

Neuropsychiatric and Mucocutaneous Manifestations of De Novo Postpartum SLE: A Diagnostic Challenge

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Introduction

Systemic Lupus Erythematosus (SLE) is a chronic, multisystem autoimmune disorder characterized by a highly variable clinical presentation and a relapsing-remitting course. The diagnosis of SLE can be exceptionally challenging when its initial manifestations mimic other acute etiologies, particularly during the postpartum period when profound physiological and neuroendocrine shifts frequently obscure autoimmune pathology. Furthermore, the concurrent presentation of an active SLE flare with severe adverse drug reaction (ADR) mimics and hepatic injury creates a convoluted clinical scenario demanding rapid differentiation and multidisciplinary management.

We report the case of a 24-year-old postpartum female who initially presented with delayed new-onset seizures, subsequently evolving over a three-month period into a severe multisystem crisis characterized by pancytopenia, acute hepatic injury, and generalized pan-epidermolysis. This case underscores the profound diagnostic complexities of SLE when masked by polypharmacy and postpartum physiological changes, specifically highlighting the imperative of differentiating an acute lupus flare from severe obstetric and iatrogenic complications.

Case Presentation

A 24-year-old female (obstetric score P2L2) presented to a tertiary care centre with a progressive, three-month history of a generalized pruritic rash and painful oral ulcers resulting in severe dysphagia. Patient also complains of right ankle pain since 1 week.

The patient's clinical trajectory began on postoperative day (POD) 34 following an emergency repeat lower segment cesarean section. She was admitted at that time for acute-onset involuntary limb movements, tongue biting, altered behaviour, and hallucinations. Despite a history of gestational hypertension, neuroimaging (CT and contrast-enhanced MRI) revealed no significant parenchymal abnormalities, effectively ruling out Posterior Reversible Encephalopathy Syndrome (PRES). She was managed empirically for late postpartum eclampsia versus encephalitis with the Zuspan regimen of magnesium sulfate, levetiracetam, and antimicrobials. She stabilized without further seizure activity and was discharged.

Interval outpatient investigations one month later revealed low blood cell counts and altered renal parameters. Three weeks prior to her current admission, she developed high-grade fever, progressive jaundice, and a generalized rash. She was prescribed unstandardized hepatoprotective agents and antimicrobials at a local clinic for suspected viral hepatitis. Serial investigations demonstrated worsening thrombocytopenia (platelets declining to 89,000/mm³) and persistent hyperbilirubinemia. Viral hepatitis and HIV serologies were negative.

Upon admission, examination revealed marked pallor, icterus, and diffuse erythematous purpuric macules progressing to plaques with crusting over the face, neck, trunk, and thighs. She exhibited diffuse alopecia, facial edema, and severe generalized oral mucosal ulcerations with active bleeding.

Laboratory evaluation confirmed severe pancytopenia (hemoglobin 7.7 g/dL, leukocytes 3,200 cells/mm³, platelets 69,000/mm³), acute transaminitis (AST 233 U/L, ALT 150 U/L, ALP 643 U/L), hypoalbuminemia, and nephrotic-range proteinuria (Spot UPCr: 3.64). Autoimmune screening demonstrated a strongly positive ANA (1:1000, homogeneous), alongside pathognomonic SLE markers: anti-dsDNA (>800 IU/mL) and anti-Sm (98.96 RU/mL). Profound hypocomplementemia was noted (C3: 30.23 mg/dL, C4: 4.66 mg/dL). A perilesional skin punch biopsy revealed epidermal separation with necrosis and a dermal mixed inflammatory infiltrate with eosinophils. Patient was diagnosed with Systemic lupus erythematosus manifesting with neuropsychiatric SLE,

musculoskeletal SLE, mucocutaneous lupus erythematosus, renal lupus nephritis, lupus hepatitis, and severe pancytopenia.

The patient was aggressively managed with pulse intravenous methylprednisolone (1 g/day for 3 days), transitioning to oral prednisolone, hydroxychloroquine, and mycophenolate mofetil. Following targeted immunosuppression, she demonstrated rapid clinical improvement, progressive resolution of mucocutaneous lesions, and stabilization of hematological and hepatic indices.

