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CASE REPORT

Severe preeclampsia in a patient with "Autoimmune Overlap": a case report

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Abstract

Objective: Introduction: Systemic lupus erythematosus and systemic sclerosis are autoimmune connective tissue diseases characterized by marked clinical heterogeneity and the potential for significant multiorgan involvement. Overlap syndromes represent a complex clinical entity, defined by the coexistence of clinical and immunological criteria of two or more rheumatologic diseases, either simultaneously or sequentially. In the context of pregnancy, these conditions are associated with a substantially increased risk of both maternal and perinatal complications, posing important diagnostic and therapeutic challenges.

Case presentation: A 26-year-old woman with a prior diagnosis of overlap syndrome between systemic lupus erythematosus and systemic sclerosis, who was 28 weeks pregnant. During the course of her pregnancy, she developed severe preeclampsia requiring urgent delivery by cesarean section. Despite the complexity of the clinical scenario, both maternal and neonatal outcomes were favorable.

Conclusions: Pregnancy in SLE–systemic sclerosis overlap requires individualized risk assessment before conception, careful evaluation of renal and cardiopulmonary involvement, continuation of pregnancy-compatible therapy, close monitoring for preeclampsia versus autoimmune renal disease, and coordinated care between rheumatology, maternal-fetal medicine, cardiology/pulmonology, and neonatology

Key words: Systemic sclerosis, Overlap, systemic lupus erythematosus, pregnancy, preeclampsia.

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Introduction

Autoimmune diseases comprise a heterogeneous and complex group of disorders resulting from the interplay of genetic, epigenetic, environmental, and immunological factors[1]. Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disease characterized by the production of autoantibodies directed against nuclear components, leading to immune-mediated inflammatory damage and highly heterogeneous clinical manifestations. Its incidence and prevalence are significantly higher among women of reproductive age [2]. Pregnancy and the postpartum period in patients with SLE are associated with an increased risk of disease flares compared with the general population, with reported rates ranging from 25% to 60% [3]. Disease activity within the six months preceding conception is a key predictor of flare occurrence, as well as of flare phenotype and organ involvement. Accordingly, maternal and fetal outcomes are more favorable when the disease has remained quiescent for at least six months prior to conception [4].

Maternal complications associated with SLE include renal and hematologic involvement, thrombotic events, multiorgan dysfunction, hypertension, preeclampsia, eclampsia, and maternal mortality. Adverse perinatal outcomes include miscarriage, fetal death, preterm delivery, and intrauterine growth restriction, among others [4]. With regard to treatment, continuation of hydroxychloroquine during pregnancy is recommended unless contraindicated, and the use of low-dose acetylsalicylic acid initiated at the end of the first trimester is advised to reduce the risk of preeclampsia [3,4].

Systemic sclerosis (SSc) is a chronic autoimmune disease of unknown etiology, characterized by progressive fibrosis and microvascular dysfunction. Clinically, it presents with skin thickening, musculoskeletal abnormalities, and multiorgan involvement, particularly affecting the gastrointestinal tract and lungs [5]. The estimated prevalence of 17.6 cases per 100,000, predominantly in women of reproductive age. Mortality remains high, primarily due to interstitial lung disease and pulmonary arterial hypertension [6]. Diagnosis is based on the classification criteria established by the American College of Rheumatology and the European League Against Rheumatism (ACR/EULAR), which include skin thickening, Raynaud's phenomenon, the presence of disease-specific autoantibodies—such as anticentromere, anti-topoisomerase I (anti-Scl-70), and anti–RNA polymerase III—and characteristic findings on nailfold capillaroscopy, in addition to a systematic assessment of target organ involvement. Current therapeutic strategies are tailored according to organ involvement and include immunosuppressive agents such as mycophenolate

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and cyclophosphamide, antifibrotic therapies, vasodilators for the management of pulmonary hypertension, and comprehensive supportive care [5,6].

Pregnant women with systemic sclerosis are at increased risk of complications, including scleroderma renal crisis, pulmonary hypertension, intrauterine growth restriction, preterm delivery, and fetal loss. Therefore, preconception counseling, thorough cardiopulmonary and renal evaluation, and multidisciplinary management are strongly recommended. Potentially teratogenic medications should be discontinued prior to conception [7]

A subset of patients with rheumatologic diseases may develop overlap syndromes, characterized by the coexistence of clinical and immunological criteria that allow the diagnosis of two or more connective tissue diseases, either concurrently or sequentially, which may hinder timely recognition and management. The prevalence of these syndromes ranges from 10% to 38.3% [8].

