OBSTETRIC APLA SYNDROME: CATASTROPHE HIDDEN IN ICEBERG

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ABSTRACT Obstetric Antiphospholipid Syndrome (OAPS) is a severe threat of pregnancy leading to, either or both, maternal and fetal morbidity/mortality. We present here a case of young primigravida, preeclamptic female with intrauterine fetal death and subsequent postpartum renal cortical necrosis. Association with antiphospholipid antibodies (APLA) as a causative factor for these catastrophic events was established only during the work-up of renal biopsy reporting. This case highlights the importance of including APLA as a screening investigation during antenatal care, especially in developing and underdeveloped countries.

KEYWORDS Obstetric, Antibodies, Renal cortical necrosis

Introduction

Pregnancy-related end-organ damage with accompanying significant maternal and fetal mortality are not rare in second and third world countries [1-3]. Antiphospholipid antibodies in the form of Obstetric Antiphospholipid Syndrome (OAPS) bears a distinctive association with these catastrophic events, however seldom taken in account. OAPS induced thromboembolic events in pregnancy are approximately 200 times higher than that in the general obstetric population [4]. OAPS is characterized by the presence of venous/arterial thrombosis, recurrent fetal losses or premature fetal birth < 34 weeks of gestation, consumptive thrombocytopenia, organ damage in the presence of elevated antiphospholipid antibodies (APLA). There are three main types of APLA viz. lupus anticoagulant (LA), anticardiolipin antibodies (aCL) and anti-beta-2 glycoprotein-I antibodies (antiβ2GPI). Positivity of LA among all APLA carries the worst prognosis. The affected patient may test positive for either, two or all of these; prognosis worsening with the involvement of LA in the positive test panel. Presence of LA is detected by phospholipid dependent coagulation assays like PT, APTT, whereas aCL and antiβ2GPI are detected by ELISA/immunoassays [5].

Antiphospholipid syndrome (APS) can have primary presentation as OAPS, or it can be secondary (SAPS) when associated with autoimmune disorders like systemic lupus erythematosus (SLE), malignant lesions or drug/infection induced [6]. OAPS may affect kidneys too in its series of complications with prominent changes being fibrous intimal hyperplasia, thrombotic microangiopathy, focal cortical necrosis and tubular thyroidization in the kidney [7-9]. We present here a case of OAPS, presenting with a multitude of complications whose association with APLA could be established only in the late course of the disease.

Case report

A 25 years old primigravida female presented with altered sensorium, oliguria, fever, vomiting and pedal oedema 12 hours after cesarean section for preeclampsia at 32 weeks of pregnancy with intrauterine fetal death. Her blood pressure was 160/90 mmHg. Laboratory parameters revealed hemoglobin 9.1 g/dl; total leucocyte count 8,600cells/mm3; differential leucocyte count revealing mild neutrophilic leucocytosis; platelet count 2.94 lakh/mm3. Urea and creatinine were 80 mg/dl and 2.5mg/dl, respectively. Urine examination revealed 1+ proteinuria along with gross hematuria and mild pyuria. Urine culture was negative for any pathogenic micro-organisms. Ultrasonography of the lower abdomen revealed increased echogenicity of the right kidney. Serological tests including complement C3 and C4 levels, ANA and ANCA were done which all came within normal range, thereby

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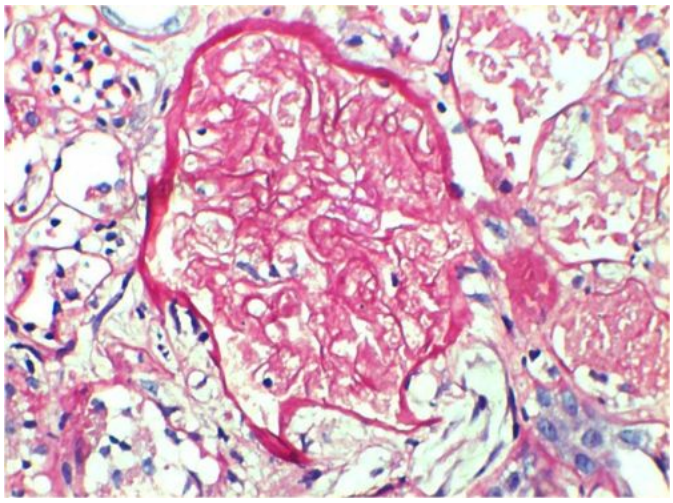

Figure 1: Renal biopsy microscopy image depicting cortical necrosis involving glomeruli as well as tubules.

excluding the possibility of complement-mediated nephropathy, lupus nephritis, Wegener's granulomatosis respectively.

