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A CASE OF ANTI PHOSPHOLIPID SYNDROME

General Medicine

Dr. Raghuramulu Ananthoju* Associate Professor, Department of General Medicine, SVS Medical College , Mahabubnagar, Telangana, India *Corresponding Author

Dr. A. RojaRani Resident,General Medicine, SVS Medical College, Mahabubnagar, Telangana, India

Dr. Baddireddy Sai Jahnavi Resident,General Medicine, SVS Medical College, Mahabubnagar, Telangana, India

Dr. Sohail Ahmed Khan Resident,General Medicine, SVS Medical College, Mahabubnagar, Telangana, India

ABSTRACT

Anti phospholipid syndrome (APS)is an autoantibody mediated acquired thrombophilia charecterized by recurrent arterial or venous thrombosis and /or pregnancy morbidity. APS may occur alone (Primary) or (secondary) in association with other autoimmune diseases mainly systemic lupus erythematoses (SLE).the major autoantibodies detected are against the negatively charged phospho lipids and/ or Beta 2 GP1, cardiolipin, lupus anticoagulant and pro thrombin. We are reporting one young woman with digital gangrene, arthritis, livedoid rash, and history of early pregnancy loss. Based on history and clinical examination we suspected this as a case of autoimmune disease and subjected her for further investigations. The subsequent investigations showed Positive some auto antibodies (anti ds DNA, sm-B, RNP-A, RNP-C and anti Histone) which were suggestive of patient had Systemic Lupus Erythematosis(SLE).

KEYWORDS

INTRODUCTION

Anti phospholipid syndrome (APS) is an auto immune disease characterized by vascular (arterial and /or venous)thrombosis and/or pregnancy morbidity in the presence of anti phospholipid antibodies. APS occurs alone or in association with other auto immune diseases, particularly systemic lupus erythamatoses (SLE). APS criteria requires evidence of persistently abnormal test results (over at least 12 weeks)by solid phase assays {anti cardiolipin (aCL) IgG/IgM, anti-beta2 GP1 IgG/IgM}, or by the lupus anticoagulant functional assay. Phospho lipids are present on the surface of cell membranes. Antiphospholipid antibodies (aPL) are heterogeneous group of autoantibodies that activate endothelial cells, platelets, and neutrophils via interactions with cell-associated phospholipids and phospholipid-binding proteins such as beta-2-glycoprotein I (β2GPI) and prothrombin.[2]In patients with APS ,arterial occlusions leading to stroke and Myocardial infarction are the most common causes of morbidity and mortality.

The exact prevalance of APS is unknown. However, a female predominance is described. About 30% with lupus anti coagulant and 30-50% of patients with moderate to high titers of anticardiolipin antibodies have clinical manifestations of APS. In indian setting, a prevalence of 27.7% has been reported in 155 females with recurrent miscarriages or late pregnancy loss from kolkatta and 40% from tamilnadu[8].The estimated incidence and prevalence among most of the population based studies ranged between 1-2 cases per 1,00,000 and 40-50 cases per 1,00,000 respectively. The prevalence of Anti phospholipid Antibodies in patients with obstretic morbidity was 6-9%, while in arterial and venous thromboembolism is 9-10 %. Mortality of patients with APS is 50-80% higher than general population[7].In a multicenter study, 53.1% of patients had primary APS, while 36.2% had SLE with secondary APS. The most frequently presenting manifestations of APS are deep vein thrombosis (31.7% of patients), thrombocytopenia (21.9%), livedo reticularis (20.4%), and stroke (13.1%). Less frequent manifestations include superficial thrombophlebitis (9.1%), pulmonary embolism (9%), transient ischemic attacks (7%), and hemolytic anemia (6.6%). Fetal loss is the presenting manifestation in 14% of female patients[3].

Here we are reporting a case of young woman who presented with digital gangrene, arthritis and with a h/o early pregnancy losses.

CASE DESCRIPTION

A 25 year old woman, presented with complaints of pain in both knees and shoulder joints since 10 days, insidious in onset, progressive in nature associated with restriction of movements in shoulder and knee. She also had pain and discoloration of all her toes in right foot and 2nd ,3rd, 4th toes in the left foot, insidious in onset and progressive. She had no history of fever, pain abdomen, chest pain, palpitations, shortness of breath, leg cramps. No recent history of bedridden state. She had no history of decreased urine output.