Flares of SLE and scleroderma renal crisis during pregnancy represent significant diagnostic challenges, as it is essential to distinguish disease-related manifestations from physiological changes of pregnancy and obstetric complications such as preeclampsia [3].

The aim of this case report is to describe a case of severe preeclampsia associated with an autoimmune overlap syndrome and to emphasize the importance of comprehensive clinical assessment, accurate diagnosis, multidisciplinary management, and close follow-up in order to reduce maternal and neonatal morbidity and mortality.

Case Presentation

A 26-year-old primigravid woman (G1P0A0) with an unplanned pregnancy and a history of systemic lupus erythematosus (SLE)–diffuse systemic sclerosis (dcSSc) overlap syndrome was admitted at 28 weeks of gestation because of progressive bilateral lower-extremity edema and newly diagnosed hypertension.

At the time of conception, the patient had a known diagnosis of SLE–dcSSc overlap syndrome complicated by biopsy-proven class V lupus nephritis (membranous lupus nephropathy), autoimmune hemolytic anemia, and nephrotic syndrome. The disease had remained clinically stable for approximately two years before conception, without documented lupus flares, progression of systemic sclerosis, deterioration of renal function, or significant changes in baseline proteinuria.

Maintenance treatment before and during pregnancy consisted of hydroxychloroquine 200 mg daily, azathioprine 50 mg twice daily, folic acid supplementation, and low-dose aspirin (100 mg/day). Pre-pregnancy blood pressure was 120/70 mmHg. Blood pressure remained within normal limits during the first and second trimesters (110/70 mmHg and 114/68 mmHg, respectively).

Autoimmune serology revealed positive antinuclear antibodies (ANA, 1:320 homogeneous pattern), anti-double-stranded DNA antibodies, anti-Smith antibodies, and anti-Scl-70 antibodies. Anticentromere antibodies, anti-RNA polymerase III antibodies, anti-Ro/SSA, anti-La/SSB, lupus anticoagulant, anticardiolipin antibodies, and anti-β2 glycoprotein I antibodies were negative.

The patient had chronic nephrotic-range proteinuria (approximately 7 g/24 h), preserved renal function, and no evidence of active urinary sediment before or during pregnancy. Renal biopsy had previously demonstrated class V lupus nephritis. Preconception serum albumin was 3.9 g/dL and remained stable during gestation (3.8 g/dL). Urinalysis showed no hematuria, leukocyturia, or urinary casts.

Regarding systemic sclerosis, the patient had diffuse cutaneous involvement with sclerodactyly and characteristic facial skin changes. She had no history of Raynaud phenomenon, digital ulcers, interstitial lung disease, pulmonary arterial hypertension, gastrointestinal complications, or cardiac involvement. Echocardiography demonstrated normal ventricular function without pulmonary hypertension or valvular abnormalities. Pulmonary function testing was not available.

Serial fetal growth assessments and Doppler studies were performed throughout pregnancy. First-trimester ultrasound demonstrated normal fetal anatomy, normal nuchal translucency, and positive fetal cardiac activity. Doppler studies during the first and second trimesters were normal, without increased uteroplacental resistance or uterine artery notching.

At 28 weeks of gestation, the patient presented with progressive lower-extremity edema and blood pressure of 150/100 mmHg. She denied headache, visual disturbances, epigastric pain, right upper quadrant pain, chest pain, dyspnea, neurological symptoms, or decreased fetal movements. Physical examination revealed bilateral grade II lower-extremity edema. Oxygen saturation remained within normal limits throughout hospitalization.

Initial laboratory evaluation demonstrated elevated liver enzymes (AST 77.4 U/L; ALT 87.8 U/L), preserved renal function (serum creatinine 0.38 mg/dL), serum uric acid of 6.2 mg/dL, normal platelet count (259×10^9/L), stable nephrotic-range proteinuria (7.12 g/24 h), normal complement levels (C3 103.8 mg/dL; C4 24.2 mg/dL), and absence of active urinary sediment. Anti-dsDNA levels remained stable and no clinical evidence of lupus flare was identified (table 1).

