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Case Report

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Lupus Nephritis Presenting with Preeclampsia

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Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multisystem involvement. The renal involvement of SLE may present with hematuria , proteinuria or acute kidney dysfunction. It is well established that pregnancy may trigger the disease activation in patients with SLE. Lupus nephritis (LN) may be diagnosed during pregnancy in very few patients. Preeclampsia is a pregnancy-related disorder characterized by maternal hypertension, proteinuria, and edema and is sometimes complicated by renal dysfunction, which usually occurs in the last trimester of pregnancy. However preeclampsia rarely occurs within 48 h of postpartum. In this report, we present the case of a 20-year-old patient with oliguria, proteinuria, edema, and hypertension who was diagnosed with preeclampsia starting at the 35th week of her first pregnancy. Acute kidney failure developed in the postpartum period after emergency cesarian delivery. Crescentic and diffuse LN was revealed by renal biopsy. While SLE is a risk factor for preeclampsia, LN should be considered in kidney failure in the third trimester or postpartum period.
Keywords: Pregnancy, preeclampsia, lupus nephritis

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease with multisystem involvement. Approximately 50% of patients with SLE may present with renal involvement. Renal involvement typically manifests as hematuria, proteinuria, or sudden onset renal dysfunction. In 1957, Muehrcke et al. (1) described lupus nephritis (LN) by kidney biopsy for the first time. LN is a serious but curable disease. Clinically, LN may also present with nephrotic syndrome, nephritic syndrome, or crescentic glomerulonephritis. Clinicopathologically, LN is classified into six types. The most frequent and the most severe prognosis is the form with diffuse proliferative glomerulonephritis (type IV) (2). Approximately 15%-25% of patients progress to end-stage renal disease within 10 years.

Several studies have demonstrated that pregnancy leads to the activation of this disease in women with SLE (3-6). Chronic LN, if activated during pregnancy, can lead to hypertension and renal failure, which can adversely affect the health of the mother and fetus. In rare cases, LN can be diagnosed during pregnancy. In particular, the clinical findings of patients who have not been previously diagnosed with LN may become apparent following activation during pregnancy. However, it is possible that the physiological changes related to pregnancy may mask some of the clinical presentations of LN including of proteinuria and edema. Otherwise, various diseases may cause renal dysfunction during pregnancy (4, 5). Among these, there are many possible causes of acute renal failure in pregnancy such as preeclampsia, hemolytic uremic syndrome, and perioperative complications (acute tubular necrosis) and rapidly progressive glomerulonephritis (2, 6). Preeclampsia is an important health problem that causes serious maternal and fetal complications in approximately 7%-10% of all pregnancies, mostly during the last trimester and rarely within 48 h postpartum. It is characterized by systemic vaso-

Table 1. Laboratory parameters of the patient at admission

Parameters	Value	Normal range
White blood cell (10^3/µL)	7.1	4.8-10.7
Hemoglobin (g/dL)	8.9	12-16
Platelets (10^3/µL)	204	130-400
Glucose (mg/dL)	110	74-106
BUN (mg/dL)	32	8-23
Creatinine (mg/dL)	1.82	0.7-1.20
Uric acid (mg/dL)	8.1	2.4-5.7
Calcium (mg/dL)	8.7	8.6-10.2
Phosphorus (mg/dL)	6.5	2.5-4.5
Magnesium (mmol/L)	1.2	0.66-1.77
Sodium (mmol/L)	136	136-145
Potassium (mmol/L)	6.03	3.5-5.1
Clor (mmol/L)	103	98-107
Total bilirubin (mg/dL)	0.15	0.2-1.2
Direct bilirubin (mg/dL)	0.09	0-0.3
GGT (U/L)	11	10-71
LDH (U/L)	411	135-225
AST (U/L)	39	0-40
ALT (U/L)	28	0-41
ALP (U/L)	151	40-130
Total protein (g/dL)	4.3	6.4-8.3
Albumin (g/dL)	2.1	3.5-5.2
PT (s)	10	10.1-14.9
APTT (s)	26	20-36
INR	0.89	0.8-1.2
UDT		
Protein (mg/dL)	100	0-10
Blood (ery/µL)	80	0-5
Leu (leu/µL)	29	0-10
Urine microscopy		
Erythrocyte (HPF)	80	0-3
Leukocyte (HPF)	29	0-5
Urine microprotein (mg/dL)	2950	28-217
Urine creatinine (mg/dL)	289	0-15

