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# Acute Systemic Lupus Erythematosus and Antiphospholipid Syndrome with Miscarriage

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**Abstract**

**Background:** Antiphospholipid syndrome is an autoimmune, hypercoagulable state that is caused by antiphospholipid antibodies. Anticardiolipin antibodies, anti-b2 glycoprotein-I, and lupus anticoagulants are the main autoantibodies found in antiphospholipid syndrome. In this brief communication, we describe the case of a woman who has been suffering from treatment-resistant and difficult to manage bipolar disorder (BPD) with fluctuating thrombocytopenia and neurological findings with positive lupus anticoagulant. This was important because it was a multi-complicated problem and showed antiphospholipid syndrome with lupus. We propose it to be a consequence of an atypical presentation of APS.

**Case presentation:** The known case of APS (antiphospholipid syndrome) and SLE (systemic lupus erythematous) with a history of kidney transplantation for 14 years, infertility, and CVA (cerebrovascular accident). According to the history of infertility, she had an abortion. Lab data reveals a positive anticoagulant antibody. The microscopy pathology data showed mainly necrotic chorionic villi admixed with extensive hemorrhage and evidence of thrombosis.

**Conclusion:** This is the report of APS with SLE (systemic lupus erythematosus) and miscarriage. Patients with menopausal history and a history of infertility should also be considered for fertility.

**Keywords:** Antiphospholipid • SLE • Bipolar disorder • Aortic stenosis

## Introduction

Antiphospholipid syndrome (APS), also known as 'Hughes Syndrome [1] is an autoimmune disease characterized by the presence of antiphospholipid antibodies, such as lupus anticoagulant, anticardiolipin antibodies, and anti-β2-glycoprotein-I antibodies [2]. In addition to the classical antiphospholipid antibodies, namely anticardiolipin antibodies, and lupus anticoagulant, new autoantibodies and antibody complexes of different immunoglobulin subtypes (IgA, IgG, IgM) are now recognized as significant contributors to the pathogenesis of the antiphospholipid syndrome. The incidence and prevalence of antiphospholipid syndrome are estimated at approximately 5 *de novo* cases per 100 000 per year and 40–50 cases per 100 000 individuals, respectively [1,3]. APS can present various clinical phenotypes, including thrombosis in the veins, arteries, microvasculature, and obstetrical complications. The pathophysiological hallmark is thrombosis, but other factors might be important, such as complement activation [4]. Obstetrical antiphospholipid syndrome is characterized by fetal loss after the 10$^{th}$ week of gestation, recurrent early miscarriages, intrauterine growth restriction, or severe preeclampsia.1 The major non-thrombotic manifestations of antiphospholipid-antibody positivity include valvular heart disease, livedo, antiphospholipid antibody-related nephropathy, thrombocytopenia, hemolytic anemia, and cognitive dysfunction.

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Antiphospholipid syndrome is often associated with other systemic autoimmune diseases such as systemic lupus erythematosus (SLE); however, it commonly occurs without other autoimmune manifestations (primary antiphospholipid syndrome) [5]. The degree of risk associated with antiphospholipid antibodies depends on the characteristics of the antiphospholipid antibody profile and the presence of additional thrombotic risk factors [6]. Although criteria for classifying the antiphospholipid syndrome have been proposed, the definition of clinically significant antiphospholipid-antibody [7]. Saccone G, et al. [8] showed in singleton pregnancies with primary antiphospholipid syndrome, the anticardiolipin antibody is the most common sole antiphospholipid antibody present, but anti-b2 glycoprotein-I is the one associated with the lowest live birth rate and the highest incidence of preeclampsia, intrauterine growth restriction, and stillbirth, compared with the presence of anticardiolipin antibodies or lupus anticoagulant alone. Aneja J, et al. [9] showed lately the thrombotic events in APS role as an etiological mechanism in the causation of certain neuropsychiatric disorders have been put forth. It has been suggested that one should suspect APS in psychiatric manifestations, which are atypical, resistant to treatment, associated with cognitive decline and dementia, abnormal involuntary movements, livedo reticularis, migraine, thrombotic events like stroke or transient ischemic attacks, obstetrical complications. Our objectives are to help both general practitioners and specialty-based physicians recognize and accurately diagnose antiphospholipid syndrome and provide basic recommendations for treating patients who are persistently positive for antiphospholipid antibodies.