Obstetric ultrasound at admission showed a male fetus with an estimated fetal weight of 907 g (approximately 10th–15th percentile for gestational age), normal amniotic fluid volume, and a posterior placenta. Doppler evaluation demonstrated increased uteroplacental vascular resistance and abnormal uterine artery Doppler findings without evidence of fetal hemodynamic redistribution. Umbilical artery Doppler showed increased placental resistance.

The differential diagnosis included severe preeclampsia, lupus nephritis flare, HELLP syndrome, and scleroderma renal crisis. Stable proteinuria, preserved renal function,

Table 1. Laboratory follow-up.

Parameter	Pre-pregnancy	15 days before admission	Admission (Day 0)	Day 1	Day 2	Day 5	Day 8
Hemoglobin (g/dL)	13.2	11.2	10.3	10.6	10.0	9.9	10.4
Hematocrit (%)	42	34	22.9	33	29	29.2	29.3
White blood cells (/μL)	5,400	4,800	6,340	6,530	7,410	6,270	5,450
Platelets (/μL)	228,000	239,000	259,000	225,000	236,000	295,000	278,000
Reticulocytes (%)	—	—	1.2	—	—	—	—
Proteinuria (g/24 h)	7.0	7.2	7.12	—	—	—	—
Total/Direct/Indirect Bilirubin (mg/dL)	0.48 (0.12/0.36)	0.7 (0.2/0.5)	0.68 (0.16/0.52)	—	—	0.9 (0.2/0.7)	—
Lactate dehydrogenase (U/L)	—	182	286	237	291	249	192
AST/ALT (U/L)	22/35	19.5/26.71	77.47/87.8	89.1/105	97.3/116	34.3/42.8	19.5/26.79
Creatinine (mg/dL)	0.35	0.42	0.38	0.45	0.35	0.34	0.39
Blood urea nitrogen (mg/dL)	12	15.5	8.5	16.3	11	8.9	8.1
Complement levels	C3: 117, C4: 28	—	C3: 103.8, C4: 24.2	—	—	—	—
anti-dsDNA /ELISA	< 30 UI/mL		< 30 UI/mL				
Anti-Ro/SSA / Anti-La/SSB	Negative						

Abbreviations: AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH: lactate dehydrogenase; BUN: blood urea nitrogen; C3/C4: complement components.
Note: (—) indicates data not available.

normal complement levels, absence of active urinary sediment, negative antiphospholipid antibodies, and lack of evidence of microangiopathic hemolysis argued against lupus nephritis flare, antiphospholipid syndrome, HELLP syndrome, and scleroderma renal crisis.

Based on the development of hypertension after 20 weeks of gestation, progressive elevation of liver enzymes, elevated serum uric acid levels, abnormal uteroplacental Doppler findings, and exclusion of alternative diagnoses, a diagnosis of preeclampsia with severe features was established.

The patient received magnesium sulfate for seizure prophylaxis, nifedipine for blood pressure control, antenatal betamethasone for fetal lung maturation, and continued treatment with hydroxychloroquine and azathioprine. Despite conservative management, liver enzyme levels continued to increase. After completion of the corticosteroid course, cesarean delivery was performed at 28 weeks of gestation because of progressive maternal biochemical deterioration and concern for worsening preeclampsia.

A male neonate weighing 942 g was delivered with Apgar scores of 6 and 7 at one and five minutes, respectively. The newborn required endotracheal intubation for five days because of respiratory distress syndrome and was admitted to the neonatal intensive care unit (NICU). After a 72-day NICU stay, the infant was discharged alive in good clinical condition with a body weight of 2108 g.

The maternal postpartum course was favorable. Liver enzyme levels progressively normalized, renal function remained stable, and proteinuria returned to baseline levels. The patient was discharged on postoperative day eight with hydroxychloroquine, azathioprine, folic acid supplementation, and antihypertensive therapy (table 2).