There is a past history of fever with rash 3 months ago associated with itching all over the body, which healed by leaving hypo pigmented multiple minute, circular macules, for which she took treatment from local rural medical practitioner (RMP) who advised Tab. Hydraxizine Hydrochloride 10mg once daily, Tab. Itraconazole 200mg twice daily, Tab. Ciprofloxacin 500mg twice daily for 3 months. She went to the same RMP for her recent joint pains, who added Tab. Hydroxychloroquine 200mg twice daily and Tab. Methotrexate 15mg once daily, Tab. Prednisolone 8mgonce daily, Tab. Caripill 1100mg twice daily (Platelet count of 1.3 lakk/microlitre) a week ago.

She is married 5 years ago. She had a bad obstetric history with 2 early/first trimester abortions. First abortion occurred in third month of gestational age(4 years ago), second abortion in second month of gestational age(2 years ago). She has no history of similar complains in her family. Patient is not a known case of hypertension, diabetes mellitus, asthma, epilepsy, Coronary artery disease, Cerebro vascular attack, Thyroid disorders.

On Examination

On examination, she had multiple hypo pigmented small, circular macules(3-4mm diameter)over both upper limbs, lower limbs and back. There is complete black discoloration of the right fifth toe (gangrene), reddish to black discoloration of 1 to 4 toes of right foot and 2nd, 3rd , 4th toes of left foot.

VITALS:

PARAMETERS	ON PRESENTATION TO EMERGENCY
Temperature	98.6^F
Pulse(per minute)	112bpm
Blood Pressure	120/80mmHg
Oxygen Saturation	99%@RA

Cardio Vascular System

Apex impulse is felt in left fifth intercoastal space 1cm medial to mid clavicular line.
JVP raised, loud P2 is present

Respiratory System

Bilateral normal vesicular breath sounds heard all over the lung fields.

Investigations

The Routine investigations showed raised Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP). Based up on history and clinical examination we suspected this as a case of autoimmune disease and further investigations were conducted .They showed positive for lupus anticoagulant antibodies and few auto anti bodies (ds DNA, sm-B, RNP-A, RNP-C and anti Histone) related to Systemic Lupus Erythematosis(SLE) were positive.

Hemogram:

PARAMETER	OBSERVED VALUE	REFERENCE VALUE
HAEMOGLOBIN	10.9g/dl	12.0 - 16.0 g/dL
RBC	4.6million/cumm	4.2-5.4 million/cumm
WBC	8,900cells/cumm	4000-11000 million/cumm
PCV/HCT	35.2%	33-51%
MCV	75.7fL	80-100fL
MCH	23.4pg	27-31 pg
MCHC	31.0g/dl	32-36 g/dL
PLATELET COUNT	1.9lakhs/cumm	1.5 - 4.0 lakhs/cumm
DIFFERENTIAL COUNT		
Neutrophils	75%	34-64
Lymphocytes	15%	25-45
Eosinophils	02%	1-6
Monocytes	08%	3-6
Basophils	00%	0-1
BLOOD GROUPING AND Rh TYPING	'B' POSITIVE	

Complete Urine Examination:

PARAMETER	OBSERVED VALUE
PHYSICAL EXAMINATION	
Volume	15mL
Colour	Yellow
Appearance	Slightly turbid
Reaction(pH)	5.5
Specific gravity	1.025
CHEMICAL EXAMINATION	
Protein	Trace
Glucose	NIL
MICROSCOPIC EXAMINATION	
Pus cells	1-2/hpf
Epithelial cells	4-5/hpf
RBC cells	NIL
Casts	NIL
Crystals	NIL
Others	NIL

Serum Electrolytes:

PARAMETER	OBSERVED VALUE	REFERENCE VALUE
Na	144 mEq/l	136-145 mEq/L
K	4.5 mEq/L	3.5-5.1 mEq/L
Cl	104 mEq/L	98-107 mEq/L
Ca	1.17 mmol/l	1.16-1.32 mmol/L

Liver Function Tests:

PARAMETER	RESULT	REFERENCE VALUE
TOTAL BILIRUBIN	0.5mg/dL	0.3-1.2 mg/dL
DIRECT BILIRUBIN	0.1mg/dL	0.0-0.3 mg/dL
ALKALINE PHOSPHATASE	79 U/L	30-120 U/L
ALANINE TRANSAMINASE	53 IU/L	<35 IU/L
ASPARTATE TRANSAMINASE	70 IU/L	<35 IU/L
TOTAL PROTEIN	8.1 g/dL	6.6-8.3 g/dL
ALBUMIN	3.8g/dL	3.5-5.2 g/dL
GLOBULIN	4.3g/dL	2.3-3.6 g/dL