BUN: blood urea nitrogen; GGT: gamma-glutamyl transferase; LDH: lactate dehydrogenase; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; PT: prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; UDT: Urine dipstick test

spasm, maternal hypertension, proteinuria, edema, increased platelet aggregation, and decreased uteroplacental blood flow and is observed in the presence of placental tissue and resolves within a short time after birth. The pathophysiology of the disease are still unclear (7-9).

In this case report, we describe the case of a 20-year-old patient without a history of any disease who developed proteinuria, edema, and hypertension at 35 weeks of her first pregnancy. She underwent emergency cesarean section (C/S) due to preeclampsia, developed oliguria and renal dysfunction in the postpartum period, and was referred to our clinic. Subsequently, she was diagnosed with crescentic LN with renal biopsy.

CASE PRESENTATION

A 20-year-old woman without a history of kidney disease presented to a private hospital with elevated blood pressure and swelling of the lower limbs during 35th week of her first pregnancy. Emergency C/S was performed due to the diagnosis of preeclampsia. Patient's postoperative urine output decreased (200 cc in 12 h) and serum creatinine level increased to 1.8 mg/dL; so urinary system ultrasound was performed and ectasia was not detected in the pelvicalyceal system. Kidney sizes were reported within normal range. In the postoperative period, 40 mg furosemide was administered intravenously (iv) due to oliguria. She was transferred to the nephrology department of our university hospital in April 2017 with the preliminary diagnosis of oliguric acute renal failure. There were no complications such as perioperative bleeding, hypovolemia, and hypotension. There was no history of nonsteroidal anti-inflammatory drug use. Complaints of fatigue and oliguria were noted in the systemic query. On physical examination, her body temperature was 37.0°C, pulse rate was 112 beats/min, blood pressure was 130/80 mmHg, and respiratory rate was 22 breaths/min; decreased breathing sounds in the lower lung fields at the bottom of the rib cage was detected by auscultation and significant amount of ascites was detected in the abdomen and pretibial +++/+++ edema was detected in the examination of distal extremities. The laboratory test results are shown in Table 1.

Ten grams of proteinuria was detected in the spot urine microprotein/creatinine test. Microscopic examination of urinary sediment revealed dysmorphic erythrocytes, leukocyte casts , and granular casts. Urinary ultrasonography revealed that both kidney sizes were normal, parenchymal echoes increased to grade 1 in both kidneys without pelvicalyceal ectasia and stones, and intra-abdominal ascites was present. The patient's renal function tests deteriorated during the following days in the nephrology clinic. There were no abnormal results in the urine gram, and no bacteria were detected in urine culture. Diuretic treatment was initiated as the patient had increased pretibial edema, oliguric course, and hypervolemia. There was no response to diuretic treatment with furosemide. At the follow-up, the patient developed anuria and diuretic-resistant hypervolemia and was treated with intermittent hemodialysis (HD) and ultrafiltration