Table 2. Clinical timeline

Gestational Age	Clinical Findings	Laboratory Findings	Fetal Assessment	Treatment
Preconception	Stable overlap syndrome	Chronic proteinuria (~7 g/24 h), normal renal function	—	HCQ + AZA
First trimester	Stable disease	No flare	Normal ultrasound, normal NT	HCQ + AZA + ASA
Second trimester	Stable disease	Normal complement, stable proteinuria	Normal Doppler studies	HCQ + AZA + ASA
28 weeks	Edema, hypertension (150/100 mmHg)	Elevated AST/ALT, normal creatinine, normal C3/C4	EFW 907 g (10–15th percentile), abnormal uterine Doppler	MgSO4, nifedipine, betamethasone
28 weeks	Maternal deterioration	Progressive liver enzyme elevation	No fetal redistribution	Cesarean section
Postpartum	Clinical improvement	Normalization of AST/ALT	NICU stay	Follow-up

Abbreviations: EFW: Estimated Fetal Weight AST: aspartate aminotransferase; ALT: alanine aminotransferase; NICU: neonatal intensive care unit; HCQ: hydroxychloroquine; AZA: azathioprine ASA: aspirin
Note: (—) indicates data not available.

Discussion

Pregnancy in women with systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) remains a high-risk clinical scenario despite advances in multidisciplinary management. Both diseases are associated with increased maternal and fetal morbidity, including hypertensive disorders of pregnancy, fetal growth restriction, preterm birth, and disease-related complications [3,4,6]. The coexistence of both conditions as an overlap syndrome is uncommon and poses additional diagnostic and therapeutic challenges because manifestations of autoimmune disease activity may mimic obstetric complications [7,8].

The present case is particularly relevant because it involved a patient with SLE–diffuse systemic sclerosis overlap syndrome complicated by biopsy-proven class V lupus nephritis and chronic nephrotic-range proteinuria. Although the pregnancy was unplanned, the disease had remained clinically stable for approximately two years before conception, with preserved renal function, stable proteinuria, and no evidence of active lupus nephritis. This favorable baseline status may have contributed to the satisfactory maternal outcome despite the subsequent development of severe preeclampsia.

One of the most challenging aspects of this case was differentiating preeclampsia from active lupus nephritis. Both conditions may present with hypertension and proteinuria

during pregnancy, making diagnosis particularly difficult in patients with pre-existing renal disease [9,10]. In our patient, several findings argued against active lupus nephritis. She had biopsy-proven class V lupus nephritis with long-standing nephrotic-range proteinuria that remained stable throughout pregnancy and hospitalization. In addition, renal function remained preserved, complement levels were within normal limits, anti-dsDNA levels showed no evidence of increased activity, and urinalysis demonstrated no active urinary sediment. Furthermore, serum albumin levels remained stable throughout pregnancy. Collectively, these findings support the interpretation that the observed proteinuria reflected chronic residual renal involvement rather than active immune-mediated nephritis [9,10].

The presence of diffuse systemic sclerosis further complicated the differential diagnosis because the onset of hypertension during pregnancy raises concern for scleroderma renal crisis, one of the most severe complications of systemic sclerosis. Scleroderma renal crisis is typically characterized by abrupt severe hypertension, rapidly progressive renal dysfunction, and frequently thrombotic microangiopathy [5,6]. Although our patient had diffuse cutaneous systemic sclerosis and positive anti-Scl-70 antibodies, renal function remained stable throughout hospitalization, platelet counts were preserved, and there was no evidence of microangiopathic hemolytic anemia. In addition, anti-RNA polymerase III antibodies, which have been strongly associated with an increased risk of scleroderma renal crisis, were negative. Therefore, this diagnosis was considered unlikely [5,6].

HELLP syndrome was also considered because of the progressive elevation of liver enzymes. However, normal platelet counts, absence of significant hemolysis, stable bilirubin levels, and preserved renal function did not support this diagnosis [10,11]. Similarly, antiphospholipid syndrome-related obstetric complications were considered unlikely because lupus anticoagulant, anticardiolipin antibodies, and anti-β2 glycoprotein I antibodies were negative [3,9].

Conversely, several clinical and laboratory findings supported the diagnosis of preeclampsia with severe features (table 3). The patient developed new-onset hypertension after 20 weeks of gestation, progressive elevation of liver enzymes, elevated serum uric acid levels, and abnormal uteroplacental Doppler findings suggestive of placental dysfunction. Although the recorded blood pressure values did not reach the threshold typically associated with severe hypertension, progressive hepatic involvement together with worsening maternal laboratory abnormalities fulfilled criteria for preeclampsia with severe features and prompted delivery [10,11]. Moreover, liver enzyme abnormalities improved following delivery, while renal function remained stable, further supporting preeclampsia as the primary diagnosis.

