Case Report

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ISSN (o):2321–7251

Primary antiphospolipid antibody syndrome- presenting as cerebral venous thrombosis and recurrent deep vein thrombosis of lower limbs- A case report

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Submission Date: 25-04-2014, Acceptance Date: 29-05-2014, Publication Date: 31-07-2014

How to cite this article:

Vancouver/ICMJE Style

Rajasekhar P, Maheshwarareddy M, Ramarao P, Reddy KBB, Bingi P, Nagesh AMA. Primary antiphospolipid antibody syndrome- presenting as cerebral venous thrombosis and recurrent deep vein thrombosis of lower limbs- A case report. Int J Res Health Sci [Internet]. 2014 Jul 31;2(3):894-7. Available from http://www.ijrhs.com/issues.php?val=Volume2&iss=Issue3

Harvard style

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Abstract:

Anti-phospolipid antibody syndrome is a disorder characterized by recurrent arterial or venous thrombosis with or without fetal loss. It can occur as an isolated diagnosis, or it can be associated with systemic lupus erythematosis or another rheumatic disease. Transient aPL but probably not the syndrome can be induced by drugs and infections. Here we report a case of primary antiphospolipid antibody syndrome with cerebral venous thrombosis and recurrent venous thrombosis of lower limbs.

Key words: Antiphospolipid antibodies; Antiphospolipid antibody syndrome; Beta2 glycoprotein 1; Fetal loss; Thrombosis

Introduction

Antiphospolipid syndrome is characterized by recurrent arterial or venous thrombosis with or without fetal loss. Diagnosis of antiphospolipid syndrome requires that a patient have both a clinical event(thrombosis or pregnancy morbidity) and the persistent presence of antiphospolipid antibody (aPL), a coagulant assay(inhibitor of phospolipid dependant clotting- the lupus anticoagulant test) or both. Low titre, usually transient anticardiolipin occurs in upto 10% of normal blood donors [1,2] and moderate to high titre anticardiolipin or positive lupus anticoagulant test occurs in less than 1%. 10-40% of SLE patients [2] and approximately 20% of rheumatoid arthritis patients [3] have positive aPL test. 14% of patients with recurrent thromboembolism disease have aPLs. 10% of first stroke victims have aPLs [4], especially those who are young (upto 29%) [2,5], as do upto 20% of women who have suffered 3 or more consecutive fetal losses [6].

Case Report

A 17 year old male patient presented with complaints of seizures, generalized tonic clonic in nature, 6 episodes associated with fever. No neurological deficit and no bowel and bladder disturbances. Patient was drowsy, pulse of 92 bpm,regular with all peripheral pulses equally felt and no delay. Blood pressure of 120/80 mm of Hg. Cardiovascular and respiratory system examination are normal. Neurological examination revealed no focal neurological deficit, plantars are bilateral extensors. In the due course of hospital stay patient gradually improved but he developed swelling of left lower limb (figure 1) which subsided and again recurred few days later.

Investigations:

1. Computed tomography brain plain: Acute ischemic infarct in right frontal lobe.

2. Magnetic resonance imaging brain: T1 hypointensity, T2, Flair hyper intensity noted in right frontoparietal and frontotemporal lobe, suggestive of acute infarct. Mild compression affect noted over right lateral ventricle. (figure 2)

3. Computed tomography brain with venogram: Hemorrhagic infarct in right frontal lobe. Irregular filling defect superior sagittal sinus (cerebral venous thrombosis). (figure 3,4)

4. Antinuclear antibody – 6U/L(<20)

Activated partial thromboplastin time- 55sec (36sec)

Prothrombin time – 15sec(15 sec)

International normalized ratio – 1.1

5. Doppler venous study of left lower limb: Hyperechogenic thrombus in external saphenous vein suggestive of Deep vein thrombosis (DVT). Other deep veins normal.

6. Doppler venous study of left lower limb(3 days later): Hyperechogenic thrombus in common femoral vein, popliteal vein with extension into common iliac vein suggestive of DVT.

7. Random blood sugar – 94 mg/dl

Blood urea - 28 mg/d

Serum creatinine – 1.0 mg/dl

Serum sodium – 132 mmol/L

Serum potassium – 4.1 mmol/L

Serum chloride - 102 mmol/L

Hemoglobin – 7.2g%

Total count -11000/mm^3

Platelets - 2.8 lakhs /pl

Urine albumin and sugar not detected.