Discussion

The presentation of SLE in the puerperium as a multisystem crisis is a complex diagnostic challenge. Diagnostic complications in this patient were multifactorial, driven by anchoring bias toward obstetric complications, confounding polypharmacy, hiding the autoimmune pathology by the physiological hyperdynamic state of recent pregnancy.[1]

Diagnostic Masking and the Assessment of Disease Ominosity

The severity of the index patient's multisystem flare can be objectively quantified utilizing the 2019 EULAR/ACR classification criteria.[2] The patient's accumulated score of 29 points, driven by seizures, severe cytopenias, nephrotic-range proteinuria, acute cutaneous manifestations, and extreme immunological derangement—firmly places her in the highest echelon of disease "ominosity." This threshold strongly predicts a higher probability of cumulative major organ involvement, accelerated damage accrual, and increased mortality.[2]

Neuroendocrine Pathogenesis of the Postpartum SLE Flare

The postpartum period is recognized as a window of extreme vulnerability for autoimmune exacerbation. The abrupt expulsion of the placenta results in a precipitous withdrawal of immunoregulatory steroid hormones, initiating a sudden restoration of Th1/Th17 inflammatory pathways.[3] Concurrently, the onset of lactation is driven by a massive surge in prolactin (PRL). Hyperprolactinemia actively subverts peripheral B-cell tolerance, rescuing autoreactive B cells from apoptosis and driving the aberrant expansion of follicular T helper cells, ultimately triggering a massive surge in pathogenic IgG3 anti-dsDNA autoantibodies.[4]

Neuropsychiatric SLE (NPSLE) Versus Late Postpartum Eclampsia

The initial clinical misstep occurred on POD 34 when the patient's new-onset seizures were empirically managed as eclampsia. Eclampsia is driven by placental ischemia and the release of anti-angiogenic factors (e.g., sFlt-1); therefore, the vast majority of eclamptic seizures occur within 48 hours postpartum.[5,6] A neurological event occurring beyond 28 days postpartum exceeds the physiological half-life of these factors and is temporally incompatible with eclampsia, mandating evaluation for NPSLE. NPSLE pathogenesis involves microvascular thrombosis and direct neurotoxicity occurring when autoantibodies breach the blood-brain barrier.[7] Brain MRI is normal in approximately 50% of patients with NPSLE. Radiographic abnormalities, when present, can be classified into vascular or inflammatory phenotypes. Vascular pathology, the predominant subtype, is largely driven by small vessel disease (presenting as small white matter hyperintensities, lacunar infarcts, microhaemorrhages, and cortical atrophy), whereas large-vessel territorial infarcts are relatively rare. Inflammatory lesions occur infrequently and are characterised by poorly marginated, medium-to-large T2/FLAIR hyperintensities that span grey or white matter irrespective of vascular boundaries, occasionally demonstrating mass effect.[8] While this patient lacked structural inflammatory or vascular lesions on MRI, her clinical presentation combined with massive autoantibody titres ultimately confirmed the neuropsychiatric involvement.

Cutaneous Lupus Erythematosus Versus Severe Adverse Drug Reactions

Three months following her neurological presentation, the patient developed pan-epidermolysis. Given her exposure to polypharmacy, standard histology suggesting epidermal separation initially prompted a diagnosis of severe ADR (e.g., Toxic Epidermal Necrolysis). However, massive serological activity confirmed TEN-like lupus erythematosus (acute syndrome of apoptotic pan-epidermolysis).[9]

Pathophysiological Distinctions

True TEN is a cell-mediated hypersensitivity reaction triggered by specific medications, resulting in a clonal expansion of CD8+ T cells that release cytotoxic granulysin.[10] Conversely, TEN-like LE is an exacerbation of

underlying SLE, typically triggered by UV light or systemic flares, wherein impaired clearance of apoptotic keratinocytes leads to massive immune complex deposition and complement-mediated cytotoxicity.[9]

Clinical and Histopathological Differentiation

True TEN progresses acutely over hours to days, whereas TEN-like LE frequently exhibits a subacute progression over days to weeks. Histologically, true TEN exhibits full-thickness epidermal necrosis with a characteristically sparse dermal infiltrate. TEN-like LE features intense vacuolar interface dermatitis and abundant dermal mucin. Crucially, Direct Immunofluorescence (DIF)—the Lupus Band Test—is uniformly negative in true TEN, whereas TEN-like LE demonstrates continuous, granular deposits of immunoglobulins and C3 along the basement membrane zone.

Differentiating Hepatic Involvement in the Multisystem Crisis

The patient's acute transaminitis required rigorous differentiation among three primary entities to guide therapy.

Drug-Induced Liver Injury (DILI)

DILI is a diagnosis of exclusion linked to a clear timeline of hepatotoxic drug exposure (e.g., unstandardized antimicrobials in this patient). Histologically, it presents variably but frequently features centrilobular necrosis and scattered eosinophils. It typically resolves upon withdrawal of the offending agent.[11]

Autoimmune Hepatitis (AIH)-SLE Overlap Syndrome

AIH is a distinct, progressive disease defined by the presence of Anti-Smooth Muscle Antibodies (ASMA $\geq 1:80$) or Anti-LKM1, alongside profound hyper-IgG. Liver biopsy confirms the diagnosis by demonstrating dense portal lymphoplasmacytic infiltrates, interface hepatitis, and hepatocellular rosetting, requiring targeted hepatospecific immunosuppression to prevent cirrhosis.[12]

