Journal of Medicine and Medical Specialities
Volume 1, Issue 3, September 2025; pp: 172-176
eISSN: 2455-2879 DOI: 10.65129/medical.v1i3.128

CASE SERIES

A Case Series of Antiphospholipid Antibody Syndrome

Ajith Kumar M.*, Geetha T. and Siva Kumar K.

Department of General Medicine, Coimbatore Medical College Hospital, Coimbatore - 641018, Tamil Nadu, India; ajithmuthuvel@gmail.com, Geethathirumal@hotmail.com

Abstract

Antiphospholipid Antibody Syndrome (APS) is an autoimmune thrombotic condition with recurrent arterial or venous thrombosis and pregnancy morbidity, due to the chronic presence of Antiphospholipid antibodies (aPL) like Lupus Anticoagulant, Anticardiolipin and Anti-β2 Glycoprotein I Antibodies. It may present as a primary syndrome or secondary to autoimmune illnesses, with the most frequent being systemic lupus erythematosus(SLE). The incidence of aPL antibodies in the general population is about 1–5%, but actual clinical APS is uncommon. There is an estimated incidence of 40–50 per 100,000 people, primarily occurring in females (F:M ratio 5:1). In SLE patients, 20–40% of them have aPL antibodies but only 10–15% manifest with clinical APS. APS is responsible for up to 20% of deep vein thromboses, 30% of strokes in young adults and 10–15% of recurrent pregnancy loss. In recurrent pregnancy loss or unexplained fetal loss, 5–15% of women have a positive test for aPL antibodies. In a rare but disabling form, Catastrophic APS (CAPS) is characterized by progressive multiorgan thrombosis and very high mortality (<1% of patients with APS).

Keywords: Antiphospholipid Antibody Syndrome, Thrombus, Catastrophic Antiphospholipid Antibody syndrome, Lupus Anticoagulant, Anti Cardiolipin Antibody. Anti-β2 Glycoprotein I Antibody

1. Introduction

APS is an important, under-recognized cause of both arterial and venous thromboembolism in young patients and a leading treatable cause of recurrent pregnancy loss. There is significant morbidity and mortality due to stroke, Deep vein thrombosis (DVT), Pulmonary Embolism (PE) and obstetric complications such as preeclampsia, intrauterine growth restriction and fetal loss. Hence, clinical suspicion and early diagnosis are crucial.

2. Aims and Objectives

- To highlight the different manifestations and complications of APS.
- To diagnose at earlier stage and provide appropriate treatment and prevent further complications.

3. Review of Literature

3.1 Historical Background of APS

The history of Antiphospholipid Antibody Syndrome (APS) dates back to 1906, when the Wassermann test was established as a diagnostic test for syphilis. The test detected the presence of antibodies against cardiolipin, a phospholipid constituent. Curiously, however, some asymptomatic patients on this assay were found to be positive — a reaction that later was recognized to be the result of anticardiolipin antibodies. Later in the 1950s patients with systemic lupus erythematosus were noted

*Author for correspondence

Article Received on: 05-May-2025 Revised on: 30-June-2025 Accepted on: 01-August-2025

to have an elevated activated Partial Thromboplastin Time (aPTT), which was not correctable by mixing studies. These patients, in spite of their prolonged clotting time, were surprisingly at risk for thrombotic complications instead of bleeding. This resulted in the discovery and the designation of the term "Lupus Anticoagulant," but it was soon realized that most patients presenting with this phenomenon were not suffering from Lupus.

It was in the 1980s that British rheumatologist Dr. Graham R.V. Hughes gave a detailed clinical account of a syndrome involving arterial and venous thrombosis, recurrent abortion, and thrombocytopenia and its association with antiphospholipid antibodies. He formally termed the condition Antiphospholipid Antibody Syndrome (APS), later also referred to as Hughes Syndrome in honor of his work. His research identified APS as a specific autoimmune prothrombotic condition, on which the present-day diagnostic and treatment methods are based[1,4,5].

