Postpartum Pulmonary-Renal Syndrome with Thrombotic Microangiopathy in Systemic Lupus Erythematosus

Abstract

Postpartum pulmonary syndrome as lupus flares in inactive or mild lupus is uncommon. The diagnosis and management of postpartum lupus flare in second pregnancy presenting with crescentic lupus nephritis (LN), secondary thrombotic microangiopathy (TMA), and severe lupus vasculitis in an undiagnosed systemic lupus erythematosus is extremely challenging. Here, in this case report, we present a young lady who presented with postpartum acute kidney injury (AKI) with systemic complaints about 4 weeks post-term uneventful delivery. Renal biopsy was suggestive of crescentic LN with severe lupus vasculitis. The stormy course was further complicated with diffuse alveolar hemorrhage, portal venous thrombosis, TMA, and anuric AKI requiring renal replacement therapy. She received multiple sessions of plasmapheresis, steroid, intravenous immunoglobulin, inj. cyclophosphamide, and started showing improvement after about 6 weeks of presentation.

Keywords: *Diffuse alveolar hemorrhage, lupus nephritis, lupus vasculitis, postpartum lupus flare, thrombotic microangiopathy*

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Introduction

Making a diagnosis of lupus flare in an undiagnosed systemic lupus erythematosus (SLE) is difficult during the postpartum period as many symptoms and laboratory findings can mimic those of SLE. The most common organs affected in lupus flares during pregnancy and the postpartum period are the skin, kidney, blood, and joints.[1] In this case report, we discuss a young lady who in her second pregnancy, presented with postpartum acute kidney injury (AKI) about 4 weeks post lower segment cesarean section (LSCS) and was diagnosed as severe crescentic LN with lupus vasculitis. She had a stormy course of hospitalization over 2 months and was managed with renal replacement therapy, plasma exchanges, immunosuppression, and other supportive measures resulting in remission of lupus flare and near-complete renal recovery.

Case Report

A 26-year-old lady, known hypothyroidism on tab thyroxine 50 mcg daily for last 6 years, underwent LSCS at 38th week of second pregnancy with an uneventful antenatal course and delivered a normal baby with a bodyweight of 3.2 kg. There was no family history of autoimmune disease, and the baby had no clinical features of neonatal lupus. There was no previous history of abortion. She had a history of LSCS around 3 years back due to premature rupture of membranes. Her blood pressure was noted as normal during the postoperative period. Breast feeding was initiated within a few hours of delivery. She reported to a general physician after 1 month of LSCS with a history of generalized swelling of 4–5 days duration. Investigations done there revealed—urine protein 3+, 4–5 red blood cells/high power field (HPF), serum creatinine 0.9 mg/dL, and serum albumin 2.5 gm/dL.

She was referred to our hospital to rule out the possibility of glomerular disease. Clinically, she was pale, had bilateral pedal edema with facial puffiness, pulse 102/min, regular, BP 140/94 mm Hg (on two antihypertensive drugs), and jugular venous pressure was not raised. Systemic examination revealed ascites and bilateral decreased breath sound in both infra-scapular areas. Fundoscopy was normal. She had no musculocutaneous features suggestive of SLE.

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Initial investigations revealed anemia, thrombocytopenia, hypoalbuminemia, azotemia, proteinuria, raised LDH, near-normal procalcitonin, and raised D dimer. Other investigations revealed urine protein 3+, numerous RBC/HPF, ultrasound kidney ureter bladder normal, renal Doppler normal, coagulation studies normal, electrocardiogram and 2 D echocardiogram, upper gastrointestinal endoscopy, iron studies, serum Vit B12 and folic acid, TSH were all normal.Ultrasound abdomen showed dilated portal vein (16 m), spleen 12.8 cm, ascites+, liver 12.6 cm, normal echotexture, multiple portosystemic and splenorenal collaterals suggestive of portal venous thrombosis, and serum ascitic albumin gradient 1.41 gm/dL. Chest X-ray PA view was suggestive of bilateral pleural effusion. Autoimmune workup revealed antinuclear antibody, IFA by indirect immunofluorescence test homogeneous nuclear pattern, titer 1:100, anti ds DNA +, C3 19 mg/dL (83–193), C4 5.80 mg/dL (15–57) [immunoturbidimetry], anti-GBM antibodies negative, antineutrophil cytoplasmic antibody (ANCA) P ANCA and c-ANCA negative, antiphospholipid antibody work up negative. Peripheral blood smear (PBS) was suggestive of microangiopathic hemolytic anemia (MAHA).

She became oligoanuric after 3–4 days of admission. She was initiated on hemodialysis for fluid overload and metabolic acidosis. She was put on empirical iv broad-spectrum antibiotics, intravenous loop diuretics, inj. Unfractionated heparin (UFH), antihypertensives, oral cotrimoxazole in a modified dose, and hydroxychloroquine (HCQ). As the mother was alone during this period of hospitalization, breast engorgement was managed by expressing breast milk periodically. In view of rapidly progressive renal dysfunction over a few days requiring dialysis, significant proteinuria, and hematuria, she underwent a renal biopsy on day 7 of admission after two sessions of hemodialysis.

