

Maternal and Fetal Complications of Antiphospholipid Syndrome: a case report with long-term follow-up

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Abstract

We report a case of a 26-year old woman having antiphospholipid syndrome in pregnancy with long-term follow up. She presented with recurrent miscarriages, venous thrombosis, avascular necrosis of femoral head, mid-cerebral artery infarction and skin ulcers. Antiphospholipid syndrome is a recognized disorder of pregnancy. Diagnosis requires a high index of suspicion when evaluating women with recurrent pregnancy losses and vascular thrombosis. A low dose aspirin combined with heparin can reduce morbidity and improves the pregnancy outcome.

Case Report

A 26-year-old Pakistani primigravida was admitted in April 1989 at 8 weeks of gestation with a painful right leg. On examination, the right leg was swollen; calf circumference measured 32cm on the right vs 29.5cm on left and the over-lying skin was congested. Passive movements of the calf were painful. A diagnosis of popliteal vein thrombosis was made on Doppler examination and patient was started on intravenous heparin (1000 units/hour). Complete blood count showed thrombocytopenia ($30 \times 10^9/L$). Further laboratory investigations revealed antinuclear antibodies positive 1+ whereas, anti-dsDNA, anti-smooth muscle antibodies, anti-mitochondrial antibodies and rheumatoid factor were negative. Prolonged activated partial thromboplastin time (APTT) was not correctable with fresh frozen plasma. The APTT inhibitor test was positive and anti-cardiolipin IgG was raised to 67GPL/ml. The repeat value 8 weeks later was 80GPL/ml (normal 9GPL/ml). Repeated antinuclear antibodies were strongly positive and anti-dsDNA was negative. The echo cardiogram and chest x-ray were also normal.

A diagnosis of antiphospholipid syndrome (APS) was made based on her clinical presentation and laboratory findings. Low-dose aspirin (75mg daily) was started. She had a miscarriage at 13 weeks of gestation. Second miscarriage occurred at 19 weeks of gestation in 1991. In her third pregnancy in addition to low-dose aspirin, she received heparin (5000U subcutaneously daily) and prednisolone (30mg twice daily). Prednisolone was gradually tapered and stopped at 24 weeks of gestation. This pregnancy was complicated by severe pre-eclampsia and Caesarean section was performed at 31 weeks of gestation. The baby died four months later due to complications of prematurity. She conceived fourth time after infertility treatment in 1995. Low-dose aspirin and heparin (5000U subcutaneously daily) was

started at 8 weeks of gestation and she was carefully observed during pregnancy. Platelet counts, blood pressure and urine for protein were checked at each visit. Fetal surveillance was monitored by kick chart, non-stress test, serial pelvic and Doppler ultrasound examination and biophysical profile. Dexamethasone was given at 30 weeks of gestation to promote fetal lung maturity. A healthy male baby (weight 3.1kg) was delivered at 37 weeks of gestation by Caesarean section. The patient was discharged on fifth post-operative day on low-dose aspirin. She conceived for the fifth time in 1997, and received treatment as mentioned earlier. A healthy baby boy (weight 2.6kg) was delivered. Due to the nature of disease, tubal ligation was discussed with the patient.

In 1999, another episode of popliteal vein thrombosis was initially managed with heparin infusion (30,000U daily). Later she was switched to warfarin followed by low-dose aspirin. Her sixth pregnancy in 2001 was complicated by severe intrauterine growth restriction (biophysical profile: 6/10 with suboptimal cardiotocography at 29 weeks of gestation). Dexamethasone was administered to promote lung maturity and an elective Caesarean section with tubal ligation was performed. A baby boy (weight 980 grams) was delivered and transferred to neonatal intensive care unit. The patient developed severe hypertension and thrombocytopenia on fourth postoperative day for which she received beta-blockers and corticosteroids. In January 2002, she developed pain in the left lower limb and skin ulcers. An MRI revealed avascular necrosis of femoral head. In view of her progressive symptoms and functional disability, a total hip arthroplasty was advised.

