

Case Report

Primary Antiphospholipid Antibody Syndrome Presenting as Recurrent Deep Vein Thrombosis.

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Introduction:

Aniphospholipid Syndrome also known as sticky blood or Hughes' syndrome, is an auto immune disease that can cause abnormal blood clotting in any blood vessels- both arteries & veins. As a result it can cause many different problems. These includes clots in the legs known as DVT, miscarriage & dangerous arterial thrombosis resulting in stroke & Heart attacks.

Aniphospholipid Syndrome accounts for about one in five DVT & may be to blame in some cases of economy class syndrome, leading to the death of young people traveling on long flight, one in five case of stroke in young people (<45 years) is associated with the condition. APS also accounts for as many as one in five case of miscarriage. Miscarriage is thought to result from disruption of blood flow through small blood vessels of the placenta.

The Syndrome has also been linked to pre-eclampsia, placental abruption & intra uterine growth restriction.

People with APS are at great risk of - Venous thrombosis in the leg (DVT), arms & internal organ (kidney, liver, lungs, brain, eye). Arterial thrombosis – which can be lead to recurrent stroke, TIA & Heart attack. Mild thrombocytopenia. Headache- which may be diagnosed as migraine. Multiple sclerosis like episode. Skin rash known as livedo reticularis.

Recurrent pregnancy loss. The diagnosis of APS is made by a combination of one clinical criteria plus one laboratory criteria (Revised Sapporo APS update 2006).The clinical criteria are vascular thrombosis & pregnancy events, with evidence from histopathological examination or imaging studies. The laboratory criterion is a medium to high level of anticardiolipin antibody, & beta-2 glycoprotein-1 or a positive lupus anticoagulant antibody 12 weeks apart .

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Case Report:

A 37 years old BD female house wife visited our CV clinic in April 2010 due to H/O recurrent DVT in her Right lower leg. She was apparently healthy with BMI about 22 kg/m².The first event occurred during December 2003 when after traveling from India about 2 days later she complaints painful Rt leg swelling. Doppler USG lower limb showed DVT Rt lower leg which involved Rt Popliteal vein. She was then admitted to a local hospital & started on SC LMW Heparin & warfarin. After taking 6 month she lost her follow up. She had two unexplained fetal abortion. She had on & off headache which was diagnosed as migraine. About 6 year later April 2010

this pt came to visited to our CV clinic with the complaints of painful swelling of the Rt leg. She was suspected to have DVT again her Rt leg & Doppler USG lower leg confirmed it again Rt Popliteal vein DVT.

She did not have any H/O fever, Loss of hair. Arthritis, Photosensitivity , Facial rash or oral ulcer. A physical examination reveled Afebril, normal BP & Heart rate & mildly Anaemic. There was no rash, oral ulcer or lymphadenopathy.

Initial laboratory result were notable for Hb-10 gm/dl, ESR -125, WBC- 8200, PLT- 190000. Normal Biochemistry including Homocystin & Troponin -I.

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Anti ds DNA –Negative, VDRL –Negative, HbAg –Negative.

Antiphospholipid IgG > 100 (Positive) .

Lower limb Doppler- Rt popliteal DVT.

So the lady was diagnosed as having primary APS with recurrent DVT Lower limb. She was appropriately counseled regarding the disease, treatment, monitoring & prognosis.

Treatment was started with SC LMW heparin with warfarin. During her whole clinical course, the Pt. did not experience any respiratory or chest symptom such as dyspnoea, tachypnoea, chest pain or tachycardia. so pulmonary embolism was not evaluated.

The Pt. was suggested to take warfarin indefinitely & to avoid standing & sitting for a long time.

Discussion:

Antiphospholipid syndrome (APS) or otherwise known as Hughes' Syndrome is a disorder which manifests itself by recurrent arterial or venous thrombosis, with persistently elevated levels of antibodies directed against membrane anionic phospholipids (e.g. anti-cardiolipin [aCL] antibody, antiphosphatidylserine) or their associated plasma proteins, predominantly beta-2 glycoprotein I (apolipoprotein H), or evidence of a circulating anti-coagulant.