## Case Presentation

A 45-year-old female patient was a candidate for fsgs in the initial biopsy 17 years ago. It was revived in 2005 to receive a proper kidney transplant but was rejected about eight months ago. The patient then underwent dialysis three times a week through a semi-permanent catheter; Due to suspicion of an infusion catheter, the catheter was removed, and the femoral catheter was inserted.

On November 24, 2019, the patient was hospitalized with symptoms of orthopnea, agitation, and full consciousness. She had a history of infertility and did not menstruate for several months.

Three days later, according to the psychiatrist's advice, the patient was completely inattentive and did not communicate verbally and visually. She was also unaware of the time, but she was relatively aware of the location.

After 4 days, on December 1, 2019, the patient's level of consciousness decreased to 8, and she suffered from agitation; and behavioral changes (shouting) and according to the neurologist's advice, the patient received treatment for delirium.

The patient's echocardiographic results showed EF: 10-15% and PAP: 50. The level of consciousness reached 4, and only the eyes were open. According to the neurologist's advice, heparin was started for the patient, and according to the psychiatrist's advice, anticholinergic drugs and delirium treatment were discontinued. The patient was tested for SLE.

After 4 days, according to the tonic-colonial movements of the right upper limb, a 400 mg dose of Depakin was given to the patient. According to the observation of the end lesions of the limbs, a calligraphy of the collar-Doppler ultrasound was performed for the patient and venous (partial) thrombosis was identified in the upper left limb.

According to the patient's clinical symptoms, the antiphospholipid syndrome was diagnosed, and methylprednisolone was started. Two days later, she was transferred to the ICU following a CVA and vaginal bleeding. During dialysis, she showed similar seizures. Until two days later, while not receiving anticoagulants, she still had gastrointestinal and vaginal bleeding, which led to an abortion, and doctors noticed that the patient was pregnant.

Due to the decrease in platelet count, plasmapheresis was performed for 6 days and then the patient was curettage. On December 17, 2019, Melna's patient became positive and intubation. Finally, she died on January 5, 2020.

Laboratory data showed that the patient had negative anticoagulants, positive anticardiolipin (45.9), and lupus anticoagulant 80.0.

MRI showed multiple small and ill-defined white matter demyelinating foci in the supratentorial level (Figure 1). The microscopy pathology data showed mainly necrotic chorionic villi admixed with extensive hemorrhage and evidence thrombosis (Figure 2).

## Discussion

Here, we describe the reported case of APS with SLE and miscarriage. APS is a rare autoimmune disease characterized by hypercoagulability and thrombosis in both the arterial and venous circulations, with or without pregnancy-related morbidity. This condition presents with various clinical manifestations, affecting multiple organs [10]. The underlying mechanism in APS can involve an imbalance between the generation and lysis of fibrin, or the cytokine cascade as in systemic inflammatory response syndrome [11]. The interaction of several autoantibodies, anti-beta-2-glycoprotein 1 antibodies, lupus anticoagulant, and anticardiolipin antibody with plasma proteins is

