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Case Report

Antiphospholipid Syndrome Associated with Lupus Nephritis in a Resource-Poor Setting: A Case Report in Orlu, Nigeria

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Abstract: The incidence of antiphospholipid syndrome (APS) in Nigeria is not well-defined. Concomitant occurrence of APS and systemic lupus erythematosus (SLE) is rare in Nigeria. Documented here is a case of APS associated with SLE, complicated by lupus nephritis, in a young woman in Nigeria. Patient was a 31-year-old woman on evaluation for 2 consecutive mid-trimester pregnancy losses, each preceded by a history of leg swelling and passage of blood in urine. Two of her sisters, about her age, have a similar history of recurrent mid-trimester pregnancy losses. Her blood pressure was normal. She has proteinuria +++, 24-hour urine protein 2942mg, and positive serology results for ANA, dsDNA, antiphospholipid antibody, and lupus anticoagulant. She was placed on Aspirin and Prednisolone, among others. Repeat urine protein was 1242mg/day at 4 weeks and 419mg/day at 12 weeks on follow-up. This case report highlights the need for consideration of the possibility of APS in association with SLE in the evaluation of miscarriages and proteinuric diseases in pregnancy.

Keywords: Antiphospholipid Syndrome, Systemic Lupus Erythematosus, Lupus Nephritis, Miscarriage, Proteinuria in Pregnancy, Hematuria in Pregnancy, Nigeria

1. Introduction

Antiphospholipid syndrome (APS), a connective tissue disease, marked by abnormalities of clotting and rarely hemorrhage, may occur in isolation or in association with systemic lupus erythematosus (SLE). [1] The incidence of APS is low in Nigeria, though that of SLE seems to be rising. [2, 3] Concomitant occurrence of APS and SLE tends to have more likelihood of lupus nephritis (LN) complicating the SLE. [4, 5]

Antiphospholipid syndrome usually manifests with thromboembolic phenomena in many parts of the body including the placenta, leading to pregnancy loss, more pronounced in mid-trimester. [2] Lupus nephritis is a common complication of SLE and tends to flare in pregnancy. [6] Proteinuria in pregnancy is not limited to pre-eclampsia or other hypertensive diseases of pregnancy, but is also a prominent feature of LN. [6]

There is a paucity of reports on APS and LN emanating from southeast Nigeria. This has prompted us to document this case report of APS occurring concomitantly with LN, and escalating nephritic activity in pregnancy. This will bring to the fore the need, by clinicians and obstetricians, for the consideration of APS and LN in the evaluation of proteinuric diseases in pregnancy in Nigeria.

2. Case Presentation

The patient presented in the Medical Out-patient Clinic of Imo State University Teaching Hospital, Orlu, Nigeria, with a history of two consecutive mid-trimester pregnancy losses, first in 2015, second in 2016. Each miscarriage was preceded by passage of blood in urine, foaming of urine and swelling of both legs and face, noticed to be worse in the morning, but waned as the day progressed. She also noticed rash on the face, neck and shoulders. She has no fever, but has headache,

palpitation and occasional scalp rash. There was no associated blurring vision, erratic or abnormal behavior, cough, breathlessness, joint pain, vomiting, or diarrhea.

She attained menarche at 14 years, and has regular menstrual cycles. Last menstrual cycle was 21/08/2016, flow of about 4 days. She is para 3, gravida 1 + 2, 1 alive following full-term normal delivery. During the past 2 miscarriages, she was found to have hematuria and proteinuria +++. The findings of proteinuria and hematuria were the reasons her gynecologist/obstetrician referred her to us after initial treatment. In both miscarriages she did not receive any blood transfusion.

Two of her sisters about her age also have a similar history of recurrent mid-trimester pregnancy losses of "unexplained cause". However, the patient denied a history of rashes in her siblings. She has no alcohol or cigarette use history. A native of Imo State, southeast Nigeria, she lives in Port Harcourt, south-south Nigeria.

Physical examination showed a young woman in no obvious distress, afebrile, not pale and has no peripheral edema or asterixis. She has discoid rashes on her scalp, and photosensitive rashes on the neck and shoulders. Pulse was 74 beats/minute, of full volume and regular. Blood pressure was 130/90mmHg sitting. Heart sound S1 and S2 were normal. There was no murmur or any other adventitious heart sound. Chest was clinically clear. Central nervous system showed she was fully conscious and oriented in time, person and place. Memory, both recent and remote, were intact. She has no meningeal irritation signs or any other neurological deficit. Abdomen was full, moved with respiration but was not tender. The liver, spleen and kidneys were not enlarged.

A presumptive diagnosis of APS and lupus nephritis was made.

Results of investigations done showed

Serological tests were positive for antinuclear antibody (ANA), anti-dsDNA antibody, anti-phospholipid IgM/IgG antibodies and lupus anticoagulant (LA) (Table 1).

Full blood count, ESR, blood film and prothrombin time were within normal range (Table 2). Urinalysis showed protein ++ and no other abnormality. Twenty four-hour urine protein (24 HUP) was elevated. Other serum biochemistry results were within normal values.