Renal Function Tests:

PARAMETER	OBSERVED VALUE	REFERENCE VALUE
BLOOD UREA	20mg/dL	17-43 mg/dL
SERUM CREATININE	0.5mg/dL	0.6-1.1 mg/dL

Coagulation Profile

PARAMETER	OBSERVED VALUE	REFERENCE VALUE
PT	13.9 sec	13.5 sec
APTT	72.8 sec	22-35 sec
INR	1.10	1.1-1.2
D-dimer	983ng/mL	220-740 ng/mL

Acute Phase Reactants:

PARAMETER	OBSERVED VALUE	REFERENCE VALUE
ESR	145mm/hr	0.0 - 20.0 mm/hr
CRP	43mg/L	0.3-1.0 mg/dL
ASO	NEGATIVE	
RA FACTOR	NEGATIVE	

Microbiology:

1. Specimen: Blood for Malaria antigen detection (Qualitative)
   Report: Negative
2. Test: Blood for Dengue NS1 antigen and IgM & IgG antibodies
   Result:
   Dengue NS1 antigen : Negative
   Dengue IgM antibody :Negative
   Dengue IgG antibody :Negative
3. Blood for RDT /VDRL - Negative

Anti Phospholipid Antibodies

1. Lupus Anticoagulant(confirmatory) Tests

Mixing studies:		
PTT- LA Mix	Result	Interpretation
Patient plasma with PNP(1:1)	64.6 Sec	Not corrected (Positive)
DRVVT Screen Mix	Result	Interpretation
Patient plasma with PNP(1:1)	55.7 Sec	Not corrected (Positive)
DRVVT Confirm Test:		
DRVVT CONFIRM	Result	
Patient plasma	33.8 sec	
Pooled Normal Plasma(PNP)	33.7 sec	
Confirm Ratio	1.00	
Normalised Ratio	1.95	
Interpretation	POSITIVE FOR LUPUS ANTI COAGULANT	

2.Anti cardiolipin(phospholipid) IgG+IgM ELISA	Anticardiolipin antibodies(IgG)-Negative (4 GPL Units)	<15 GPL Units - Negative
	Anticardiolipin antibodies(IgM)-Negative (14MPL Units)	<15 MPL Units - Negative
3.Beta 2 Glycoprotein IgG + IgM ELISA	Anti Beta 2 Glycoprotein 1 antibodies(IgG)-Negative(1U/mL)	<7U/mL - Negative
	Anti Beta 2 Glycoprotein 1 antibodies(IgM)-Negative(3U/mL)	<7U/mL - Negative

Ana Profile:

Band order	Band name	Position (mm)	Intensity (%)	Evaluation	Antibodies found against
1	IgG Control	-3.73			
2	Jo-1	2.96	1.50	Negative	
3	PL-7	5.16	1.50	Negative	
4	PL-12	7.11	2.47	Negative	
5	PmScl	8.89	1.98	Negative	
6	CENP-A	12.53	1.50	Negative	
7	CENP-B	13.89	0.00	Negative	
8	Scl-70	16.43	1.99	Negative	
9	Ro52	19.30	1.99	Negative	
10	Ro60	21.34	5.87	Negative	

11	La	23.28	3.93	Negative	
12	RNP-A	25.40	51.51	positive	U1-RNP antigen
13	RNP-C	28.36	36.29	Positive	U1-RNP antigen
14	RNP-68	30.31	3.93	Negative	
15	SmB	32.26	29.53	Positive	Sm antigen
16	SmD	34.29	2.97	Negative	
17	P0	37.25	1.00	Negative	
18	PCNA	39.37	1.00	Negative	
19	dsDNA	41.32	10.53	Positive	
20	Histone	43.26	12.41	Positive	Histone
21	Nucleosom	46.40	1.99	Negative	
22	DFS70	48.85	0.50	Negative	
23	M2	51.90	0.00	Negative	
ANA	Positive				
Possible association with: SLE,MCTD SLE drug-induced SLE					

Complement C3/c4:

TEST NAME	OBSERVED VALUE	BIOLOGICAL REF. RANGE
Complement C3	1.04g/L	0.9-1.8g/L
Complement C4	0.21g/L	0.1 - 0.4g/L

