A RARE CASE OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A MALE PATIENT ASSOCIATED WITH ANTIPHOSPHOLIPID SYNDROME, PRESENTING WITH SEVERE AUTOIMMUNE HEMOLYTIC ANEMIA

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ABSTRACT

This case report describes an unusual case of Systemic Lupus Erythematosus (SLE) in a male patient associated with antiphospholipid syndrome who presented with recurrent episodes of jaundice secondary to severe autoimmune hemolytic anemia. SLE is rare in males and very few cases have been reported so far. Our patient was a middle-aged gentleman diagnosed case of SLE, presented with fatigue, generalized weakness and shortness of breath. He also had multiple episodes of jaundice. Diagnostic workup confirmed autoimmune hemolytic anemia, that was refractory to steroid therapy and Azathioprine, but responded to IV methylprednisolone and Mycophenolate. The antibodies for antiphospholipid syndrome were also positive. Although lupus and antiphospholipid syndromes are rare in males, these entities should be considered especially among those with unexplained anemia and hemolysis.

Keywords: *Antiphospholipid Syndrome, Autoimmune Hemolytic Anemia, Immunosuppression, Systemic Lupus Erythematosus*

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder affecting various body organs. The etiology has been attributed to environmental, genetic and idiopathic factors. The condition involves inflammatory process which leads to activation of autoimmunity in body leading to a wide spectrum of clinical presentation that may vary from a mild disease to severe fatal organ involvement.[1] Female gender, identical twins and genetic conditions like Klinefelter's syndrome have more predisposition to the development of SLE. Various medication like Procainamide, Hydralazine, Isoniazid have been found to be linked with drug induced SLE. Environmental factors include viral infections, sunlight exposure and vitamin D deficiency.[2] Diagnosis of lupus requires clinical symptoms as well as laboratory tests particularly autoimmune profile. According to the diagnostic criteria by the European Alliance of Associations for Rheumatology (EULAR)/American College of Rheumatology (ACR) in 2019 auto antibody positivity is required with anti-nuclear antibody (ANA) in majority of the patients however this antibody is less sensitive and is even found in healthy individuals. Some patients with SLE have negative ANA antibody so extractable nuclear antibody particularly anti double stranded DNA (anti- ds DNA) is used, which is more specific and also provides information regarding disease activity. Other auto antibodies like anti SS-A, SS-B and anti-RNP antibodies can also be present in patients with SLE. Treatment of lupus is aimed at reduction of the symptoms to minimum, prevention of acute flares and acquire disease remission.[3]

Antiphospholipid antibody syndrome (APS) is a chronic autoimmune disease mediated by the antibodies that target membrane surface phospholipids. This in turn leads to a spectrum of clinical manifestations including arterial and venous thrombosis along with the multi system involvement. The condition has been linked with other autoimmune disorders especially lupus and the diagnosis involve detection of antibodies including anticardiolipin, anti-phospholipids, Anti-beta

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2 glycoprotein antibodies and lupus anti coagulant.[4] SLE has been found to be associated with antiphospholipid syndrome and other autoimmune disorders. Interestingly, patients suffering from SLE and associated antiphospholipid syndrome who develop autoimmune hemolytic anemia as complication are more prone to develop thrombosis[5] highlighting the timely recognition of these associated medical disorders. SLE is more common in females and the purpose of presenting this case was the fact that our patient was male with SLE and antiphospholipid syndrome who presented with severe autoimmune hemolytic anemia that was refractory to corticosteroid therapy.

CASE REPORT

A 37 years old gentleman already diagnosed as a case of SLE in July 2021 on the basis of symptoms and biochemical parameters and was prescribed low dose hydroxychloroquine that improved his joint pains and rashes, now presented to the medical outpatient department in a tertiary care hospital with history of vomiting, lethargy and reduced appetite for the last one week. The vomiting which started a week ago, was sudden in onset, non-projectile, not associated with abdominal pain or fever. Vomitus contained food particles and he experienced multiple episodes over the past 48 hours. There was associated lethargy and reduced appetite. Anorexia and vomiting were likely related to gastritis as he was taking hematinic and anticoagulant since 2021. The systemic inquiry revealed history of joint pains, rashes, photo sensitivity to sunlight. There was no history of weight loss or bleeding from any site. There was no history of any surgical intervention in the past however there was history of multiple blood transfusions. There was history of deep venous thrombosis (DVT) of his left leg in 2021 for which he was given anticoagulant therapy with oral Rivaroxaban in a therapeutic dose for 3 months followed by a prophylactic dose of 10mg daily that was continued. He also revealed the history of chronic headaches and numbness in the body. He also revealed progressive lethargy and history of multiple hospital visits due to anemia.

On examination, he was pale as well as jaundiced. His temperature was 98.6^{0}F. His pulse was 110/min, respiratory rate 16/min and blood pressure was 105/60 mm Hg. Abdominal examination revealed splenomegaly. There was no clinical suspicion or findings of thrombosis in his recent admission.

