A Rare Case of Anti-Phospholipid Antibody Syndrome with Bleeding Manifestation

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ABSTRACT

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The Antiphospholipid syndrome or Antiphospholipid antibody syndrome (APS or APLS), is an acquired autoimmune thrombophilic disorder in which patient have vascular thrombosis and/or pregnancy complications attributable to placental insufficiency accompanied by presence of anti-phospholipid antibodies in blood. Bleeding manifestations are uncommon in APS. Prolongation of aPTT is an usual manifestation of APS but not accounting for any bleeding manifestations. In rare occasions, a hemorrhagic diathesis can occur due to the occurrence of anti-prothrombin antibodies causing severe hypoprothrombinemia.
We are reporting a case Antiphospholipid Syndrome with rare atypical bleeding manifestations.

Keywords: Antiphospholipid Syndrome, Anti-prothrombin Antibodies, Lupus Anticoagulant

*See End Note for complete author details

INTRODUCTION

Antiphospholipid syndrome or antiphospholipid antibody syndrome (APS or APLS) is an acquired autoimmune thrombophilic disorder caused by antiphospholipid antibodies. APS provokes blood clots (thrombosis) in both arteries and veins as well as pregnancy-related complications such as miscarriage, stillbirth, preterm delivery, and severe preeclampsia. Prolongation of aPTT is usual manifestation of APS but not accounting for any bleeding manifestations. Presentations of hemorrhagic diathesis due to antiprothrombin antibodies causing severe hypoprothrombinemia are a very rare occurrence.

We are reporting a case Antiphospholipid Syndrome with rare atypical bleeding manifestations

CASE REPORT

A 43 year old female presented with headache, multiple episodes of vomiting and decreased responsiveness. She was diagnosed to have right frontotemporal chronic subdural hematoma and underwent right frontal burr hole craniotomy. She developed loss of vision in the right eye after the event. She was found to have persistently elevated coagulation profile.

She was diagnosed with Addison's disease secondary to an episode of adrenal hemorrhage since 3 years and now on steroid therapy. She had seven pregnancies in which first one was a 3rd trimester loss. The two, three and 4 pregnancies were a 2nd Trimester loss. Fifth one was live baby born at 7th month due to uteroplacental insufficiency. The sixth & seventh pregnancies were 3rd month losses.

On examination vitals were stable, bilateral pitting pedal edema was present. Other systemic examination was within normal limits. Examination of the eyes showed; left eye visual acuity 6/60 and in the right eye only perception of light present, which was diagnosed asrelative afferent pupillary defect (RAPD) by ophthalmologist due to ischemic optic neuropathy.

INVESTIGATIONS ON ADMISSION

Routine investigations showed, Hb –8.2 gm%, HCT – 28.7%, Total count – 11900 cells/cmm (P-82%, L-12%, E- 1%, M-5%, B- 0) PLT –90,000cells/cmm initially, then 196000cells/cmm, RBS – 97mg/dl, B. Urea – 54, Creatinine – 0.6mg/dl, Sodium – 138meq/l, Potassium –2.9meq/l. Peripheral blood smear showed moderate hypochromic microcytic anemia, mild thrombocytopenia an neutrophilia with toxic neutrophils. Thyroid

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function test was within normal limits (T3 – 1.08ng/ml, T4 – 9.87mcg/ml, TSH – 3.20microIU/ml). USG Abdomen showed only a large calculus in gall bladder. Venous Doppler both lower limbs was done and DVT was ruled out.

Coagulation profiles showed elevated prothrombin time (PT) - 23.8 initially (then 19.9 and 20.1) and INR –2.25 initially (then 1.88 and 1.9), aPTT –93.4 initially (then 72.9). Other investigations, D-Dimer– 571ng/ml, S. Albumin– 2.7 g/dl, Pro calcitonin – negative, DCT – negative, ANA and Anti ds DNA – Negative. Out of Anti-phospholipid antibodies: Anti-cardiolipin IgG – 95 u/ml and Beta 2 glycoprotein 1 IgG – 16.5 u/ml was positive. Anti-cardiolipin IgM – 3.37 u/ml and Beta 2 glycoprotein 1 IgM – 2.1u/ml were negative. Lupus anti-coagulant was in the upper limit 1.3 (normal 0-1.3)

Mixing Study was done for prolonged aPTT .Patient's aPTT was 75.3 and control was 30 sec. On mixing with pooled normal plasma – aPTT was 70.7.On mixing with factor VIII deficient plasma aPTT was 95.7. On mixing with factor IX deficient plasma, aPTT was 93.3. So, aPTT was not normalized even after mixing, indicating the presence of lupus anticoagulant.For the evaluation of prolonged PT and to confirm the presence of hypoprothrombinemia, prothrombin assay have to be done which is not possible in a tertiary care centre.