Total bilirubin – 0.9mg/dl

SGPT – 160U/L

SGOT - 29 U/L

Alkaline phospatase – 300 U/L

8. Coagulation profile:

Phospolipid antibody IgG - 4.68 GPL U/ml.(<10.00)

Phospolipd antibody IgM - 22.23 MPL U/ml (<10.00)

Antithrombin activity - 89% (80-120)

Protein C, functional - 63% (70-140)

Protein S, functional - 20% (60-140)

Factor V, Leiden mutation analysis- not detected.

Lupus anticoagulant by DRVVT- Lupus like anti coagulant present.

Discussion:

APS is characterized by the presence of autoantibodies against phospolipid binding plasma protein namely beta2 GP1 (apolipoprotein H). In vivo beta2 GP1 binds to phospotidyl serine on activated or apoptotic cell membrane, including those of trophoblasts, platelets and endothelial cells. Under physiologic conditions beta2 GP1 may function in the elimination of apoptotic cells and as a natural anticoagulant[7]. aPL is mostly related to thrombosis through multiple mechanisms. One is beta2 GP1 binds to phospotidyl serine expressed on activated or apoptotic platelets, endothelial cells or trophoblasts and then aPL binds to beta2 GP1 dimer [8]. This complex induces a prothrombotic phenotype. Second through down regulation of signal transducer and activator of transcription5 (STAT5), aPLs inhibit the production of placental prolactin and SGF binding protein1 and they adversely affects the formation pf trophoblast syncitium, placental apoptosis and trophoblast invasion- all processes required for normal establishment of placental function.

APS can be diagnosed based on the revised Suppuro classification criteria 2004 [9].

Clinical criteria:

1. Vascular thrombosis—one or more clinical episodes of arterial, venous or small vessel thrombosis in any tissue or organ.

2. Pregnancy morbidity—

a. One or more unexplained deaths of a morphologically normal fetus at or beyond 10^{th} week of gestation or

b. One or more premature births of a morphologically normal neonate before the 34^{th} week of gestation because of eclampsia, severe

preeclampsia or recognised features of placental insufficiency or

c. Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation with maternal anatomic or hormonal abnormalties and paternal and maternal chromosomal causes excluded.

Laboratory criteria:

1. Lupus anticoagulant present in plasma on 2 or more occasions atleast 12weeks apart.
2. Anticardiolipin antibody of IgG or IgM isotype in serum or plasma, present in medium or high titre(>40 GPL or MPL or >99 percentile) on two or more occasions atleast 12 weeks apart.
3. Antibeta 2 glycoprotein1 antibody of IgG or IgM isotype in serum or plasma(in titres >99 percentil) present on two or more occasions atleast 12 weeks apart.

Definitive APS is present if atleast one of the clinical criteria and one of the laboratory criteria are met. Catastrophic APS is a rare, abrupt, life threatening complication. It consists of multiple thrombosis of medium and small arteries occurring over a period of day and causin stroke; cardiac, hepatic, adrenal, renal and interstitial infarction and peripheral gangrene [1,2].

No treatment for asymptomatic patients. Warfarin to be given indefinitely for patients with venous or arterial thrombosis with INR to be maintained at 2.5 and for patients with recurrent thrombosis INR should be maintained between 3-4. For greater than or equal to one fetal loss or greater than or equal to 3 embryonic loss without thrombosis prophylactic heparin plus low dose aspirin through out the pregnancy, discontinue 6-12 weeks peripartum. Thrombosis regardless of pregnancy history- therapeutic heparin or low dose aspirin through out pregnancy, warfarin postpartum.

Conclusion

Antiphospolipid antibody syndrome is uncommon in men. If a young patient presents with a thrombotic state, we need to suspect a hypercoagulable state which may be hereditary or acquired, as later case for APLAS.

Source of Funding: Nil

Conflict of Interest: None

Acknowledgement:

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors/editors/publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

References:

1. Vila P, Hernandez MC, Lopez- Fernandez MF, Batlle J. Prevalence, follow up and clinical significance of the aCL in normal subjects. Thromb Haemost. 1994 Aug;72(2):209-13.
2. Petri M: Epidemiology of antiphospolipid antibody syndrome. J auto immune. 2000;15:145-151.
3. Olech E, Merrill JT: The prevalence and clinical significance of antiphospolipid antibodies in rheumatoid arthritis , wrr rheumatic rep 8: 100-108, 2006.
4. Ginsberg JS, Wells PS, Brill- Edwards, Donovan D, Moffatt K, Johnston M, et al. Anti phospolipod antibody and venous thromboembolism. Blood. 1995 Nov 15;86(10):3685-91.
5. Levine SR, Brey RL, Savvaya KL, Salowich-Palm L, Kokkinos J, Kostrzema B, et al. Recurrent stroke and thrombooclusive events in the antiphospolipid syndrome. Ann Neurol. 1995 Jul;38(1):119-24.
6. Stephenson MD: Frequency of factors associated with habitual abortion in 197 couples, Fertil Steril 16:24-29, 1996.
7. Mori T, Takeya H, Nishirka J, Gabazza EC, Suzuki K. beta 2-Glycoprotein 1 modulates the anticoagulant activity of activated protein C on the phospolipid surface. Thromb Haemost. 1996 Jan;75(1):49-55.
8. Lutters BC, Derksen RH, Teketenburg WL, Lenting PJ, Arnout J, de Groot PG. Dimers of beta 2-Glycoprotein 1 increase platelet deposition to collagen via interaction with phospholipids and apolipoprotein E receptor 2'. J Biol Chem. 2003 Sep 5;278(36):33831-8. Epub 2003 Jun 13.
9. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. Interactional consensus statement on an update of the classification criteria for definite antiphospolipid antibody syndrome (APS). J Thromb Haemost. 2006 Feb;4(2):295-306.

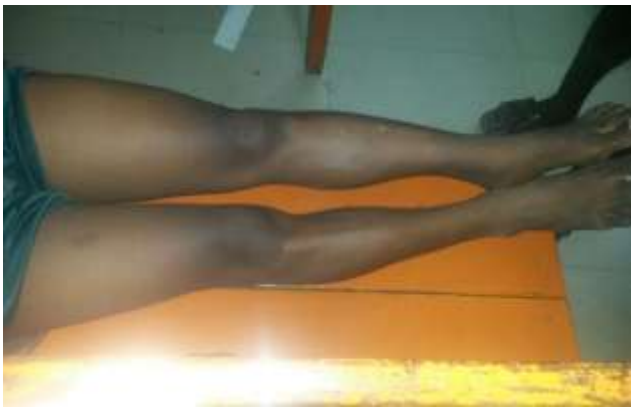

Figure 1: Swelling of left lower limb suggestive of deep vein thrombosis

Figure 2: MRI Brain T1 weighted images showing hypointensity in right frontoparietal and frontotemporal lobe, suggestive of acute infarct

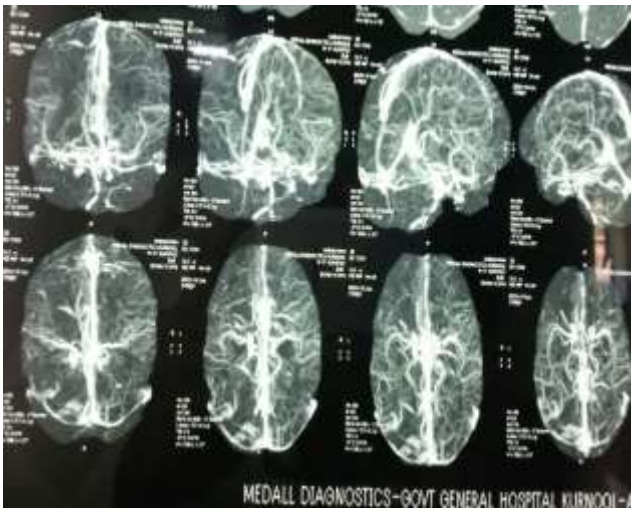

Figure 3: Computed tomography brain with venogram showing irregular filling defect superior sagittal sinus (cerebral venous thrombosis)

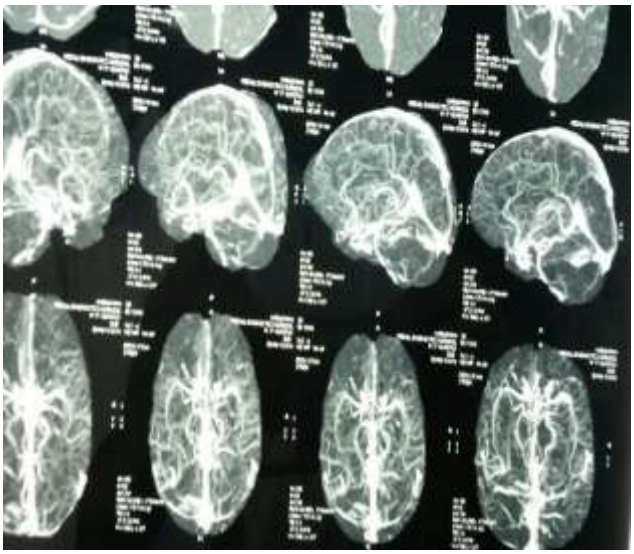

Figure 4: Computed tomography brain with venogram showing irregular filling defect superior sagittal sinus