3.2 Pathogenesis of APS

The main mechanism in Antiphospholipid Antibody Syndrome (APS) includes the generation of pathogenic antiphospholipid antibodies (aPL), mainly Anti-β2 Glycoprotein I (anti-β2GPI), Anticardiolipin (aCL) antibodies and Lupus Anticoagulant (LA). These are not directed against phospholipids per se but against phospholipid-binding proteins, particularly β2 glycoprotein I. Upon formation, these antibodies bind to β2GPI on the surface of endothelial cells, platelets, and monocytes. This interaction results in endothelial cell activation, upregulation of adhesion molecules such as VCAM-1 and ICAM-1, platelet aggregation, and activation of monocytes with augmented tissue factor expression — all tending toward a procoagulant state[1-3].

Aside from facilitating coagulation, aPL antibodies are also responsible for activating the classical pathway of complement, particularly the production of C5a, a potent inflammatory molecule. This complement activation attracts neutrophils and leads to further damage to the endothelium and thrombosis. This pathway is especially significant in obstetric APS, where it results in placental infarction and miscarriage[1,2].

APS antibodies interfere with natural anticoagulant mechanisms. They interfere with Annexin V (which functions as a natural anticoagulant barrier), the protein C–protein S system, and Tissue Factor Pathway Inhibitor (TFPI), thus inhibiting fibrinolysis and promoting the potential for clot formation. The "two-hit hypothesis" is generally believed in APS pathogenesis: the first hit consists in the occurrence of aPL antibodies that make the environment prone to thrombosis, and the second hit is an exogenous trigger such as infection, surgery, immobilization, and hormonal changes, which ultimately trigger the clot formation[1,3].

In obstetric APS, these antibodies induce placental injury by resulting in thrombosis of the spiral arteries, complement activation, and disrupting normal trophoblast growth. This leads to pregnancy complications like recurrent pregnancy loss, preeclampsia, intrauterine growth restriction, and fetal loss[1,2].

3.3 Clinical Features

Antiphospholipid Antibody Syndrome (APS) is clinically expressed with a broad range of thrombotic and obstetric phenomena. The most frequent clinical manifestation is vascular thrombosis, which may occur in the arteries, veins, or small vessels. Venous thrombosis is more common compared to arterial disease, with lower limb Deep Vein Thrombosis (DVT) being the most frequent. Arterial thrombosis can manifest as ischemic stroke, transient ischemic attack, or myocardial infarction in younger patients without conventional risk factors. Small vessel thrombosis can involve practically any organ and manifests as skin ulceration, livedo reticularis, or renal microangiopathy. A minority of patients can present with Catastrophic APS (CAPS), a potentially life-threatening disorder with extensive small vessel thrombosis and multiorgan failure[1-3].

Pregnancy-associated morbidity is another major clinical characteristic. These include repeated early miscarriages, idiopathic fetal loss after 10 weeks, preeclampsia- or placental insufficiency- induced preterm delivery, and intrauterine growth restriction. Infertility through failure of implantation can also be present in APS women[1,4,5].

Other non-criteria manifestations are thrombocytopenia, livedo reticularis, migraine, chorea, seizures, cognitive impairment, and abnormalities of heart valves like Libman–Sacks endocarditis. Involvement of the kidneys occurs as APS nephropathy, characterized by hypertension, proteinuria, and renal insufficiency[4,5].

3.4 APLA/APS- Classification Criteria: Revised Sapporo (Sydney) Criteria

Requires at least one clinical criterion and at least one laboratory criterion, present on two occasions, 12 weeks apart[1,2].

1. Clinical Criteria

a. One or more episodes of arterial or Venous thrombosis confirmed by imaging/histopathology (with no vessel wall inflammation).

b. Any one of the following pregnancy morbidity:

1. ≥1 unexplained death of morphologically normal foetus of >10 weeks gestation.

2. ≥1 premature birth of morphologically normal neonate before 34 weeks.

3. ≥3 consecutive, unexplained spontaneous abortions <10 weeks gestation.

