Primary Antiphospholipid Antibody Syndrome Presenting as Venous Infarct and Deep Vein Thrombosis

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Abstract
We report the case of a young lady with primary antiphospholipid antibody syndrome, who had two spontaneous abortions and cerebral venous thrombosis and subsequently deep vein thrombosis of the leg veins. Three classes of antiphospholipid antibodies (IgG, IgM, IgA) were elevated. There was no clinical or laboratory evidence for other autoimmune or systemic illnesses. We are presenting the case due to the rarity of the same.

INTRODUCTION
Antiphospholipid antibodies (APLA) are a group of auto-antibodies, all recognizing various combinations of phospholipids, phospholipid binding proteins, or both. Primary antiphospholipid syndrome occurs in patients without clinical evidence of another autoimmune disease, whereas secondary antiphospholipid syndrome occurs in association with other autoimmune diseases. Primary APLA syndrome is an extremely rare condition.1 We report a case of primary antiphospholipid antibody syndrome, and reviewed the literature.

CASE REPORT
A 25 years housewife presented to our OPD with history of holocranial headache and progressive bilateral impairment of vision of one and a half years duration and left lower limb edema of one month duration. Complaints started during fourth month of her second pregnancy 1 ½ years back when she developed severe holocranial continuous headache and vomiting. Seven days later she developed sudden onset of weakness of right side of the body with facial deviation to the opposite side. She did not have dysphagia, dysarthria, diplopia, or bladder and bowel disturbances. She was admitted to a local hospital and as per the old records she had bilateral papilloedema, right sided hemiparesis with, grade 3 power of right upper and lower limbs. On the eight day after admission she developed left sixth cranial nerve palsy. There was no other neurological deficit. Her routine blood, urine, serum electrolytes, RBS, LFT, RFT, ECG, chest X-ray were within normal limits. CT scan head showed a small hypodense area suggestive of infarct in the left frontal region. There was no hemorrhage or dense/empty delta sign. ANA was negative. CSF studies were normal.

She was put on antioedema measures. Hemiparesis completely cleared in one week.

Oral steroids were given for a total of five weeks and acetazolamide was continued for eight weeks. Diplopia got cleared by three weeks. She had spontaneous abortion at the seven month of gestation. She continued to have recurrent holocranial headache with transient obscuration of vision. There was no history of skin rashes, photosensitivity, joint pain or swelling. She had a first trimester spontaneous abortion two years ago. There was no history of hypertension and diabetes. No history of any substance abuse or drugs.

Fig. 1 : CT of brain shows left parasagittal cortical infarct
On admission in our centre, she was conscious with normal vital signs. She had edema of left lower limb below the knee with a positive Homan’s sign. Neurological examination revealed a visual acuity of 6/60 on both eyes with peripheral concentric of visual field and optic atrophy. Only other neurological defect was a pronator drift of the right hand. Thus 25 years lady with history of two abortions, raised intracranial pressure and cortical infarct and the findings of optic atrophy and deep vein thrombosis we considered the possibility of a hypercoagulable state. Investigations revealed the following findings. Blood routine, urine routine, serum electrolytes, renal, liver and thyroid functions, lipid profile, chest X-ray and ECG were normal. Platelet count was 1,00,000 per cmm. Activated partial thromboplastin time (aPPT) was 50 seconds (control of 34 seconds). Doppler study showed evidence for deep vein thrombosis of left lower limb affecting the leg veins.

ANA, anti ds DNA and VDRL tests were negative.

Antiphospholipid antibody titers were as follows: IgA-22EU (normally <10), IgM-39 MPL (normally <10), Ig G -<48 GPL (normally <10). Lupus anticoagulant tests were done using DRVVT which was prolonged. Procoagulant work up including protein C and S, antithrombin, urine homocystine assays were normal. Factor V leiden mutation was not seen. Based on the clinical and laboratory findings we made a definite diagnosis of primary APLA syndrome. We repeated the lab tests after six weeks, which confirmed the diagnosis of primary antiphospholipid antibody syndrome. We started her on inj. Heparin and was later switched over to oral anticoagulation.