Table 3. Differential diagnosis of hypertensive and renal complications during pregnancy

Feature	Severe Preeclampsia	Lupus Nephritis Flare	HELLP Syndrome	Scleroderma Renal Crisis	Present Case
New-onset hypertension	Yes	Possible	Yes	Yes	Yes
Elevated AST/ALT	Yes	Rare	Yes	Rare	Yes
Stable proteinuria	Yes	No	Variable	Variable	Yes
Low complement levels	No	Yes	No	No	No
Active urinary sediment	No	Yes	No	Variable	No
Thrombocytopenia	Variable	Variable	Yes	Variable	No
Renal dysfunction	Variable	Common	Variable	Common	No
Improvement after delivery	Yes	No	Yes	No	Yes

Current EULAR recommendations emphasize preconception counseling, continuation of hydroxychloroquine during pregnancy, and individualized risk assessment based on disease activity, nephritis history, complement levels, anti-dsDNA antibodies, anti-Ro/SSA and anti-La/SSB antibodies, antiphospholipid antibody status, hypertension, and major organ involvement [5,9]. Although the present pregnancy was unplanned, conception occurred during a period of relative disease quiescence, characterized by stable renal function, absence of active urinary sediment, and no evidence of progressive systemic sclerosis. This observation reinforces the importance of disease control before conception whenever possible.

From an obstetric perspective, fetal surveillance played a central role in clinical decision-making. Serial ultrasound examinations demonstrated normal fetal development during the first and second trimesters, whereas third-trimester Doppler studies revealed increased uteroplacental vascular resistance. Current recommendations support serial fetal growth assessment and Doppler surveillance in pregnancies complicated by autoimmune diseases because of the increased risks of placental insufficiency, fetal growth restriction, stillbirth, and preterm delivery [3,4]. Although the estimated fetal weight of 907 g at 28 weeks corresponded approximately to the 10th percentile for gestational age and did not definitively meet criteria for fetal growth restriction, abnormal Doppler findings suggested progressive placental dysfunction and increased fetal risk.

The decision to terminate the pregnancy at 28 weeks of gestation was based primarily on progressive maternal biochemical deterioration despite antihypertensive treatment and completion of antenatal corticosteroid therapy. Although expectant management may be considered in selected cases of early-onset preeclampsia, worsening liver

enzyme abnormalities raised concern for disease progression and justified delivery [10,11]. Cesarean section was selected to expedite pregnancy termination and optimize maternal safety in the context of severe preeclampsia and extreme prematurity.

The neonatal outcome reflected the expected consequences of extreme prematurity. The infant required endotracheal intubation for five days, respiratory support, and prolonged neonatal intensive care. Nevertheless, survival to discharge after 72 days of hospitalization with a discharge weight of 2108 g represents a favorable outcome considering the gestational age at delivery and the complexity of the maternal disease. In addition, the absence of anti-Ro/SSA and anti-La/SSB antibodies reduced the risk of neonatal lupus and congenital heart block [3,4].

This case highlights the importance of multidisciplinary collaboration in the management of pregnancies complicated by autoimmune overlap syndromes. Careful interpretation of clinical findings, serological markers, renal parameters, and obstetric assessments is essential to differentiate preeclampsia from autoimmune disease activity and to guide timely intervention. Additional reports of pregnancies complicated by SLE–diffuse systemic sclerosis overlap syndrome are needed to improve risk stratification and optimize evidence-based management strategies for these rare but clinically challenging cases.

Conclusion

Pregnancy in SLE–systemic sclerosis overlap requires individualized risk assessment before conception, careful evaluation of renal and cardiopulmonary involvement, continuation of pregnancy-compatible therapy, close monitoring for preeclampsia versus autoimmune renal disease, and coordinated care between rheumatology, maternal-fetal medicine, cardiology/pulmonology, and neonatology..

Authors' contributions

MMAJ (Conceptualization, Data curation, Investigation, Resources, Writing – original draft, Writing – review & editing)

WDEP (Conceptualization, Project administration, Resources, Supervision, Writing – original draft)

JAPO (Conceptualization, Data curation, Formal Analysis, Visualization, Supervision, Writing – original draft, Writing – review & editing)

Conflict of interest

None to declare..

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