2. Laboratory Criteria

Lupus Anticoagulant (LA)/ Anticardiolipin antibody (aCL) (IgM/IgG)/Anti-β2 Glycoprotein-I Antibody (IgM/IgG) positive on 2 occasions at least 12 weeks apart.

To classify a patient as having definite APS, at least one clinical and one laboratory criterion must be present[1,2].

4. Materials and Methods

Patients admitted in the Coimbatore Medical College and Hospital, General Medicine Department have been chosen for case series. Complete history, detailed examination, relevant biochemical, microbiological and radiological investigations were done. Patients were treated discharged and followed up.

CASE 1

A 28 years old male patient, who was a known case of Cerebral Venous Thrombosis (CVT) not on treatment, presented with the complaints of sudden onset left sided chest pain associated with palpitation with H/O high grade intermittent fever of 2 days duration. O/E: Patient had dyspnea and icterus. ECG was taken – It showed ST elevation in leads V1 to V4.

On investigations- Patient had platelet count 98,000/uL, Urea- 65 mg/dL, creatinine -1.6 mg/dL, Total bilirubin- 5.4 mg/dL, SGOT- 135 U/L , SGPT- 112 U/L , IgM Leptospirosis was positive (Evaluated in view of persistent fever).

Diagnosis- STEMI/Old CVT/ Leptospirosis.

CASE 2

A 47 years old female patient, a known case of hypertension and old ischemic stroke with recently diagnosed leprosy not on regular treatment was admitted with complaints of altered sensorium of one day and one episode of generalized tonic clonic seizures.

O/E: Patient was drowsy and irritable. Patient had madarosis, ill defined hypo pigmented patches involving both elbows and legs. Left sided ulnar nerve thickening was present.

Investigations- Patient had anemia (Hb- 6.1 g/ dl), Platelet count- 67,000/ ul, Renal and liver function tests within normal limits. MRI brain showed – Acute infarct in right middle cerebral (MCA) territory, old infarct with gliotic changes in left MCA territory.

Diagnosis- CVA- Multi infarct state with Leprosy and Systemic Hypertension.

CASE 3

A 38 years old male patient presented sudden onset bilateral lower limb weakness with sensory loss. O/E: Both lower limbs were cold and all the lower limb pulses from femoral artery were absent.

Investigations: CBC and biochemical investigations were within normal limits and ECG was in normal sinus rhythm. CT lower limb angiography showed-

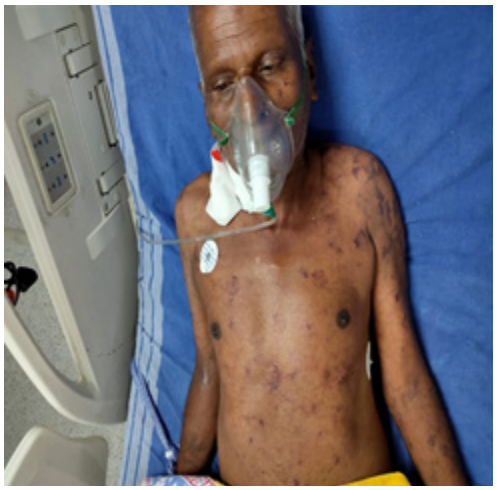

Figure 1. Ecchymosis all over body in caps.

Figure 2. Gangrene over little finger.

Thrombus at aortoiliac bifurcation and right femoral artery and ECHO showed left ventricular apical clot.

Diagnosis- Acute limb ischemia of both lower limbs with LV apical clot.

CASE 4

A 65 yrs old male patient presented with H/O intermittent Fever with bilateral leg swelling and skin lesions all over the body. After admission, we noticed blackish discoloration of fingers and toes and altered sensorium.

O/E: Patient was drowsy, not responding to oral commands, he had tachypnea, Grade 2 clubbing, bilateral pitting pedal edema. Pulses were absent in both radial, dorsalis pedis artery and posterior tibial artery. Ecchymosis and purpura was seen all over the body and gangrenous changes were seen in right little finger, right 5 toe, left 3rd and 5th toes (Figure 1, 2, 3).

