CASE REPORT

Primary Antiphospholipid Syndrome Associated with Autoantibodies Against Golgi Bodies: A Case Report of a 32-Year-Old Female

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Abstract Antiphospholipid syndrome is an autoantibody mediated disorder characterised by thrombotic manifestations and/or obstetric morbidity. The autoantibodies are directed against phospholipid binding plasma proteins. Amongst the clinical features abdominal presentation is an unusual feature in this syndrome. We present the case report of a 32-year female whose complaints was abdominal pain for one week and no history of previous foetal loss, who responded well to warfarin and has not developed systemic lupus erythematosus even after follow up. Characteristic of this patient is the appearance of auto antibodies against Golgi bodies. Although antinuclear antibodies are seen in patients of rheumatic disease like systemic lupus erythematosus, its presence in individuals with unusual presentation of antiphospholipid syndrome may facilitate in diagnosis.

Keywords Antiphospholipid syndrome · Thrombosis · Antinuclear antibodies

Introduction

Antiphospholipid syndrome (APS) is an autoantibody mediated disorder characterised by thrombotic manifestations and/or obstetric morbidity. The common antibodies detected are lupus anticoagulant, anticardiolipin and anti β -2 glycoprotein 1 antibodies. These antibodies can interfere with both pro and anticoagulant pathways. The disease

presents in an extremely diverse manner, with abdominal manifestations unusual and varied. As this may pose a threat to life so a high degree of suspicion is necessary to spare dire consequences.

Case Report

A 32-year-old female presented at our hospital with complaints of insidious pain in the abdomen for 1 week, the nature of which was episodic, spasmodic and non-radiating in nature. There were no relieving factors for the subsiding of the pain. The pain aggravated after taking meals and also after drinking water. She had a single episode of low grade fever in near past which was relieved with medications. There was no past medical history of hypertension, diabetes or any other chronic illness. On examination, her vitals were normal, with mild pallor and no icterus, cyanosis, clubbing, oedema or lymphadenopathy. Abdominal examination revealed distension with diffuse tenderness more in right hypochondrium and epigastric region. No organomegaly could be elicited. She has had menarche at 14 years of age with three living children, her last born child being 13 years. She had no history of miscarriages and was not on oral contraceptive drugs or used any other forms of contraception. There was no history of drug intake in the recent past and no such similar history. There was no history of smoking, intake of alcohol or any form of addiction. Her laboratory investigations at time of admission indicated a low haemoglobin, packed cell volume (PCV) and RBC count (Table 1). The liver function and renal function tests were within normal limits. Her homocysteine was higher than normal with low folic acid and Vitamin B12. Her investigations for prothrombin, partial thromboplastin time, dilute Russell viper venom time and

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Table 1 Laboratory investigations (routine and special) at time of admission

Parameter	Value	Biological reference range
Haemoglobin	10.1 gm/dL	12.0–15.0 gm/dL
Packed cell volume	31.6%	36.0–46.0%
Total red cell count	3.67 million/ μ L	3.80–4.80 million/ μ L
Mean cell volume	86 fL	83.0–101.0 fL
Mean cell Haemoglobin	27.5 pg	27.0–32.0 pg
Mean cell Haemoglobin conc	31.9 gm/dL	31.5–34.5 gm/dL
Red cell distribution width	11.6%	11.6–14.0%
Total leucocyte count	7.8 $10^3/\mu$ L	4.0–10.0 $10^3/\mu$ L
Polymorph	64%	40–75%
Lymphocytes	22%	20–45%
Monocytes	9%	2–10%
Eosinophils	5%	1–6%
Basophils	0%	0–2%
Platelet count	374 thou/ μ L	140–400 thou/ μ L
Prothrombin time	21.7 s	12.2–15.1 s
INR	1.56 s	0.80–1.20 s
PTT (clot based assay)	50.3	30.11–40.55
DRVV screen test (clot based assay)	57.40	32.82–48.90
DRVV screen control (clot based assay)	36.30	32.82–48.90
DRVV screen ratio	1.58	0.82–1.22
DRVV confirmatory test (clot based assay)	41.20	27.89–34.55
DRVV confirmatory control (clot based assay)	32.20	27.89–34.55
DRVV confirm ratio (clot based assay)	1.28	0.93–1.17
Lupus anticoagulant (clot based assay)	Present	Absent
Anti-phospholipid IgG Ab (enzyme immunoassay)	6.57 U/mL	< 12
Anti-phospholipid IgM Ab (enzyme immunoassay)	3.59 U/mL	< 12
Anti- β_2 glycoprotein 1 IgG Ab (enzyme immunoassay)	24.61 RU/mL	< 20 (negative), $\geq$ 20 (positive)
Anti- β_2 glycoprotein 1 IgM Ab (Enzyme immunoassay)	17.86 RU/mL	< 20 (negative), $\geq$ 20 (positive)
Protein C activity (clot based assay)	74%	67–195
Protein S activity (clot based assay)	56%	55–123
ANA-IF Hep2	Antibodies against golgi bodies (1 +), 1:80 endpoint titre	Absent
Vitamin B12 (chemiluminescence immunoassay)	200 pg/mL	211–911 pg/mL
Folic acid (chemiluminescence immunoassay)	4.71 ng/mL	> 5.38 ng/mL
Homocysteine (chemiluminescence immunoassay)	18.38 μ mol/L	< 12 μ mol/L with folate supplementation < 15 μ mol/L without folate supplementation

