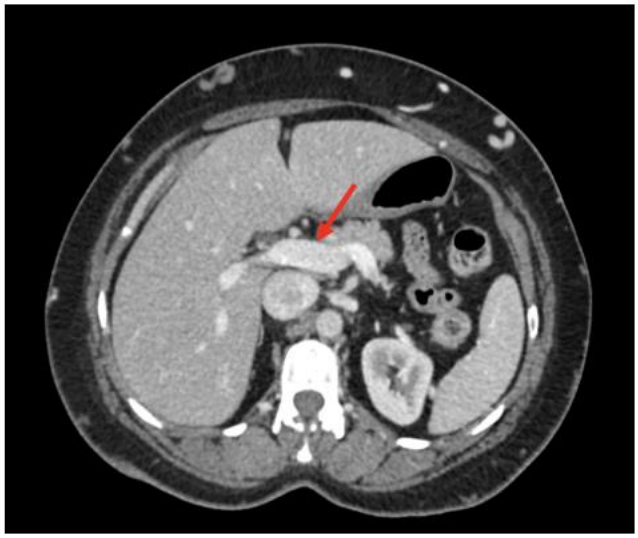

Figure 2. Dilated portal vein (red arrow) with no evidence of portal vein thrombosis

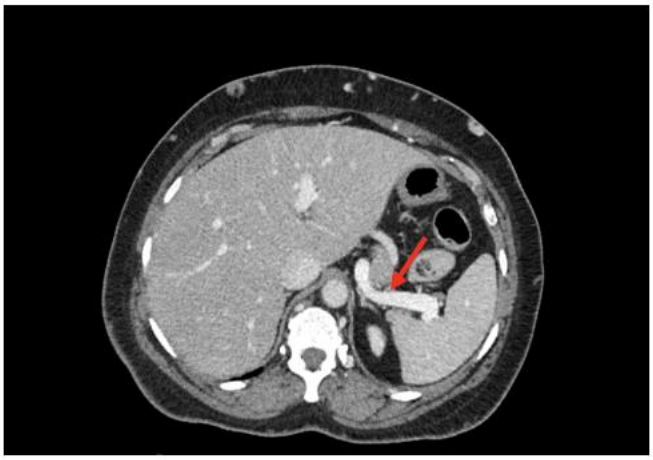

Figure 3. Mildly dilated splenic vein (red arrow) with no splenomegaly

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