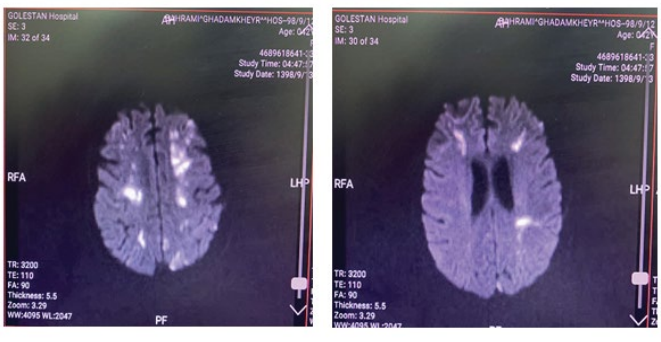


**Figure 1.** MRI with multiple small and ill-defined white matter demyelinating foci in the supratentorial level.

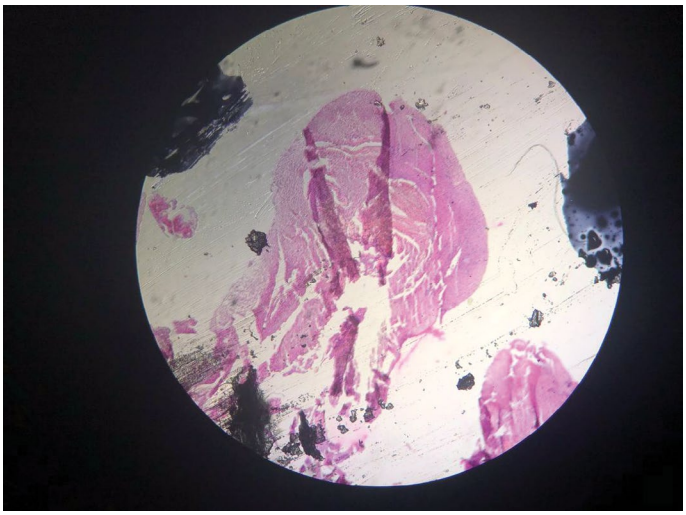

**Figure 2.** Microscopy pathology with mainly necrotic chorionic villi admixed with extensive hemorrhage and evidence thrombosis.

associated with a heightened procoagulant state. As a result, physicians need to recognize this syndrome in a patient presenting with thrombosis in multiple organs. Not only this, but physicians must be aware of traditional cardiovascular risk factors that increase a patient's risk of atherosclerosis, such as diabetes, hypertension, hypercholesterolemia, and smoking that increase these patient's clot risk. Primary care doctors must be diligent in recognizing and aggressively controlling traditional risk factors to prevent further endothelial and vascular injury that can precipitate thrombosis [12]. Physicians should also consider the possibility of patient fertility, even in the context of a history of infertility and menopausal age.

APS is characterized by the development of thrombosis in the form of DVT, pulmonary thromboembolism, and stroke. The cardiac manifestations of APS include mainly valvular disease and intracardiac thrombus formation. Myocardial infarction occurs only 4% of the time [13]. Autoimmune disorders, including systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, and APS, are known states of chronic inflammation that induce premature atherosclerosis [12]. While the involvement of APL antibodies in the pathogenesis of thrombosis in APS is very much established in the literature, the presence of certain cardiovascular risk factors or medical conditions such as pregnancy in these patients raises their risk for thrombosis. Recognizing and controlling these risk factors can help establish an effective treatment plan and prevent future thrombotic events.

Shayestehpour M, et al. [14], recently found an APS associated with gastric signet ring cell adenocarcinoma. The clinical findings described in the present case and the positivity of antiphospholipid antibodies suggested an association between the 2 disorders. Thrombosis is one of the first manifestations of malignancy. Cancer patients are at high risk of thromboembolic events. Therefore, antiphospholipid antibodies may be linked to tumor-related thrombosis. These antibodies may be increased due to cancer immunotherapy by interferon $\alpha$ or immune response to tumor antigens. Cancers can increase the production of antiphospholipid antibodies by several mechanisms, including the following: 1) autoantibody production in response to tumor antigens; 2) secretion of anticardiolipin antibodies from tumor cells; and 3) production of monoclonal immunoglobulins with lupus anticoagulant and anticardiolipin-antibodies activities.

Antiphospholipid syndrome (APS) is associated with thrombosis and morbidity in pregnancy. Morbidity in pregnancy includes unexplained stillbirths at ≥ 10 weeks of gestation, preterm delivery due to eclampsia, preeclampsia, or placental insufficiency, and three or more consecutive miscarriages [15]. The APS is associated with recurrent miscarriage (RM). The incidence of aPLs in RM patients is between 15% and 20%. Given the complexity and heterogeneity of RM, the etiology remains unknown in about 50% of couples [4]. Santos, et al. found recurrent miscarriage is related to the specificity of antiphospholipid antibodies, with relationships to anticardiolipin antibodies, lupus anticoagulant,

anti-β2-glycoprotein I antibodies, and antiphosphatidylserine [16]. The number of recurrent miscarriage does not appear to be influenced by the presence of antiphospholipid antibodies. The lack of standardization between antiphospholipid antibodies tests, not applying the strategy of repeated tests for diagnostic and not using two tests for confirming the lupus are factors that may hinder the diagnostic of antiphospholipid syndrome determination. But in our case, the patient had a history of infertility and did not have a period for about a few months, and because he was in the menopausal age, no doctor suspected that the patient was pregnant. Therefore, it is important for physicians to consider the possibility of patient fertility even in the context of a history of infertility.

## Conclusion

We have presented the reported case of APS with SLE and miscarriage. Overall, it has been proven time and time again that traditional thrombotic risk factors greatly increase the miscarriage risk. Patients with APS already have a high thrombotic burden with the presence of APL antibodies and chronic inflammation leading to premature miscarriage. Primary care doctors must be diligent in recognizing and aggressively controlling traditional risk factors to prevent further thrombotic.

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