lupus anticoagulant, performed by a clot based assay and anti- β_2 glycoprotein1 IgG by enzyme immunoassay were suggestive of APS. However, the antiphospholipid Ab, protein C and protein S were all within normal limits. Antinuclear antibody (ANA) using HEp-2010/Liver (monkey) biochip (EURO IMMUNE AG) detected by

indirect immunofluorescence with an endpoint titre of 1:80 was positive for antibodies for golgi bodies which was noted in cytoplasm that are clustered on one side of the nucleus (Fig. 1), with an intensity of 1 +. Further confirmatory test done for ANA by immunoblot assay which was also positive for antibodies for golgi bodies.

Fig. 1 Autoantibodies against Golgi bodies (HEP-2 cell line)

Ultrasonography of abdomen showed portal vein thrombosis and mild ascites. CECT abdomen gave an interpretation suggestive of thrombus involving the portal vein, splenic vein and superior mesenteric vein. Few collateral vessels were seen adjacent to the portal vein in porta hepatic region. Hepatic artery and vein were normal, with no focal lesion in liver. Free fluid was seen in perihepatic region, hepatorenal pouch, bilateral paracolic gutters and in pelvis. Rest of abdominal organs were normal.

Based on the above findings, a diagnosis of portal vein thrombosis and mesenteric vein thrombosis with antiphospholipid syndrome was made on this documented case. She was treated with antibiotics, analgesics and low molecular weight heparin twice daily and kept on a vitamin K restricted diet. The patient stabilised and was discharged with acenocoumarol and advice of Vitamin K restricted diet, Vit B12 and folate supplementation and to visit the hospital at the end of 3 months. She was also advised for routine PT/INR assay. Later when the patient visited the hospital the lupus anticoagulant activity and anti- β_2 glycoprotein1 were still high, but vitamin B12 and folate had reached values within normal limits.

Discussion

The autoimmune nature of APS has always been observed by the presence of antiphospholipid antibodies. Our patient had no history of recurrent miscarriages, no history of drug use or any other autoimmune disease but the abdominal pain was identified to be portal vein thrombosis. Gastrointestinal involvement is an unusual clinical manifestation of APS. Systemic arterial and venous thrombosis are typical features of APS, however portal vein thrombosis is rare [1], still rarer is the mesenteric and splenic vein

thrombosis [2]. CECT abdomen commented on the presence of collateral vessels adjacent to the portal vein thereby protecting the vital organs resulting in a normal liver function test.

Anticardiolipin antibodies IgG type has been suggested to be a risk factor for thrombosis [3, 4], but it was within normal limits in our patient. However, the presence of prolonged aPTT, lupus anticoagulant and a dilute Russell viper venom time and antibodies to anti- β_2 glycoprotein1—IgG helped in the diagnosis. One of the other antibodies which was identified was the presence of antinuclear antibodies (ANA HEP-2). There are few studies showing the presence of ANA, the predominant pattern when positive being nuclear homogenous followed by speckled [5]. Our patient had antibodies against golgi bodies, in cytoplasm that are clustered on one side of the nucleus. This unusual staining pattern is generally seen in patients with systemic rheumatic disease like Sjogren's syndrome, SLE. None of the antibodies were positive for anti-ANA antibodies. Patients with ANA Hep-2 positive are also more likely to develop SLE in the future, in some cases after 6 years [6, 7]. This patient is on follow up and for the last one year after her admission she is asymptomatic without any evidence of SLE or other connective tissue disease.

Carvalho et al. [5], has also shown that patients who are positive with ANA Hep-2 may have a higher frequency of deep vein thrombosis. Our patient had no history of miscarriages, rather with three living children, with last child born being 13 years. Even in the absence of the above history the development of thrombosis points towards positivity to antinuclear antibodies. Antiphospholipid antibodies bind to the cell wall of endothelial intimal layer in a restricted manner and activate endothelial cells, monocytes and platelets. This is followed by increased expression of certain adhesion molecules on endothelial cells and tissue factor upregulation. The release of thromboxane A2 altering the prostacyclin-thromboxane balance favour thrombosis. Further, fibrinolysis is impaired by interfering with thrombomodulin-protein C-protein S pathway [8]. The antinuclear antibodies bind to the intimal layer causing its damage and also affect its functionality by binding to intracellular structures like nucleus and cytoplasm [9]. Thus, its ability to promote thrombotic changes is more direct.

Homocysteine, formed during methionine metabolism has also been associated with prothrombotic activity and could be responsible for thromboembolic effect [10]. This case had a raised homocysteine, associated with low folate and vitamin B12. However, after dietary supplementation her folate and vitamin B12 returned to normal. Carvalho et al. [11], have showed that a certain proportion of patients with primary antiphospholipid syndrome can have elevated

serum levels of homocysteine. A recent study in SLE has also highlighted that patients with antiphospholipid antibodies with high homocysteine levels is associated with higher vascular events like deep vein thrombosis [12].

In conclusion, a clinician needs to be aware of the fact that antinuclear antibodies can serve as a marker for thrombosis for antiphospholipid syndrome even in the absence of characteristic clinical findings and in individuals with unusual presentations.

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