The diagnosis of a definite APS is made by referring to the revised Sapporo Criteria 2006, whereby it consists of at least one clinical criteria, which involves one or more episodes of vascular thrombosis and also one laboratory criteria with positive anti-cardiolipin (aCL), anti-beta-2 glycoprotein I, or lupus anticoagulant antibody on at least 2 occasions at least 12 weeks apart. The episode of vascular thrombosis must be confirmed by imaging, doppler studies, or histopathology.

This patient fits the clinical diagnosis of antiphospholipid syndrome in view of he presented with two proven episodes of recurrent venous thrombosis, the first one involving the lower limb deep vein thrombosis in 2003, and the second one is the current problem which involved thrombosis of the Rt popliteal vein & a positive antiphospholipid antibody IgG > 100.

The antiphospholipid antibodies associated with APS are anticardiolipin antibodies (aCL), lupus anticoagulants (LAs) which are immunoglobulins directed against plasma proteins (prothrombin or annexin V) and anti-beta-2 glycoprotein-I (anti-beta-

2GPI)antibodies. According to a few studies, the prevalence of anti-beta-2 glycoproteins in APLS ranges from zero percent to 90 percent. Anti-beta-2 glycoprotein-I antibodies have higher specificity than aCL for thrombosis.

There were two evaluations conducted of the proposed and revised Sapporo criteria. In the first evaluation by Kaul et al. whereby a retrospective analysis of 200 aPL-positive patients who met the previous diagnostic criteria for APLS (1999 Sapporo criteria), only 59 percent can be diagnosed with APLS by using the 2006 revised criteria. Thus, the 2006 revised criteria is likely to exclude a significant number of patients presented with APS clinically. However, the 2006 criterion is useful in defining a more homogeneous population, especially for research studies.

This patient is likely to have APLS in view of the recurrent venous thrombosis & the laboratory criteria of positive Antiphospholipid IgG >100. There was also no history of trauma and we have ruled out other possibilities like hypercoagulable state and thrombophilia, which can also cause recurrent thrombosis.

Another issue in this patient is whether the APLS is primary or secondary. Primary antiphospholipid syndrome means that the APLS occurs by itself and not associated with a connective tissue disease, particularly with the spectrum of systemic lupus erythematosus. In this patient, he has primary antiphospholipid syndrome in view of negative connective tissue disease screening, namely anti-nuclear antibody (ANA), Anti dsDNA, complement level C3/C4, rheumatoid factor. There are also no other signs or symptoms suggestive of a related connective tissue disease in the patient. In the European Multicenter Study of 114 patients comparing primary APLS with secondary disease, the two groups were found to have similar clinical and laboratory manifestations of APS.

The patient is treated with lifelong warfarin, with a target INR of 2.0 to 3.0. Anticoagulation is the mainstay treatment for antiphospholipid syndrome. Based on a few studies, the optimum target INR is at a conventional range of 2.0 to 3.0.6 In patients with recurrent thrombosis despite conventional doses of warfarin, the target INR will be higher at 3.0–4.0 based on expert recommendations, and the effect of adding aspirin to warfarin may increase the frequency of

bleeding. However, there is no randomized controlled trial to point towards the effectiveness of increasing INR in recurrent thrombosis. The duration of anticoagulation is also another issue. The optimum duration of anticoagulation after the first event of venous thromboembolism is debatable. It has been shown that the presence of anticardiolipin antibodies at the end of six months of treatment was

associated with a doubling of the risk of recurrent thrombosis (29 versus 14 percent). Another study has shown that patients with venous thromboembolic episode and antiphospholipid antibodies have an extremely high risk for recurrent venous thrombosis after withdrawal of treatment with oral anticoagulants. Therefore, based on these recommendations, lifelong anticoagulation is the preferred choice.

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