(UF). The patient received intermittent HD+UF treatment in the following days. After dialysis, regression was observed in hypervolemia findings. Urine output remained oliguric. An autoimmune panel was obtained from the patient, who showed signs of proteinuria, hypoalbuminemia, edema, oliguric renal failure, and active urine sediment. Renal biopsy was performed. After the pathological examination of the kidney biopsy revealed crescent formation, the patient was given pulse steroid treatment (1 g/day for 3 days), followed by cyclophosphamide + mesna iv (750 mg/day) immunosuppressive therapy. Based on the autoimmune panel findings, the patient was diagnosed with SLE with antinuclear antibody (ANA) positivity, anti-double stranded DNA antibody (anti-dsDNA) positivity, and lupus anticoagulant positivity, and low levels of complement factor 3 (C3) and complement factor 4 (C4) were noted. The patient was evaluated for other SLE findings. There was no history of oral aphthae or arthralgia. Mild hyperemia was noted on the face. However, typical malar rash was not detected. As a result of the pathology, type IV diffuse LN+crescentic glomerulonephritis was reported (Figure 1). Hydroxychloroquine treatment was initiated after the ophthalmology consultation. Simultaneous plasmapheresis treatment was planned. The patient underwent plasmapheresis for seven sessions. At the follow-up, her urine output increased after the 6th session of plasmapheresis (Figure 2). Intermittent dialysis was also administered during this period.

The patient's serum blood urea nitrogen (BUN)/creatinine (Cre) level decreased from 61/5.7 mg/dL to 47/2.43 mg/dL. She was discharged with a twice weekly intermittent HD program and monthly cyclophosphamide treatment plan. She received six cycles of cyclophosphamide treatment. Dialysis treatment was discontinued in July 2017 when her renal function improved. In November 2017, BUN/Cre level of 6.2/0.48 mg/dL and proteinuria of 6.7 g/day were noted. Maintenance therapy of mycophenolate mofetil was started, and out-patient clinic controls were continued in remission.

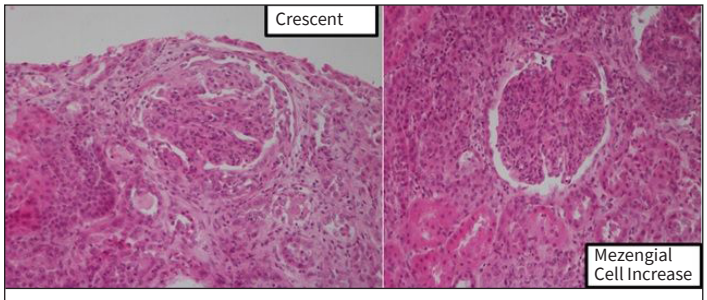
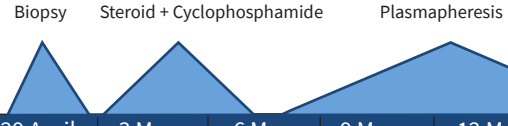


Figure 1. Presence of crescent formation and mesangial cell increase in glomeruli in renal biopsy specimen (H&E, ×40).

DISCUSSION

Systemic lupus erythematosus is the most common rheumatologic disease in pregnancy because it is usually observed in women in the reproductive age group. Fertility in women with SLE is similar to that in the normal population. The exacerbation of the disease during pregnancy and in the postpartum period is approximately 50%. In patients with lupus and pregnancy, the disease is usually exacerbated in the last trimester of pregnancy and within a few weeks after birth. Lupus exacerbations during pregnancy are frequently associated with renal and hematologic systems (1-4). Many complications in lupus can occur during pregnancy. These complications include exacerbation of the disease (leukomotor-hematologic-renal), abortion (especially in the presence of antiphospholipid antibodies), premature birth, intrauterine growth retardation, hypertension, increased risk of preeclampsia (especially in nephritis cases), risk of renal failure development, and maternal death. Therefore, the follow-up of pregnant women with SLE, which can cause significant maternal and fetal complications, should be performed with care. On the other hand, patients who become pregnant before the diagnosis of SLE may admit to the hospital with lupus complications. In the present report, we described a patient diagnosed with preeclampsia and LN due to oliguric acute renal failure after C/S.