**DISCUSSION**

The occurrence of aPL antibodies associated with vasoclusive events without any underlying disease process is termed the primary antiphospholipid antibody syndrome. The most commonly detected subgroups of antiphospholipid antibodies are lupus anticoagulant antibodies, anticardiolipin antibodies and anti beta2 glycoprotein 1 antibodies. Possible mechanisms by which aPL might be generated include: 1) auto immunity may be a factor-a break in the tolerance may lead to an “escaped clone”; 2) closely related to the same is the concept that aPL antibodies are a response to inner membrane (i.e. phosphoserine) that are exposed in apoptotic blebs on cells not eliminated from the circulation because of an overloaded or defective clearance system; 3) aPL may also be cross-reactive antibodies induced by exogenous antigens from infectious organisms. Possible mechanisms by which aPL might induce thrombotic events include: the following: 1) aPL may combine with platelet membrane phospholipids, resulting in increased platelet adhesion and aggregation; 2) aPL may combine with the endothelial cell membrane phospholipids along with beta2 GPI and induce endothelial cell damage, impaired prostacyclin production, increased platelet adhesion and aggregation (which is responsible for thrombocytopenia); endothelial cell damage may also result in decreased production of endothelium derived relaxing factor and thus, increased vasospasm and ischemia. Venous thrombosis, especially deep venous thrombosis of the legs, is the most common manifestation of the antiphospholipid syndrome occurring in 29 to 55 percent of patients with the syndrome during an average follow-up of less than six years. Arterial thromboses are less common than venous thromboses and most frequently manifest with features consistent with ischemia or infarction. The brain is the most common site, with strokes and transient ischemic attacks accounting for almost 50 percent of arterial occlusions. Cerebral venous thrombosis has many causes like local and systemic infection, cranial trauma and procoagulant states. Only 25-30% cases are idiopathic. Thus a thorough investigation to identify the etiological factor is warranted in every case. Other prominent manifestations of the antiphospholipid syndrome include thrombocytopenia (in 40 to 50 percent of patients), hemolytic anaemia (in 14 to 23 percent), and livedo reticularis (in 11 to 22 percent). Placental infarction due to microthrombi, increased occurrence of IUGR, toxemia are the causes of fetal loss. Since pregnancy itself is a hypercoagulable state presence of aPL antibodies can precipitate any of the above mentioned complications at anytime, either during pregnancy or during postpartum state. So in short, suspect the presence of aPL antibodies when there is clinical symptoms such as DVT, arterial occlusive events, recurrent fetal loss, vasospastic phenomenon, TIA etc. So in case of doubt along with the criteria required for diagnose, and excluding other disease processes, patient should be screened for this rare syndrome. International consensus statement on preliminary criteria for the classification of antiphospholipid antibody syndrome is as follows.

**Clinical criteria**

Vascular thrombosis: i.e., one or more clinical episodes of arterial, venous, or small vessel thrombosis, occurring within any tissue or organ.

Complications of pregnancy: One or more deaths of morphologically normal fetuses at or after the 10th week of gestation; or one or more premature births of morphologically normal neonates at or before the 34th week of gestation or three or more unexplained consecutive spontaneous abortions before the 10th week of gestation.

**Laboratory criteria**

Anticardiolipin antibodies: aCL IgG or IgM antibodies present at moderate or high levels in the blood on two or more occasions at least six weeks apart. (significance of IgA aCL antibodies is not well established). Lupus anticoagulant antibodies: Lupus anticoagulant antibodies detected in the blood on two or more occasions at least six weeks apart.

The minimum criteria: A patient must meet at least one clinical and one laboratory criterion for a diagnosis of APLA. Women with recurrent preembryonic and embryonic pregnancy loss and no history of thromboembolism may be treated with 5000 U of heparin twice daily, but experts recommend higher doses, sufficient to produce full
anticoagulation, for women with prior thromboembolism. Experts agree that low-molecular-weight heparin may be substituted for standard heparin in the treatment of pregnant women with the antiphospholipid syndrome.

Our plan is to maintain her on oral anticoagulation with an INR of 2-3 and to switch over to inj heparin during the next pregnancy.

**REFERENCES**


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**Book Review**

**Adherence to Long-Term Therapies Evidence for Action**

*World Health Organization 2003*

Adherence to therapies is a primary determinant of treatment success. Poor adherence attenuates optimum clinical benefits and therefore reduces the overall effectiveness of health systems.

“Medicines will not work if you do not take them” - Medicines will not be effective if patients do not follow prescribed treatment, yet in developed countries only 50% of patients who suffer from chronic diseases adhere to treatment recommendations. In developing countries, when taken together with poor access to health care, lack of appropriate diagnosis and limited access to medicines, poor adherence is threatening to render futile any effort to tackle chronic conditions, such as diabetes, depression and HIV/AIDS.

This report is based on an exhaustive review of the published literature of the definitions, measurements, epidemiology, economics and interventions applied to nine chronic conditions and risk factors. These are asthma, cancer (palliative care), depression, diabetes, epilepsy, HIV/AIDS, hypertension, tobacco smoking and tuberculosis.

Intended for health managers, policy-makers and clinical practitioners this report provides a concise summary of the consequences of poor adherence for health and economics. It also discusses the options available for improving adherence, and demonstrates the potential impact on desired health outcomes and health care budgets. It is hoped that this report will lead to new thinking on policy development and action on adherence to long-term therapies.

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