ANTI-PHOSPHOLIPID SYNDROME IN NIGERIA: REPORT OF FIVE CASES

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SUMMARY

Five cases of secondary anti-phospholipid syndrome (APS) are presented and literature reviewed. Pregnancy loss was the most common presentation but neurologic manifestations are also seen. IgG ACA was more commonly seen than IgM ACA. Although APS has been infrequently reported in black Africans, an awareness of this condition is needed especially among females with previous recurrent pregnancy losses.

INTRODUCTION

Anti-phospholipid syndrome (APS, Hughes Syndrome) is an acquired, autoimmune thrombophilia, usually associated with significant morbidity and mortality. The diagnosis requires clinical manifestations of recurrent arterial and venous thrombosis: recurrent pregnancy losses, as well as the demonstration of serum anti-phospholipid antibodies (APA) (1).

APS could either be primary or secondary to connective tissue diseases such as systemic lupus erythematosus, polymyositis, scleroderma, and inflammatory arthritis like rheumatoid arthritis. It could also be associated with infectious diseases and neoplasms (2).

Clinical manifestations may also include thrombocytopenia, livedo reticularis, cutaneous necrosis, haemolytic anaemia, heart valvular disease, chorea, migraine, foetal growth retardation and pre-eclampsia.

A particularly severe form is catastrophic anti-phospholipid syndrome (CAPS) which is characterised by widespread microthrombi, in multiple vascular beds culminating in fulminant multiple organ failure. Organ manifestations in CAPS may include renal impairment, abnormal liver enzymes and failure as well as respiratory failure and adrenal insufficiency (3).

Anti-phospholipid antibodies are found in 1-5% of young healthy subjects with the frequency rising with age and presence of co-existent chronic diseases. Prevalence of these antibodies among SLE patients is about 12-30% for anti-cardiolipin antibodies (ACA) and 15-34% for lupus anticoagulant (LAC) (4,5). It has been suggested that the lupus anticoagulants are immunologically distinct from ACA; though the associated clinical complications exhibited by the two groups of antibodies are similar (6,7).

It has been shown that the binding of anti-phospholipid antibodies to cellular phospholipids requires the serum co-factor, beta-2 glycoprotein 1. Among patients with SLE selected for the presence of lupus anticoagulant, thrombosis or foetal loss, 36% had anti-beta 2 glycoprotein 1. The effect of this protein has been associated with inhibitory effects on platelet aggregation, platelet thrombokinase activity as well as the intrinsic pathway of coagulation. These further support the hypothesis that implicates this protein in the pathogenesis of unwanted thrombotic events (8).

Systemic lupus erythematosus is not commonly reported among black Africans (9) and associated APS has rarely been reported. The objective of this case is to show the presentation and management of APS among Nigerians.

We hereby present five patients with Anti-phospholipid syndrome among 66 diagnosed SLE patients seen in a private practice rheumatology clinic.

CASE REPORTS

Case 1: Mrs. M. O., a 34 year old female who presented with photosensitivity rash; polyarthritis of the shoulder, elbows, hands, ankles associated with joint morning stiffness; generalised macular body rashes; pleuritic chest pain; and two previous abortions at 18 and 20 weeks. Physical examination showed a young lady with marked tenderness in most of the joints. Respiratory system examination showed pleural rubs at the right basal region.

Laboratory investigations - Urine dipstick showed proteinuria of 2+, no casts, no haematuria.
Haematocrit was 39% with normal white blood cell count and differentials. Erythrocyte sedimentation rate - 106 (Westergren mm/hr). Serum urea - 20.5mg/dl.

SeroLOGY - Rheumatoid factor 25(normal 0-20); anti nuclear antibody - 320 (normal 0-40): 1 gG Cardiolipin - 44mpl/ml(normal 0-15); IgM Cardiolipin 6.4mpl/ml (normal 0-13.5).

The diagnosis was SLE with APS. She was treated with methotrexate tablets - 15mg once weekly, aspirin tablets - 75mg daily and prednisolone tablets - 15mg daily. She is still being followed up.

Case 2: Mrs. E. U; a 28 year old female who presented with generalised urticaria rashes - nine months before presentation; pruritic maculo papular rashes on the trunk and face and polyarthralgia affecting joints of the hands, ankles and knee. Physical examinations showed a young, cachetic lady with maculo papular rashes on the trunk and face. She also had tenderness of the metacarpophalangeal and proximal interphalangeal, wrist joints of both hands as well as the knees.

Laboratory investigations - white blood cell count-3,800 (neutrophils - 86%; lymphocytes - 14%). Platelet count showed thrombocytopenia - 87,000 per cu.mm. Serum urea was normal- 16.8 mg/dl. SeroLOGY - ANA positive 1: 5120 speckled pattern; Anti RNP positive; anti DNA - negative. IgM ACA - 20; anti nuclear antibody - 320 (speckled). IgG ACA - 41.6 mpl/ml(0-13.5). Diagnosis was SLE. She was placed on azathioprine 100 mg daily and prednisolone tablets - 10mg daily. About two years after presentation, she became pregnant but had a miscarriage at 22 weeks. Examination of the placenta by the obstetrician showed a small placenta with areas of infarction. Additional diagnosis of antiphospholipid syndrome was made.