Torch Profile-23/03/2021 (Done following miscarriages):

TEST NAME	RESULT
Anti Toxoplasma-IgG Antibodies	Non Reactive
Anti Toxoplasma IgM Antibodies	Non Reactive
Anti Rubella IgG Antibodies	REACTIVE
Anti Rubella IgM Antibodies	Non Reactive
Anti CMV IgG Antibodies	REACTIVE
Anti CMV IgM Antibodies	Negative
Anti HSV I IgG Antibodies	Negative
Anti HSV I IgM Antibodies	Negative
Anti HSV II IgG Antibodies	Negative
Anti HSV II IgM Antibodies	Negative

2D ECHO -

- Grossly dilated RA/RV
- Severe TR/Severe PAH
- No LV RWMA
- No MS/MR/AS/AR
- Good Biventricular function
- No Pericardial effusion/ clots/ vegetations

Suggestive of severe pulmonary arterial hypertension

Doppler Study:
Arterial Doppler -(both lower limbs)-NORMAL STUDY
Venous Doppler -(both lower limbs)-BILATERAL MILD SAPHENO FEMORAL JUNCTION INCOMPETENCE

Viral Markers:
Specimen: Blood (Qualitative detection)
HV1&2 antibody: Negative
HCV antibody: Negative
HBsAg: Negative

Biochemistry:

PARAMETER	OBSERVED VALUE	REFERENCE VALUE
Spot urine protein	82.4 mg/dL	5-24 mg/dL
Spot urine creatnine	112.5 mg/dL	20-275 mg/dL
Spot urine protein creatnine ratio	0.7	<0.2

Thyroid Profile:

PARAMETER	OBSERVED VALUE	REFERENCE VALUE
T3	0.86 ng/mL	0.7-2.04 ng/mL
T4	17.71 ug/dL	5.5-11.0 ug/dL
TSH	5.01 uIU/mL	0.4-4.2 uIU/mL

USG Abdomen Impression
Likely focal fatty infiltration in segment IV of Liver

Livedoid Rash

Hypo Pigmented Macules

Digital Gangrene

DISCUSSION

TABLE 357-2 Clinical Features of Antiphospholipid Syndrome

MANIFESTATION	%
Venous Thrombosis and Related Consequences	
Deep-vein thrombosis	39
Livedo reticularis	24
Pulmonary embolism	14
Superficial thrombophlebitis	12
Thrombosis in various other sites	11
Arterial Thrombosis and Related Consequences	
Stroke	20
Cardiac valve thickening/dysfunction and/or Libman-Sacks vegetations	14
Transient ischemic attack	11
Myocardial ischemia (infarction or angina) and coronary bypass graft thrombosis	10
Leg ulcers and/or digital gangrene	9
Arterial thrombosis in the extremities	7
Retinal artery thrombosis/amaurosis fugax	7
Ischemia of visceral organs or avascular necrosis of bone	6
Multi-infarct dementia	3
Neurologic Manifestations of Uncertain Etiology	
Migraine	20
Epilepsy	7
Chorea	1
Cerebellar ataxia	1
Transverse myelopathy	0.5
Renal Manifestations Due to Various Reasons (Renal Artery/Renal Vein/Glomerular Thrombosis, Fibrous Intima Hyperplasia)	3
Musculoskeletal Manifestations	
Arthralgias	39
Arthritis	27
Obstetric Manifestations (Referred to the Number of Pregnancies)	
Preeclampsia	10
Eclampsia	4
Fetal Manifestations (Referred to the Number of Pregnancies)	
Early fetal loss (<10 weeks)	35
Late fetal loss (≥10 weeks)	17
Premature birth among the live births	11
Hematologic Manifestations	
Thrombocytopenia	30
Autoimmune hemolytic anemia	10

Features Of Our Patient That Match With The Criteria

Clinical Findings

- LIVEDOID RASH
- DIGITAL GANGRENE
- EARLY FETAL LOSS
- ARTHRITIS
- PULMONARY HYPERTENSION

Laboratory Findings

- RNP-C -Positive
- Sm-B -Positive
- dsDNA - Positive RNP-A -Positive
- Histone - Positive
- Lupus anti coagulant - Positive

Our intention of publishing this case is to appraise the medical fraternity that APS is not an unknown entity in our area.

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