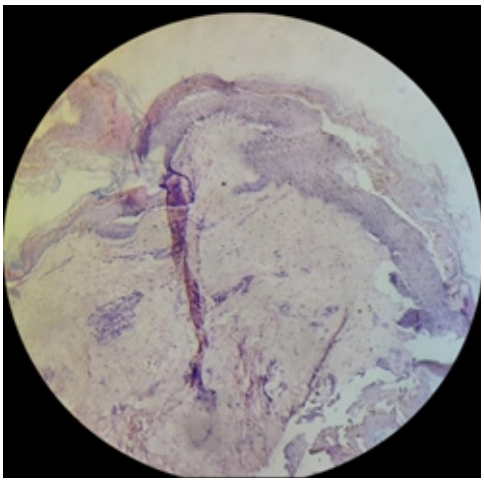

Figure 3. Skin biopsy showing thrombosis in caps.

On investigations: WBC – 17,000/uL, Urea- 298 mg/dL, creatinine – 4.4 mg/dL, Total bilirubin – 2.7 mg/dL, aPTT- 41.8 sec. CT chest showed features of Acute Respiratory Distress Syndrome (ARDS). ECHO – EF-58%, No vegetations.

Differential diagnosis: Sepsis, Meningococcemia, Thrombotic Thrombocytopenic Purpura (TTP), Antiphospholipid Antibody Syndrome (APLA), Vasculitis.

In all the above mentioned cases, development of thrombus is the main pathogenic mechanism.

5. Results (Including Observations)

We evaluated the cause for thrombophilia in all the above cases which included- Protein C, Protein S, Anti-thrombin-III, Homocysteine and APLA antibodies. All four patients were APLA positive.

6. Discussion

In CASE 1- Patient already had APS induced endothelial dysfunction. Leptospirosis acted as a "second hit."

APS-induced endothelial dysfunction combined with infection-related inflammation precipitated the arterial event causing acute coronary thrombosis.

In CASE 2- Chronic infections such as leprosy can precipitate or reveal APS by inducing chronic autoantibody production and endothelial activation resulting in thrombotic manifestations like strokes or DVT. The persistence of aPL positivity with clinical events establishes the diagnosis.

In CASE 3- The patient probably had primary APS, where the antibody mediated endothelial injury and hypercoagulability led to large-vessel arterial thrombosis – aortoiliac bifurcation thrombosis.

In CASE 4- It is the case of CAPS. Since, it fulfills all four criteria- Acute onset, multiorgan thrombotic involvement, positive serology and histopathological confirmation. Early recognition is crucial as CAPS carries high mortality and mandates urgent initiation of combined therapy with anticoagulation, corticosteroids and plasma exchange or IVIG.

7. Summary and Conclusion

Hughes Syndrome or Antiphospholipid Antibody Syndrome can present with a wide spectrum of thrombotic manifestations—from young myocardial infarction and stroke to acute limb ischemia and thrombotic microangiopathy. Early recognition and evaluation for APS is crucial in atypical or recurrent thrombotic events, especially in young individuals. These cases highlight the need for a high index of suspicion and comprehensive workup to guide timely anticoagulation and improve outcomes.

8. References

1. Harrison 's principle of internal medicine. 21st ed.
2. API text book of medicine, 12th ed.
3. Knight JS, Branch DW, Ortel TL. Antiphospholipid syndrome: advances in diagnosis, pathogenesis, and management. BMJ. 2023; 380:e069717. https://doi.org/10.1136/bmj-2021-069717 PMid:36849186.
4. Garcia D, Erkan D. Diagnosis and management of the antiphospholipid syndrome. N Engl J Med. 2018; 379(13):1290. https://doi.org/10.1056/NEJMc1808253
5. Erkan D, Yazici Y, Sobel R, Lockshin MD. Primary antiphospholipid syndrome: functional outcome after 10 years. J Rheumatol. 2000; 27(12):2817-21.