Lupus Hepatitis (LH)

LH is intrinsic hepatic inflammation caused by the SLE disease process itself, characterized by generic SLE markers and a specific association with anti-ribosomal P antibodies. Histologically, it shows non-specific reactive changes and mild lobular inflammation. Given the patient's severe hypocomplementemia and multisystem crisis, her transaminitis overwhelmingly represents LH, which, unlike AIH, responds briskly to the systemic corticosteroids utilized for the primary SLE flare.[13]

Given the patient's immense SLE disease activity score (EULAR/ACR ≥ 29), the AST/ALT elevations >150 U/L most likely represent acute Lupus Hepatitis occurring as a component of the profound systemic inflammatory response. While transient DILI cannot be entirely excluded without a definitive liver biopsy, the expected absence of specific AIH markers (such as SMA or anti-LKM1) firmly pushes the clinical diagnosis toward LH, justifying the use of high-dose pulse methylprednisolone without the immediate need for liver-specific adjunctive therapies.

Nephrotic-Range Proteinuria and Lupus Nephritis

A Urine Protein Creatinine Ratio of 3.64 strongly correlates with severe, immune complex-mediated Lupus Nephritis (LN). The pathogenesis involves in situ immune complex formation triggering complement cascade activation. During early postpartum stages, maternal hyperfiltration physiology can effectively mask the early stages of LN until it rapidly breaches the nephrotic threshold.[5]

Severe Pancytopenia and Hematological Collapse

Severe pancytopenia in highly active SLE results from both peripheral antibody-mediated destruction and central bone marrow suppression driven by a cytokine storm.[14] In a postpartum patient presenting with pancytopenia and acute transaminitis, secondary Macrophage Activation Syndrome (MAS) must also be considered. In the index patient, Serum Ferritin levels of 1 ng/mL rules out the possibility of MAS.[15]

Conclusion

The postpartum period represents a window of extreme immunological vulnerability, capable of triggering fulminant, de novo manifestations of Systemic Lupus Erythematosus. This case vividly illustrates the profound diagnostic challenges encountered when massive autoimmune flares are obscured by obstetric anchoring bias and extensive polypharmacy. A high index of clinical suspicion, precise interpretation of histopathology, and a

coordinated multidisciplinary approach are essential to accurately differentiate true SLE activity from obstetric or iatrogenic mimics, thereby preventing irreversible end-organ morbidity.

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Fig 1: Clinical picture of the patient on presentation (A) and after 5 days of pulse dose of steroids (B,C).

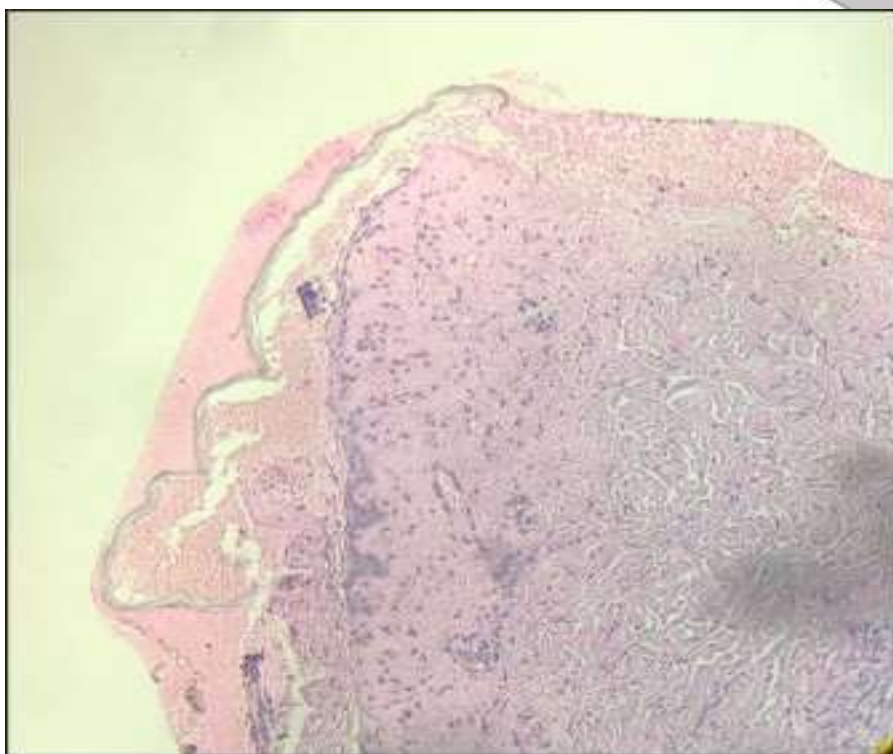


Fig 2: Punch biopsy of skin showing epidermal separation with necrosis and Dermal mixed inflammatory infiltrate with eosinophils.