Renal biopsy [Figures 1 and 2] on light microscopy revealed 15 glomeruli with none globally sclerosed. Eight (53.3%) glomeruli revealed overlying crescents (seven cellular and one fibro cellular crescent) and two (13.3%) glomeruli revealed secondary segmental tuft necrosis. Tubular atrophy and interstitial fibrosis involved about 10–12% of sampled cortex. Several arterioles and occasional arteries revealed necrotizing lesions, RBC fragmentation, and fuchsinophilic deposits in walls. Direct Immunofluorescence: full house pattern. Overall renal biopsy findings were suggestive of diffuse lupus nephritis: (International Society of Nephrology/Renal Pathology Society ISN/RPS 2018 modification): Class IV. Indices (Modified National Institutes of Health- NIH) of activity 18/24 and chronicity 2/12.

Post renal biopsy, she was given iv methylprednisolone pulse 500 mg × 3 days followed by oral prednisolone. She also received inj. cyclophosphamide in a modified dose thereafter. A total of six doses of inj. cyclophosphamide (500 mg each) were given over 16 weeks at the interval of 14–21 days. In view of microvascular lesions in renal biopsy and PBS suggestive of MAHA/thrombocytopenia, a possibility of lupus TMA was considered. She received a total of 16 sessions of plasma exchanges (60 mL/kg each session) over 6 weeks due to persistent thrombocytopenia and PBS showing schistocytes. She was also administered 140 gm of intravenous immunoglobulin (IVIG) twice over 5 days each at 21 day intervals during hospitalization. She developed streaky hemoptysis, breathlessness, and desaturation on day 11 of admission despite regular hemodialysis with adequate ultrafiltrate. High-resolution computed tomography chest [Figure 3] was suggestive of diffuse alveolar hemorrhage (DAH). Her repeat coagulation studies were normal. Her saturation started improving over 2 weeks with the continuation of hemodialysis, plasma exchanges, immunosuppressive drugs, and other supportive measures. Urine output started improving after 4 weeks, and she became dialysis independent thereafter. There was no evidence of MAHA and thrombocytopenia on PBS after 3 months. Heparin was switched to warfarin after 2 months and was stopped after

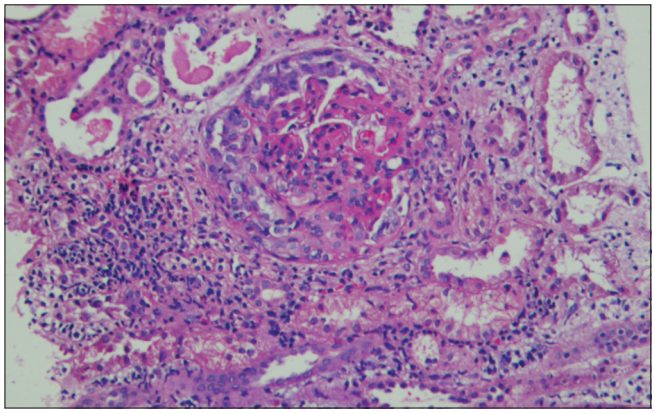

Figure 1: Glomerulus reveals circumferential active cellular crescent, with proliferative component and wire-loop lesions in the underlying tufts. Adjacent tubules show moderate degree of acute tubular injury and scattered lymphoplasmacytic infiltrates in the interstitium (PAS, 20×)

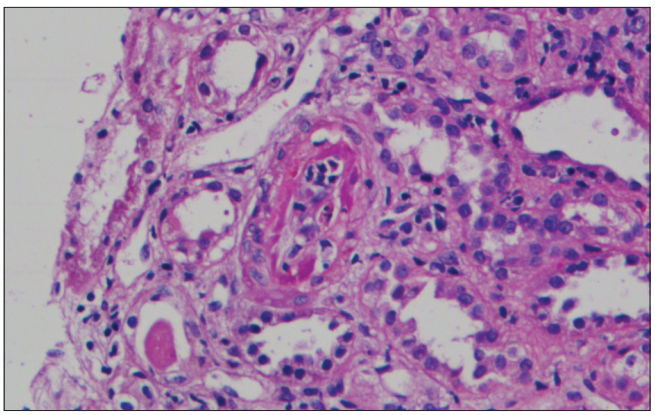

Figure 2: Interlobular artery revealing vascular lesions, in the form of eosinophilic deposits in the intimal aspect, in the presence of inflammatory cell infiltrates (PAS, 40×)

