Primary antiphospholipid syndrome with multiple organ involvement: case report

Kuria MA[1], Oyoo GO[1,2], Namasaka P[1], Akunga O[1]

[1]Department of Internal Medicine, Mater Misericordiae Hospital, Nairobi, Kenya
[2]Department of Clinical Medicine and Therapeutics, School of Medicine, College of Health Sciences, University of Nairobi, P. O. Box 19676-00202, Nairobi, Kenya

Corresponding author:
Dr. Anne M. Kuria, Department of Internal Medicine, Mater Misericordiae Hospital, Nairobi, Kenya.
Email: kuriaannemukami@gmail.com

Abstract

Antiphospholipid syndrome is a systemic autoimmune disease, characterized by the occurrence of venous and arterial thrombosis, and the detection of circulating antiphospholipid antibodies. Thrombosis mainly affect the deep veins and cerebral circulation, but can also occur in other sites such as visceral arteries, cerebral venous sinuses, and micro vessels in the lungs, heart and eyes. This is a case of a 32 year old African male with AntiPhospholipid Syndrome (APS) presenting with multiple organ involvement-left central retinal artery occlusion, right MCA infarct, superior mesenteric artery thrombosis with multiple splenic infarcts, and severe aortic regurgitation with heart failure.

Key words: Antiphospholipid syndrome, Superior mesenteric artery thrombosis, Anticoagulation, Middle cerebral artery infarct, Aortic regurgitation

Introduction

Antiphospholipid antibody syndrome (APLA) is a complex disease entity, rarely seen in day to day clinical practice. APS can be primary or secondary. Primary APS will occur in absence of other diseases, whereas secondary APS occurs with other autoimmune diseases such as Systemic Lupus Erythematosus (SLE).

Antiphospholipid antibodies are heterogenous antibodies acting on specific phospholipids-binding proteins. Antibodies against β2-glycoprotein-1(aβ2GP1), cardiolipin (aCL), together with the functional assay lupus anticoagulant (LAC) done at-least 12 weeks apart, are the three laboratory tests considered in the revised criteria for diagnosis. The authors hereby present a 32 year old male with multiple microvascular and large-vessel thrombotic events that led to multiple-organ involvement.

Case report

Our patient was a 32 year old male who had been on follow-up for spontaneous left central artery occlusion for the past 3 months in a different facility. He presented to us with a 3-day history of sudden onset left sided weakness, which was worse in the upper limb compared to the lower limb on the same side. He had a preceding severe generalized headache, throbbing, minimally relieved by analgesia, not affected by position, no nausea, vomiting, visual or disturbances or changes in level of consciousness. He was a lifetime non-smoker and non-alcohol user. His family history was negative for cardiovascular and autoimmune disease.

Physical exam

Vital signs: GCS 15/15, BP 119/45mmhg, HR 92 beats/min, regular, Sp02 96% on room air, RR 18 breaths/min,Temp 36.5° Celcius.

Neurological exam: Revealed left upper motor neuron facial nerve palsy, reduced muscle power on the left side, 3/5 in the upper limb flexors and extensors, 4/5 in the lower limb flexors and extensor. NIHSS score was 8/31

Cardiovascular exam: Significant for a dilated apex beat in the 7th intercoastal area, mid-clavicular line, and a grade 3/6 early diastolic murmur at the left sternal boarder, 4th intercostal space.

Ophthalmology assessment: Revealed left macula atrophy.

Abdominal exam: Negative for ascites, hepatomegaly or splenomegaly.

Respiratory exam: Revealed fine bilateral crepitations.

Initial investigations

Table 1: Laboratory investigations

MRI/MRA/MRV	Filling defect in the M1 segment of the right MCA
2D ECHO	Dilated cardiomyopathy with LVH, severe aortic regurgitation, mild aortic stenosis, No clots visualized
HIV/HBV/HCV	Negative
VDRL	Negative
p-ANCA	Negative
c-ANCA	Negative
Autoimmune screen	Negative
Anti-prothrombin igM antibody (100units)	High
Cardiolipin igM	94MPL U/mL(<41MPL U/mL (sample collected on 4/11/22)
C3/C4	Normal
CBC/UECs/LFTs,TFTs	Normal

Initial management

He was admitted for cardiac and neuro-monitoring. Initial treatment included; double antiplatelet (Aspirin 75mg OD, Clopidogrel 75mg OD), high dose statin (Artovastatin 80mg OD), prophylaxis enoxaparin 40mg subcut OD and solumedrol 125mg IV OD for 5 days. Heart failure regimen included eplerenone 25mg OD and bisoprolol 2.5mg OD, sacubitril-valsartan. He was also started on both physical and occupational therapy as part of stroke rehabilitation.

Progress

He did well in the ward and regained full neurological functions. He was discharged on the 7th day of admission on; Hydroxychloroquine 200mg BD, eplerenone 25mg PO OD, clopidogrel 75mg PO and bisoprolol 2.5mg OD. He was scheduled for repeat thrombophilia as an outpatient and elective aortic valve replacement.

Readmission

He presented 2 months later with 2 day history of sudden onset severe, left upper quadrant pains, persistent, pain-score 10/10 and not relieved by oral paracetamol. Pain was not positional and not affected by feeding. He had normal bowel movements and no vomiting episodes.