Further renal biopsy was performed and subjected to histopathology and immunofluorescence. Nine of the total 11 glomeruli present revealed marked coagulative necrosis along mesangium and capillaries, with preserved ghost cell outlines. At places, capillary lumina were seen congested with RBCs and leucocytes. Tubules depicted moderate degenerative changes and interstitium revealed scattered mononuclear inflammatory cell population. Minor vessels showed prominent mucointimal proliferation. Immunofluorescence was negative for all markers. Microscopic findings were in consistence with the diagnosis of renal cortical necrosis. (Figure 1) To further elucidate the etiology of the histomorphological picture, APLA panel was performed, which showed positive confirmatory results for LA, and IgM type aCL. A provisional diagnosis of OAPS was framed, which needed to be confirmed 12 weeks after too by repeating serology for APLA, as per defined criteria for antiphospholipid syndrome. Nonetheless, the possibility of OAPS existed to maxima as it could explain all the clinical history, signs & symptoms and subsequent clinical course of the patient. The patient was put on hemodialysis with few intervening sessions of plasmapheresis. After four weeks, her urine output partially improved with a marginal decline in serum creatinine too. She continued to be dialysis dependent for next eight weeks when her APLA panel was repeated. LA depicter PT, APTT values and IgM type aCL titres were found to be in declining trends but still above cutoff limits that confirmed the diagnosis of OAPS. The patient underwent a few more sessions of hemodialysis and showed further improvement too, but was eventually lost to follow-up after one month.

Discussion

APS is a well-recognized entity since more than 30 years, and lately OAPS has also been regarded as a distinct subclass of APS, in view of its significant association with maternal and fetal morbidity during the entire course of pregnancy. However, epidemiological data supporting it is still very scant owing to challenges in diagnosing OAPS because of involvement of multiple specialities [9]. A large proportion of cases remain undiagnosed or diagnosed at a very advanced morbid stage, like in the case described above. Thus OAPS can be presumed to be an iceberg entity with a larger proportion of cases being always hidden, particularly in developing or underdeveloped countries.

OAPS is diagnosed taking in consideration both clinical and laboratory criteria. Clinical criteria include pregnancy-related maternal and fetal morbidities, including recurrent thrombosis, hypertension, premature birth or fetal loss. Laboratory criteria include positive titres for one, two or all the APLA on two separate occasions separated by 12 weeks at least and not more than five years. There may be an association with some other non-criteria events too like skin ulcers, ischaemic nephropathy leading to renal failure, heart valve disease etc. in the course of OAPS like in case presented here.

Acute renal failure in pregnancy in the modern era is considered as a rare complication in developed countries, with an estimated incidence of less than 1 in 20,000 pregnancies. However obstetric related acute renal failure, although on the decline, still constitutes about 25% of the referrals for dialysis in the developing world with a high risk of maternal mortality of 9-55% [2,9,10]. There is no epidemiological data available on the contribution of APLA in obstetric related acute renal failure despite a high degree of suspicion. Pregnancy is a hypercoagulable state and may contribute to the development of APS [11].

Renal cortical necrosis is defined as the destruction of the renal cortex except for a thin rim of tissue under the capsule and usually a thick layer under corticomedullary junction due to disturbed blood flow into the interlobular and afferent arterioles. It is an uncommon entity, accounting for only 2% of all cases of acute renal failure. Pregnancy has a high risk of renal cortical necrosis owing to the well-described entity of Schwartzman phenomenon [12]. Its incidence range from 14.28% to 23.8% in India as compared with 1.5% in the developed countries [3,13]. Renal manifestations of APS are possibly due to synthesis of large amounts of nitric oxide (NO) by mesangial cells and synergy between prostacyclin (PGI2) and NO in their platelet inhibitory action, which may contribute to a lower incidence of thrombosis in the glomerular capillaries [14]. Various manifestations of APS are renal artery thrombosis, thrombotic microangiopathy, renal vein thrombosis, systemic hypertension, renal cortical necrosis, progressive renal failure and proteinuria [12,15].

Our patient presented with typical signs of renal cortical necrosis as altered sensorium, oliguria, vomiting and pedal oedema requiring dialysis support in postpartum, owing to positivity for APLA. This was a case of catastrophic OAPS that could be diagnosed only during the workup of an associated "non-criteria" complication. Such cases can be effectively managed if screened or diagnosed in time, and resulting morbidities be significantly reduced. Screening for APLA in antenatal period should be done in obstetric cases if there is any suggestive family history. Epidemiological data regarding OAPS should also be tried to framed especially in developing /underdeveloped countries, and if prevalence rates affirm, screening should be extended to all antenatal females, to warrant early diagnosis and management of OAPS.

Conflict of interest

The authors have no conflicts to disclose. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

FK AS wrote the manuscript. AS SB diagnosed the case. AS finally approved the manuscript to be sent for application.

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