Table 1. *Serology tests.*

(a) Antinuclear Antibody (ANA) Screen	(b) Anti-dsDNA Antibody screen	(c) Anti-phospholipid IgM/IgG Antibodies	(d) Lupus Anticoagulant (LA) Screening
OD ratio of sample: 2.79 Interpretation Negative specimens (OD ratio) ≤ 0.90 Equivocal specimens (OD ratio) 0.90-1.09 Positive specimens (OD ratio) ≥ 1.10 (OD = optic density, same as index value) Patient's result for ANA screen: positive Comment: ANA level is three times more than in a healthy subject	Patient's OD ratio 1.55 Interpretation: Negative specimens (OD ratio) ≤ 0.90 Equivocal specimens (OD ratio) 0.91-1.09 Positive specimens (OD ratio) ≥ 1.10 Patient's result for Anti-dsDNA Antibody Screen: Positive. Comment: Anti-dsDNA level is about two-fold higher than in a healthy subject.	Patient's OD 16.2U/ml. Reference range: normal < 10. Elevated ≥ 10. Method of analysis ELISA	Method of Analysis: Dilute Russel's Viper Venom Time (DRVVT) Patient's DRVVT Result: 45sec (Reference range in healthy subjects: 28-35 seconds. Patient's DRVVT ratio: 1.28 (Reference range in healthy subjects < 1.16.

Table 2. *Results of investigations.*

Urinalysis, urine microscopy and culture	pale/amber color, pH 6.0, SG 1.025, protein ++, others normal. Urine microscopy showed WBC 2-3/hpf, RBC nil, epithelial cells ++, crystals nil, casts nil. There was no bacterial growth on culture
Serum electrolytes, urea and creatinine	serum urea 23mg/dl, serum creatinine 0.5mg/dl, serum sodium 138mmol/l, serum potassium 4.2mmol/l, serum chloride 88mmol/l, serum bicarbonate 26mmol/l
Fasting serum lipid profile	cholesterol 4.6mmol/l, low density lipoprotein cholesterol 2.2mmol/l, high density lipoprotein cholesterol 1.4mmol/l, triglyceride 1.4mmol/l
Full blood count, ESR, blood film	PCV 40%, white blood cells (WBC) count 5200cells/ml, neutrophils 42%, lymphocytes 58%, platelets count 186 x 10^9/ml, ESR 93mm/1^{st} hour. Peripheral blood film showed normocytic normochromic red blood cells (RBCs)
Prothrombin time	20.3seconds INR 1.2
24-hour urine protein	2292mg
Other biochemistry tests	Serum calcium 2,2mmol/l, serum phosphate 1.8mmol/l, serum albumin 3.8g/dl

Diagnosis of APS in association with SLE, complicated by Lupus nephritis, was made.

She was placed on Aspirin and Prednisolone in addition to hydroxychloroquin. Follow-up at 4 weeks showed a 24HUP of 1242mg, down from 2292mg, and 419mg at 12 weeks.

Her sisters could not be reached for evaluation for APS/SLE, a challenge in our setting.

3. Discussion

The incidence of isolated APS, or APS in association with SLE, is low in Nigeria. [2] Our index patient has APS and lupus nephritis as a complication of SLE. This is the first case in four years observed in this center, one of the two tertiary hospitals in the state, suggesting the rarity of both isolated APS and concomitant occurrence of APS and SLE with LN in this part of Nigeria. The presentation of APS is thromboembolic phenomena that may involve all organs of the body, including the placenta. Placental involvement leads to ischemia and miscarriages, dominantly noted in mid-trimester [6, 7] as was observed in our index patient who has consecutive mid-trimester miscarriages.

On the other hand, LN flare is common as pregnancy progresses. [6, 7] Quiescent LN may, in fact, become active

and only be clinically manifest in pregnancy, with poor maternal and fetal outcomes. [6, 7, 8] This perhaps, could explain the apparent development of features of hematuria, leg swelling and proteinuria in this patient during pregnancy, detected in the course of antenatal checks, for which reason she was referred to us for evaluation.

The diagnosis of APS and LN in our patient was based on the history of two consecutive mid-trimester pregnancy losses, associated with leg swelling that has morning accentuation, scalp and photosensitive neck rashes, normal blood pressure, hematuria, nephritic-nephrotic proteinuria, positive tests for anti-cardiolipin antibody, lupus anticoagulant, ds-DNA, and ANA. Isolated APS nephropathy was not considered as the cause of the nephropathy because of the overwhelming evidence of SLE and LN. [9] A renal biopsy, however, was not done on this patient. This would have helped in confirming not only the diagnosis of LN but also in staging the disease, for prognostic and therapeutic evaluation. [10] In our setting, renal biopsy is not routinely done because many patients would not consent to it. In addition, histological evaluations are limited to light microscopy, as both immunoflorescent and electron microscopy facilities are not available locally and their costs are usually out of reach of our people. The specimens should be considered for overseas analysis. There was dipstick proteinuria of 4+ but the serum creatinine and urea values in our index patient were within normal range, implying that she obviously was not in LN stage I. Her initial 24-hour urine protein was clearly in excess of the values seen in LN stage II. Perhaps, she has LN stage III with preserved renal function. [10]

Screening of female family members of child-bearing age for APS, though not a standard recommendation, was not done for our index patient's two sisters who also were said to have a similar history of consecutive mid-trimester miscarriages. This strain is not peculiar to APS or SLE, as many people from this part of the world express nonchalance for screening of family members in conditions that call for this. [11]

4. Conclusion

This case report illustrates a concomitant occurrence of APS and SLE, complicated by LN in a woman in Orlu, Nigeria. It highlights the need for consideration of the possibility of APS in association with SLE in the evaluation of miscarriages and proteinuric diseases in pregnancy. Early detection and appropriate intervention will avert complications of the syndromes.

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