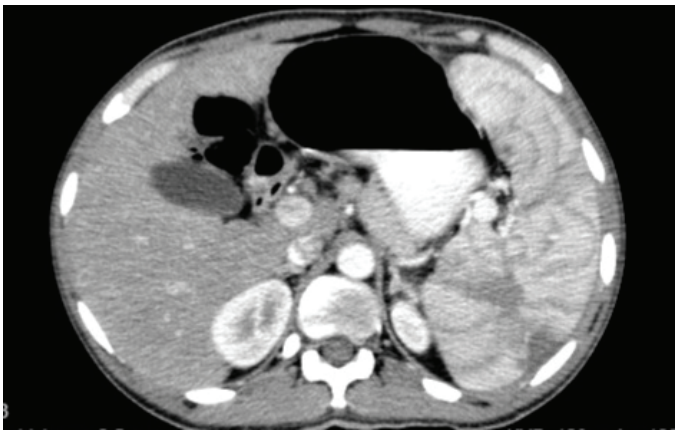
Examination

Vital signs: Within normal range except for a sinus tachycardia of 110 beats/min.

Abdominal exam: Revealed left upper quadrant tenderness on deep palpation. There were no palpable masses. Respiratory and neurological exams were unremarkable.

Investigations: CT scan abdomen done-revealed a 6.2cmx0.4cmx0.9cm intra-mural, hypodense non occlusive thrombus within the superior mesenteric artery. Enlarged spleen (15cm) with multiple splenic infarcts. Right renal cortical infarct. Small and large bowel were intact.

Figure 1: Abdominal CT scan



Management

Initial management included pain control with IV analgesics and initiation of treatment dose enoxaparin 80mg sub cut BD. He was allowed oral feeds as tolerated, but with close monitoring for any symptoms/signs of gut necrosis. He was then transitioned to warfarin on day 4 of admission with a target INR of 2.5 to 3.5. He did well, and did not require surgery. Repeat CT scan prior to discharge showed resolving thrombosis, with no new organ infarcts. He was discharged on: Warfarin 5mg OD, clopidogrel 75mg OD, hydroxychloroquine 200mg OD, aldactone 25mg OD, bisoprolol 2.5mg OD and empagliflozin 10mg OD. Repeat thrombophilia screen is shown in Table 2.

Re-admission

The patient was then re-admitted for the 3rd time 3-months after discharge, in acute decompensated heart failure, acute kidney injury with severe metabolic acidosis requiring intubation and emergency dialysis. Two days after admission, he went into cardiac arrest, and resuscitation was unsuccessful.

Table 2: Lupus anticoagulant mixing studies

Test	Results	Normal range
APTT	47.7sec	28.8-33.8s
PT	24.2 sec	11.9-14.4s
Lupus anticoagulant screen		
dRVVT	56.2sec	(31-44)sec
VV ratio	1.45	<1.20
dRVVT neutralisation	Confirmed	
Repeat anticardiolipin IgM 102MPL		<41MPL
Sample collected on 7/02/23	102MPL U/mL	U/mL

Table 3: Clinical classification criteria of APS (revised Sapporo APS criteria)-must meet atleast one of the following:

Vascular thrombosis	One or more clinical episode of arterial venous or small-vessel thrombosis in any tissue or organ, confirmed by objective validated criteria
Pregnancy morbidity	One or more premature death of a fetus beyond 10th week of gestation OR One or more premature deaths before 34th week due to severe pre-eclampsia/placental insufficiency OR Three unexplained consecutive spontaneous miscarriages before week 10

Discussion

Anti-phospholipid syndrome (APS) is a prothrombotic clinical state with multi-organ involvement. Its found in 30% of all systemic lupus cases, but primary anti-phospholipid can occur in the absence of autoimmune disease[1,2]

Revised Sapparo Laboratory criteria- must meet one of the following :

(i) Lupus anticoagulant present on two or more occasions at-least 12 weeks apart
(ii) Anticardiolipin antibodies (IgM/IgG) present in medium or high titres (>40GPL or 99th percentile) on two or more occasions at -least 12 weeks apart.
(iii) Anti-B2 glycoprotein-1 antibody (IgG or IgM) present in titer>99th percentile on two or more occasion at least 12 weeks apart 1

Valvular manifestations of APS most include valvular thickening >3mm, and irregular nodules on the atria area of the mitral valve, or the vascular side of the atrial valve[3]. Libman-sack endocarditis is also a common finding. Mitral valve is commonly affected, usually followed by aortic valve. Deposits of immunoglobulins including anticardiolipina commonly observed of valves of these patients[3]. Patients with valvular lesions, especially aortic nodules are predisposed to cardio-embolic strokes. They can also develop acute coronary syndrome secondary to coronary thrombo-embolism, accelerated artherosclerosis of the coronary arteries,and microvascular injury[3].

Acute superior mesenteric ischemia is a rare but life-threatening event in the setting of antiphospholipid syndrome. Venous thrombosis usually leads to venous congestion, increased intravascular pressure within the mesenteric circulation, and fluid leakage into the surrounding tissue with eventual bowel wall oedema and mucosal haemorrhage[4]. This can eventually cause bowel infarction, necrosis and sepsis unless promptly treated. Treatment would involve bowel rest, adequate intravenous fluids, analgesia and prompt anticoagulation to prevent propagation of the thrombus and allow recanalization of the affected circulation, as was done in our patient[5]

Treatment recommendation

(i) Patient with definite APS and a venous thrombotic event should be treated with warfarin therapy indefinitely, with a target INR of 2-3.
(ii) Patient with definite APS and arterial thrombosis and/or recurrent events should be treated with indefinite warfarin, target INR of 2-3, plus low dose asprin.
(iii) Patient with venous thromboembolism, or arterial thrombosis and a singly positive aPL detection not confirmed by confirmatory tests, should be treated similar to general population[6].

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Consent to publish the study: This was obtained from the Ethics Committee, Mater Misericordiae Hospital, Nairobi, Kenya

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