Case 3: Mrs. J. N., a 29 year old diagnosed SLE. She presented with a flare up of polyarthralgia, fatigue, malar rashes and fever. History also revealed that she has had a previous miscarriage at sixteen weeks.

Physical examination revealed that she was febrile and had macular and malar rashes. Examination of other systems were essentially normal. Blood pressure was 110/80mmHg.

Laboratory investigations - haematocrit - 38%; white blood cell count 6,800/cu.mm with normal differentials. Erythrocyte sedimentation rate was 86mm/hour.

SeroLOGY - ANA positive 1:80 (speckled pattern); IgG cardiolipin antibody 42.9gpl/ml (0-15); IgM cardiolipin antibody - 4.8mpl/ml (0-13.5).

Diagnosis of SLE and elevated Anti phospholipids antibody was made. She became pregnant later and was continued on hydroxychloroquine, prednisolone and aspirin. In addition, she was placed on subcutaneous low molecular weight heparin, (enoxaparin). Heparin and aspirin were discontinued at 34 weeks cyesis. She had a normal, uneventful delivery at 38 weeks and is still being followed up.

Case 4: Mrs. E. E., a 36 year old female who presented with polyarthralgia; recurrent sore throat and mouth ulcers; hair loss; recurrent temporal headaches. She has had both pleural and pericardial effusion before presentation for which anti-tuberculous drugs had been initiated elsewhere. Physical examination showed a cachetic lady, slightly pale. Pulse was 120 beats per minutes. Blood pressure was 110/70mmHg. Central nervous system examination revealed weakness in both lower limbs with muscle power Grade III. Tendon reflexes were brisk and there was Babinski response on plantar reflex. There was no sensory loss. Laboratory investigations - haematocrit - 40%, white blood cell count 5,600 per cu.mm with normal differentials. Platelet count was 230,000 per cu.mm. Erythrocyte sedimentation rate - 120mm/hour. Serum Urea - 44.3 (1.0); creatinine kinase - 48 (1 0-70); urine analysis and microscopy were normal. SeroLOGY showed ANA titre of 1:320 (0-39) homogeneous pattern; ENA positive, Anti DNA negative; IgG cardiolipin antibody-77.0gpl/ml (0-15); IgM cardiolipin antibody-119mp/ml (0-13.5).

Diagnosis was SLE myelopathy and antiphospholipid syndrome. She was placed on azathioprine, prednisolone, aspirin and warfarin. She was also started on physical therapy. She is still being followed up.

Case 5: O.O was a 24 year old female who presented with polyarthralgia; recurrent sore throat and mouth ulcers; hair loss; recurrent temporal headaches. She has had both pleural and pericardial effusion before presentation for which anti-tuberculous drugs had been initiated elsewhere. Physical examination showed a cachetic lady, slightly pale. Pulse was 120 beats per minutes. Blood pressure was 110/70mmHg. Chest examination revealed bilateral dullness to percussion and reduced breath sounds in the lower and middle chest zones. Other systems were essentially normal.

Laboratory investigations - elevated erythrocyte sedimentation rate - 80mm/hour. Dipstick urine examination showed albuminuria - 3+ with pus and epithelial cells. SeroLOGY - anti nuclear antibody - 1:1280 (speckled). IgM ACA-41.6 mpl/ml (0-13.5). IgGmpl/ml ACA-30 (0-15).

Treatment was initiated with pulse methylprednisolone, azathioprine and aspirin.

A week following initiation of medications, she had two episodes of seizure and thereafter, became weak in both lower limbs. Central nervous system
examination showed hypereflexia in both lower limbs as well as Babinski response on plantar reflex.

Diagnosis was SLE with myelopathy from anti-phospholipid syndrome. She was placed on low molecular weight heparin and warfarin. Physiotherapy was also initiated. She is still being followed up.

**DISCUSSION**

The five cases presented represent part of the spectrum of anti-phospholipid syndrome. All the cases were secondary to SLE. Three of the cases had presented with pregnancy losses at one time or the other while the remaining two had neurological manifestations. Recurrent pregnancy losses among those affected could be particularly distressing. In many cases, unnecessary investigations are carried out all to no avail. An awareness and effective management of this syndrome could prevent this, especially in those with primary APS.

Neurological manifestations are among the most common presentation in APS and includes cerebral ischaemia, cognitive dysfunction, dementia, psychosis, depression, seizures, chorea and myelopathy (10). This was corroborated in a study by Miesbach et al (11) which showed a prevalence of antiphospholipid antibody in 15% of 350 unselected patients attending a neurology clinic.

IgG ACA was elevated in four of the patients while IgM ACA was elevated in three patients. Both antibodies were elevated in two cases, both of whom had neurological manifestations.

IgA anti cardiolipin antibodies have been reported to be the most prevalent among African Americans with APS (12). However, this test was not performed in our patients. Secondary APS, though rarely reported among black Africans, should be considered in patients presenting with unexplained recurrent abortions and neuropsychiatric lupus.

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**REFERENCES**