In 2003 she developed stroke and MR angiography showed middle cerebral artery infarction. On a recent follow-up, she was undergoing physiotherapy. Her current therapy includes warfarin, beta-blocker, low-dose aspirin, and cholesterol lowering agent.

Discussion

Antiphospholipid syndrome (APS) is characterized by the presence of antiphospholipid (aPL) antibodies belonging to a family of immunoglobulins that bind negatively charged phospholipids, phospholipids binding proteins or both. These include lupus anticoagulants (LAC), anticardiolipin (aCL) antibodies and anti beta 2 glycoprotein -1; a co-factor required for the action of LAC and aCL. Antiphospholipid syndrome is a complex multisystem disorder. This syndrome occurs in isolation (primary APS) or

within context of several autoimmune disorders (secondary APS).¹

Sapporo criteria are considered acceptable for the diagnosis of APS. These include unexplained or repeated pregnancy loss around 10 weeks of gestation and positive aCL IgM and IgG or LAC antibodies on at least 2 occasions 6 weeks apart.² The reported patient manifests several features of APS such as venous thrombosis, repeated pregnancy loss and high titres of aCL and LAC antibodies.

Prevalence of APS varies according to the population assessed, and the Immunoassay used to detect aPL antibodies. The study published by Lockwood et al found a prevalence of 2.2% for aCL and 0.27% for LAC antibodies in low risk obstetrics patients.³

The association of positive aPL and LAC antibodies with recurrent fetal loss is well established and varies between 4.6 and 50.7% (mean 15.5%) and 0 and 14% (mean 8.3%) respectively.⁴ The presence of aPL antibodies is also associated with placenta insufficiency, fetal growth restriction, preeclampsia and preterm delivery.⁵

In addition to influencing pregnancy outcomes, APS may affect any organ of the body and display a broad-spectrum of manifestations. These include deep venous thrombosis (31.7%), thrombocytopenia (21.9%) pulmonary embolism (9%), transient ischaemic attacks (7%), stroke (13.1%), myocardial infarction (2.8%), skin ulcers (3.9%) and rarely a catastrophic syndrome characterized by widespread vascular occlusion (0.8%).⁶ Most of these systemic features can be explained by vasculopathy and occlusion of small vessels due to platelet aggregation and subsequent thrombosis.

Asymptomatic avascular necrosis (AVS) of femoral head is seen on MRI in 20% of patients with primary APS. Though sporadic cases of bilateral or unilateral AVN of femoral and tibial head has been reported in patients with primary APS who were not receiving corticosteroids.^{7,8} Use of corticosteroids in treatment of APS may aggravate the risk of avascular necrosis of bones.

It is difficult to interpret the current literature to determine the optimal treatment of APS in pregnancy. The recent trials have focused on comparison of low-dose aspirin alone with steroids or heparin. In a multicenter randomized trial no difference was found in live birth rates when low-dose aspirin and heparin was compared with low-

dose aspirin and prednisolone, but patients who received prednisolone were reported to have increased risk of maternal morbidity and preterm delivery.⁹ The review of therapeutic trials has revealed that the combination of heparin and aspirin may reduce pregnancy loss by 54%.¹⁰

In conclusion, APS is a well-recognized disorder of pregnancy and is characterized by recurrent miscarriages and vascular thrombosis. Routine screening of pregnant women for APS is not recommended as the prevalence is low. However, anticardiolipin and lupus anticoagulants antibodies must be checked in women presenting for evaluation of recurrent pregnancy loss. Management of APS is aimed to improve maternal and fetal outcome. It can be achieved by preconceptional counseling, referral to specialist and careful monitoring of pregnancy. Low-dose aspirin combined with heparin may be an appropriate treatment in women with recurrent pregnancy loss and thrombotic events.

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