Preeclampsia is defined as a combination of proteinuria , edema and increased blood pressure as >140/90 mmHg or increase in systolic blood pressure by 30 mmHg and increase in diastolic blood pressure by 15 mmHg in pregnant women at >20th week pregnancy, and the definitive treatment of preeclampsia is delivery of the fetus. Although preeclampsia and LN may coexist during pregnancy, it is very important to establish the differen-



Date	21 April	25 April	29 April	3 May	6 May	9 May	12 May	15 May	18 May	21 May
BUN (mg/dL)	32	17	13	22	48	47	34	39	53	47
Creatinine (mg/dL)	1.89	2.34	2.6	5.2	5.2	5.2	3.2	3.2	2.6	2.4
Received (volum-cc)	1300	2500	2200	3350	1700	2600	3000	4250	1350	2100
Removed (volum-cc)	350	150	50	Yok	50	200	750	4850	3250	4250

Figure 2. Patient's clinical follow-up and treatment schedule.

tial diagnosis as their treatments are different. Steroids are used to treat LN, which worsens preeclampsia. Therefore, signs and symptoms that are more reliable in showing SLE exacerbation and diagnosis in pregnancy can be summarized as ANA positivity, increased anti-dsDNA autoantibody titer (if known before), lymphopenia, active urine sediment, erythrocyte casts, direct Coombs test positivity, hemolytic anemia, fever, lymphadenopathy, typical oral mucosal ulcers, inflammatory arthritis, and cutaneous vasculitis. However, findings such as hypertension, edema, proteinuria, impaired renal function, and thrombocytopenia are common factors in both preeclampsia and exacerbation of SLE. In addition, proteinuria that occurs during pregnancy may be at physiological limits or may be related to lupus. In this context, the presence of hematuria and examination of urine sediment may be suggestive of renal involvement due to SLE (2, 3, 8). Anti-dsDNA positivity with hypocomplementemia, even in the absence of clinical activity, may be a predictor of abortion or preterm birth, particularly in the second trimester of SLE pregnancies. C3 and C4 levels are typically reduced by 25% in LN. In contrast, their levels may increase by 10%-15% in pregnancy and preeclampsia.

Performing renal biopsy in LN is crucial in determining the treatment, identifying patients who need urgent treatment, evaluating the response to treatment, and predicting the prognosis (10).

The prognosis is better if SLE is in clinical remission for at least 6 months before pregnancy. The live birth rate is approximately 90%. However, the maternal mortality rate of patients with active disease in the last 6 months before the conception is approximately 15%. Approximately 60% of infants born from these mothers have morbidity or mortality. If SLE first appeared during pregnancy, maternal and fetal prognoses are similar to those patients with SLE who have active disease in the last 6 months before the conception. Only heart blocks have been reported as congenital problems in infants of mothers with SLE (11). Even in the case series with best results, some patients with LN develop renal failure that requires dialysis. Dialysis support may be discontinued in 10%-28% of these patients. These are usually patients with rapid renal dysfunction, suggesting acute and potentially reversible disease activation. Only 1%-4% of the chronic dialysis and transplant population are patients with lupus. The clinical and serological activities of lupus usually decrease after reaching end-stage renal failure. The majority of deaths in patients with lupus occurs during the first 3 months of dialysis and is usually caused by an infection. After three months mortality causes are cardiovascular disease and infection. The prognosis of patients surviving during the first 3 months of dialysis is not different from that of patients without lupus (12).

Our patient was admitted to the hospital with suddenly elevated blood pressure and swelling of the lower limbs when she was in the 35th week of pregnancy. . Emergency C/S was performed with a diagnosis of preeclampsia. Urinary system ultrasound were reported as normal after the patient's urine output decreased (200 mL in 12 h) and postoperative serum creatinine increased to 1.8 mg/dL. She was transferred to our nephrology clinic with a preliminary diagnosis of oliguric acute renal failure. She was diagnosed with LN after autoimmune serology and renal biopsy results. The patient underwent dialysis for approximately 1 month, and her renal function improved with immunosuppressive and plasmapheresis therapy.

CONCLUSION

SLE may be the underlying cause of preeclampsia during pregnancy with concomitant renal dysfunction. Physicians should be aware of SLE as an unusual cause of preeclampsia during pregnancy.

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