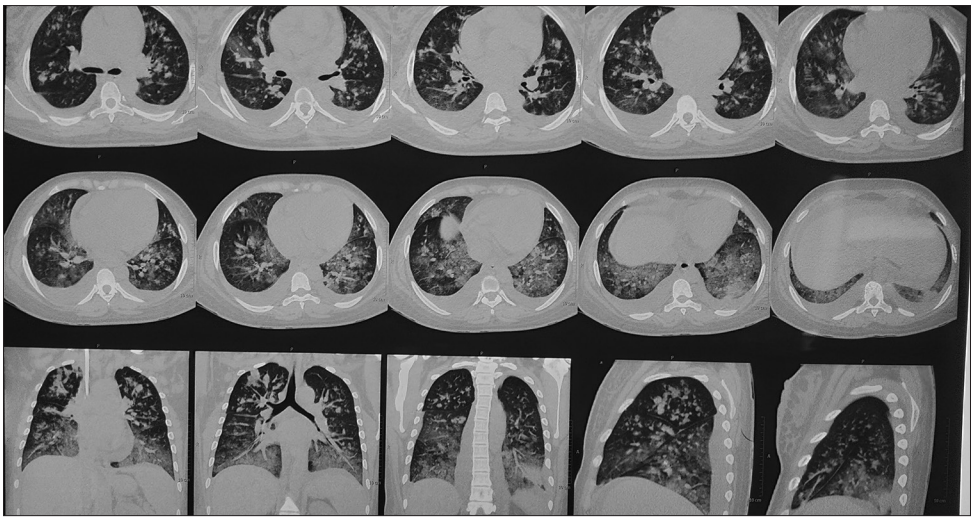

Figure 3: Non-contrast computed tomography (NCCT) chest showing multifocal patchy areas of consolidation with diffuse ground glass opacities in bilateral lungs, suggesting diffuse alveolar hemorrhage

about 6 months once serum albumin became normal. Six months after presentation, she had attained near-normal renal function (serum creatinine 1.1 mg/dL), normal serum albumin (3.8 gm/dL), no ascites but had persisting sub-nephrotic range proteinuria (24 h urinary protein 800 mg), and microscopic hematuria (3–4 RBCs/HPF). Her anti-ds DNA antibody was still positive with a normal complement level. Repeat antiphospholipid antibody work up at 12 weeks was negative. She is at present on steroid 10 mg/day (0.15mg/kg/day), mycophenolate mofetil (1 gm twice a day), tab furosemide 20 mg + tab spironolactone 50 mg once a day, tab telmisartan 40 mg twice a day, tab HCQ 300 mg/day, and calcium supplements.

Discussion

The presentation of SLE as rapidly progressive glomerulonephritis (RPGN) in the postpartum period is difficult to diagnose as hypertension, proteinuria, and renal dysfunction may present in postpartum preeclampsia too. Active lupus nephritis at the time of conception poses the greatest risk for disease flares and poor obstetric outcomes. In the PROMISSE (Predictors of Pregnancy Outcome: Biomarkers in Antiphospholipid Antibody Syndrome and Systemic Lupus Erythematosus) study, a prospective, multiethnic, multiracial cohort of pregnant SLE patients with inactive or stable mild disease activity at baseline, only 2.5 and 3.0% of patients had severe flares during the second trimester and third trimester, respectively, mostly consisting of nephritis, pleuritis, and arthritis.[2] Postpartum flares were studied in the PROMISSE cohort in 234 patients with study visits 2–6 months postpartum and only 1.7% of patients had severe lupus flares.[3] Based on these results,[3-6] it can be inferred that in patients with inactive or stable mild disease at conception, lupus disease flares during and after pregnancy are mostly mild. In the index patient, the lady with no past history of SLE was asymptomatic during her pregnancy and one month postpartum suggesting no disease activity.

The renal biopsy also had features suggestive of lupus vasculitis in this case. The renal survival rates are significantly different between the groups with and without renal vascular lesions, in which the TMA group shows the poorest renal outcome.[2,7] The rationale for the use of plasmapheresis for vascular injury, in this case, is supported by the literature.[8] Sudden onset AKI, especially when associated with anuria during the postpartum period, also supports complement-mediated TMA. However, improvement in renal function with immunosuppression and plasma exchanges favored the diagnosis of lupus TMA. In the index case, IVIG was used empirically a second time, due to worsening disease activity including crescentic LN and lupus TMA.

SLE may be associated with the development of DAH syndrome, which may be secondary to lupus vasculitis/pulmonary capillaritis.[9] In the index case, the presumptive diagnosis was made based on symptoms, radiological findings, and response to plasma exchange/immunosuppression. Patients with lupus have an increased risk for both arterial and/or venous thrombosis. Also, in the immediate postpartum period, there is a marked increase in some coagulation factors, reduced fibrinolysis, and increased platelet reactivity, which result in increased risk for thromboembolic complications. We have continued inj. UFH with close monitoring of APTT despite DAH and thrombocytopenia due to portal venous thrombosis and severe hypoalbuminemia in this case.

Different types of microangiopathies in pregnancy may mimic or overlap with lupus flares.[10] Thrombotic thrombocytopenic purpura (TTP) may occur rarely in conjunction with systemic lupus.[11,12] Severe renal

dysfunction requiring intermittent hemodialysis also does not favor the diagnosis of TTP.[11,12] This patient had achieved adulthood and two full-term pregnancies without a prior hint of TTP/hemolytic uremic syndrome (HUS), making the diagnosis of a hereditary form of TTP or atypical HUS less likely.

Conclusion

Postpartum lupus flare may present heterogeneously with multiple organ involvement and with varying severity. An aggressive approach to crescentic LN with lupus TMA and vasculitis is needed to facilitate a timely diagnosis and treatment to prevent long-term complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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