His laboratory workup showed the presence of autoimmune hemolytic anemia. In his current admission, the lab tests showed marked anemia with hemolysis as evident in table I given below. Serum bilirubin, LDH and reticulocyte count were elevated however serum ALT, AST and ALP were within the normal limits. Renal parameters including serum urea and creatinine were also normal. Rheumatology consultation was sought and complete autoimmune profile including ANA and ENA was done as shown in table II. ENA (Extractable nuclear antigen) test was positive for lupus (positive ANA and anti-double stranded DNA) while the rest of the ENA antibodies were negative. Test for antiphospholipid antibodies was also done that showed positive lupus anticoagulant, positive anticardiolipin antibodies and positive anti beta 2 glycoprotein 1 antibodies with high titer (table II). The oral course of Prednisolone was given in a dose of 1mg/kg/day for 4 weeks that was gradually tapered. Azathioprine was also started along with oral hematinic, however there was no significant improvement in his anemia over a period of time.

Following no improvement, he was admitted and IV methylprednisolone along with Mycophenolate mofetil was instituted, which resulted in a significant improvement in hemoglobin and bilirubin levels as can be seen in table II.

He was discharged on oral Prednisolone, Mycophenolate mofetil, Rivaroxaban, PPI then followed up fortnightly regularly in OPD. The compliance to treatment was good and the repeat tests showed good sustained response without any further fall in hemoglobin levels. There was no limitation during the management as he was an entitled patient in that institution.

Table I: Complete Blood counts

Parameter	Normal range	Before Methylprednisolone and MMF therapy	After Methylprednisolone and MMF therapy
WBC	4000-11,000/ul	4650	6650
RBC	3.8-5.8 m/ul	2.8	3.5
Hb	11.5-16.5 g/dl	8.8	10.1
Platelets	150,000-450,000	100,000	140,000
MCV	76-96 fl	104	95
MCH	27-33pg	31	32
MCHC	32-38 g/dl	29	33
Reticulocytes	0.5- 2 %	9.5	2.5

Table II: Autoimmune profile / Chemistry

Test	Result	Normal value
ANA	Positive	Negative
Anti-ds DNA Ab	Positive	Negative
Alegria Antiphospholipid Ab panel (IgM)	10.0	<10
Alegria Antiphospholipid Ab (IgG)	>80	<10
Coombs test	+ve	-ve
LDH	558	135-225U/L
Anti RNP Ab	2	<5
Total Bilirubin	4.05	0.1-1.2mg/dl

DISCUSSION

SLE and anti-phospholipid syndrome are often associated together as both are autoimmune mediated and are primarily seen in females. Both the conditions when coexist together lead to an increased propensity to develop complications particularly thrombosis.[6] Suzuki E et al. found mixed type autoimmune hemolytic anemia in a female patient with SLE and antiphospholipid syndrome[7] that highlights the importance of evaluation of these three conditions in a patient with unexplained anemia. The hemolytic anemia in these conditions usually resolves to steroids however we often see refractory cases that may require immunosuppressive agents and intravenous immunoglobulins. Our patient was a young male who had SLE with antiphospholipid syndrome with severe refractory autoimmune hemolysis. It is described that out of 10 cases of SLE, only one will be male whereas nine will be females.[8] Antiphospholipid syndrome often remains undiagnosed in males and this case highlights the importance of suspecting these autoimmune conditions in males. A single center retrospective study conducted at University college London hospital found that in patients with Antiphospholipid syndrome, the presence of concomitant SLE does not appear to increase the risk of thrombotic complications[9] however various other studies showed that patients with SLE and associated antiphospholipid syndrome who have autoimmune hemolytic anemia are more prone to develop thrombotic complications. A study conducted in Khairpur, Pakistan compared the different modalities of treatment in patients with autoimmune hemolytic anemia that showed more aggressive and longer duration of therapy is required in secondary AIHA as compared with primary AIHA.[10] In refractory cases, combination therapies should be preferred over steroid alone treatment as in our case the dual therapy was effective. For more severe and life-threatening cases, IVIG can be considered. Studies have highlighted various ongoing trials on monoclonal antibodies and newer modalities of treatment for autoimmune hemolytic anemia[11] and we hope they would be helpful in reducing the thrombotic complications as well. Future multi centric larger studies are required for better assessment of the thrombotic risk in these autoimmune mediated disorders.

CONCLUSION

Any male patient with SLE and coexisting antiphospholipid syndrome who presents with unexplained anemia should be evaluated for associated autoimmune hemolytic anemia. People with antiphospholipid syndrome are more prone to thrombosis and the chances of thrombosis are more when these patients have associated autoimmune hemolytic anemia.

Authors' contributions:

Nimra Riaz: Conception of study/Designing/Planning, Manuscript Writing, Data Collection, Critical Review

Muzamil Jamil: Conception of study/Designing/Planning, Manuscript Writing, Data Collection, Critical Review

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Naveed Akhter Malik: Manuscript Writing, Critical Review, Analysis of Data, Recommendations in Writing

Sara Ahmed: Manuscript Writing, Review of Data, Analysis, Review of Investigations, Critical Review

CONFLICT OF INTEREST

None.

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