Considering the presentation of intracranial bleed, thrombocytopenia and abnormal coagulation profiles, adrenal hemorrhage and recurrent abortions in the past, on evaluation showing positive antiphospholipid antibodies, lupus anticoagulant on mixing study, a final diagnosis of Anti-Phospholipid Syndrome (APS) with rare atypical bleeding manifestations was made. She was treated with high dose steroids and supportive therapy. On follow up, there was no further bleeding or thrombotic events.

DISCUSSION

The Antiphospholipid syndrome or Antiphospholipid antibody syndrome (APS or APLS), is an acquired thrombophilic disorder in which patient have vascular thrombosis and/or pregnancy complications attributable to placental insufficiency accompanied by presence anti-phospholipid antibodies on blood.

At least 1 clinical and 1 laboratory criteria must be fulfilled for diagnosis. This patient fulfilled all the 3 pregnancy morbidities along with 2 anti phospholipid antibodies

The *Clinical Criteria*: Firstly, vascular thrombosis, defined as one or more clinical episodes of arterial venous or small vessel thrombosis in any tissue or organ. Secondly pregnancy morbidity, i.e., one or more unexplained deaths of a morphologically normal fetus at or beyond 10th week of gestation or one or more premature births of a morphologically normal neonate before 34 week of because of eclampsia, severe pre-eclampsia or placental insufficiency or three or more unexplained consecutive spontaneous abortions before 10th week of gestation.[2]

Lab Criteria: Presence of Lupus anti-coagulant, Anti-Cardiolipin antibody, Anti- Beta 2 glycoprotein antibody at intermediate or high titers on two occasions 12 weeks apart.[2]

The causes of bleeding in APS are hypoprothrombinemia, thrombocytopenia, acquired platelet abnormality, acquired inhibition to specific coagulation factor eg. Factor VIII, acquired Von Willebrandsyndrome.[1] The aPTT measures the length of time (in seconds) that it takes for clotting to occur when certain substances are added to the plasma of blood in a test tube. One of these substances is phospholipid. The lupus anticoagulant is one of the antibodies that binds to phospholipids and frequently causes the aPTT to be prolonged. (LA effect)[1]

In mixing studies, when the aPTT of a particular plasma sample is prolonged and is not correctable with immediate mixture of normal plasma than Lupus anticoagulant should be suspected.[1]

Recurrent small vessel thrombosis causing consumptive coagulopathy, cause aPL-associated thrombocytopenia → usually moderate without clinical manifestations.[3] In rare occasions a hemorrhagic diathesis due to the occurrence of non-neutralizing anti-prothrombin antibodies causing severe hypoprothrombinemia (HPT) can be observed – causing PT to be prolonged

Severe thrombocytopenia causing bleeding in antiphospholipid syndrome has been reported earlier.[3,4] In rare occasions a hemorrhagic diathesis due to the occurrence of non-neutralizing anti-prothrombin antibodies causing severe hypoprothrombinemia (HPT) can be observed. Levels of prothrombin in plasma are less than 10-20% in cases with HPT-related bleeding requiring transfusion and/or corticosteroid treatment.[5]

The APS mainly causes thrombosis, and pregnancy losses. However, other clinical manifestations are also associated with the presence of persistent autoimmune APL.[55] Bleeding is uncommon but can be the first clinical manifestation in patients having severe thrombocytopenia or prothrombin deficiency.

In patients with bleeding and prolonged aPTT, antiphospholipid syndrome has to be suspected and mixing studies to rule out presence of Lupus anticoagulant should be done. High dose of corticosteroids, tapering slowly is the mainstay of treatment.

END NOTE

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Conflict of Interest: None declared

Editor's Remarks: This case highlights a rare manifestation of an unusual case. It is reported for awareness of the clinicians in general.

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