

Acute Renal Failure Associated with a Minimal Change Nephrotic Syndrome in a Systemic Lupus Erythematosus Patient

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In systemic lupus erythematosus (SLE), acute renal failure (ARF) is usually associated with severe lupus nephritis and ARF associated with other glomerular diseases is extremely rare. We recently encountered a patient with ARF that was associated with a minimal change nephrotic syndrome (MCNS) in SLE. A 41-year-old woman presented with a nephrotic syndrome and ARF. She fulfilled four of the American College of Rheumatology criteria for the classification of SLE. However, a renal biopsy revealed that there were no glomerular abnormalities and no deposition of immune complex. The generalized edema disappeared and the high creatinine levels decreased after prednisolone therapy.

Key Words: Systemic lupus erythematosus, minimal change nephrotic syndrome, acute renal failure

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown cause, which appears to result from pathogenic autoantibodies and immune complexes, and is characterized by the overproduction of autoantibodies and the deposition of immune complexes in various organs. In SLE, renal involvement is common and a lupus nephritis is one of the major predictor of end-stage renal disease and survival.¹

Lupus nephritis is caused by an immune com-

plex deposition in the glomerulus, presumably by anti-double-stranded DNA antibody complexes.² The nephrotic syndrome is the predominant clinical manifestation in about one third of the patients with lupus nephritis.³ Other glomerular diseases including minimal change nephrotic syndrome (MCNS) in SLE patients occurs rarely. It is difficult to differentiate between lupus nephritis and other glomerular diseases including MCNS without a renal biopsy in SLE patients.

We recently encountered a patient with acute renal failure (ARF). Lupus nephritis was considered to be the cause of ARF as the first impression, but a biopsy revealed the MCNS. Steroid administration by itself improved the patient's symptoms and signs.

CASE REPORT

A 41-year-old female was referred from another hospital because of a rapidly progressive edema and oliguria. Her past history was non-specific. Her height was 157.5 cm and weight was 67.4 kg. Physical examination revealed that she had malar rash and edema of the face and legs. The blood pressure was 140/90 mmHg. The heart and lungs were normal. No liver, spleen or lymph node enlargement was found. Laboratory investigations showed the following values: urine protein 4+, RBC 3-5/HPF; 24 hour urine protein 5.8 g/day; blood urea nitrogen 69 mg/dL; creatinine 2.2 mg/dL; serum total protein 4.2 g/dL; albumin 1.6 g/dL; total cholesterol 424 mg/dL; ESR 93 mm/

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hr, CRP 0.1 mg/dL; hemoglobin 13.3 g/dL, white blood cell counts $3400/\text{mm}^3$; platelets $325,000/\text{mm}^3$; Complement 3 87 (normal range: 88 - 201) mg/dL; Complement 4 18 (normal range: 16 - 47) mg/dL; antinuclear antibody 1:320 positive (homogenous pattern) and anti-DNA antibody 1:320 positive, anti-phospholipid antibody negative; anti-Sm antibody negative; anti-RNP positive; anti-Ro antibody positive; anti-La antibody negative. Chest PA, Abdominal ultrasonography, and renal artery Doppler were normal. While undergoing the investigations, the edema became aggravated, the urine output decreased to 150 - 400 ml/day and the serum creatinine level began to rise up to 3.8 mg/dl (Fig. 1).

Our first diagnostic impression was of lupus nephritis. On the 3rd hospital day, a percutaneous renal biopsy was performed. On light microscopy, glomeruli showed a normal appearance (Fig. 2). Immunofluorescence microscopy revealed an absence of glomerular deposits of immunoglobulin, complements or fibrinogen. On electron microscopy, a diffuse foot process effacement was evident and no electron-dense deposits were seen (Fig. 3). Under a diagnosis of MCNS, a high dose

steroid regimen (prednisolone 60 mg/day) was administered orally.

A few days after the initiation of the high-dose steroids, the edema and the high creatinine level remitted slowly. By the 11th day of therapy the serum creatinine decreased to 1.6 mg/dl,

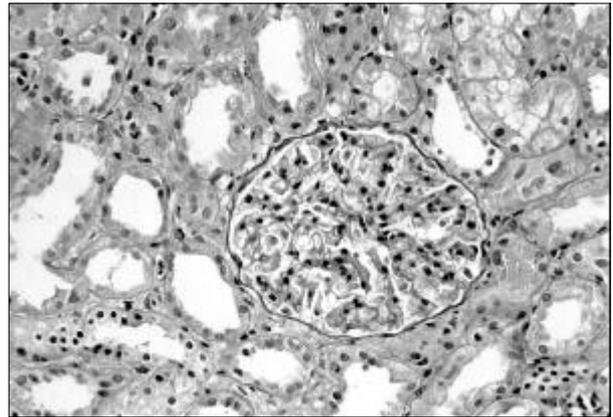


Fig. 2. Glomeruli show an almost normal appearance. The capillary lumina are patent. The basement membranes are intact and not duplicated. The mesangium is not widened and not proliferated. The interstitium shows a multifocal mild mononuclear cell infiltration. The tubules are minimally atrophic. The vessels are unremarkable.

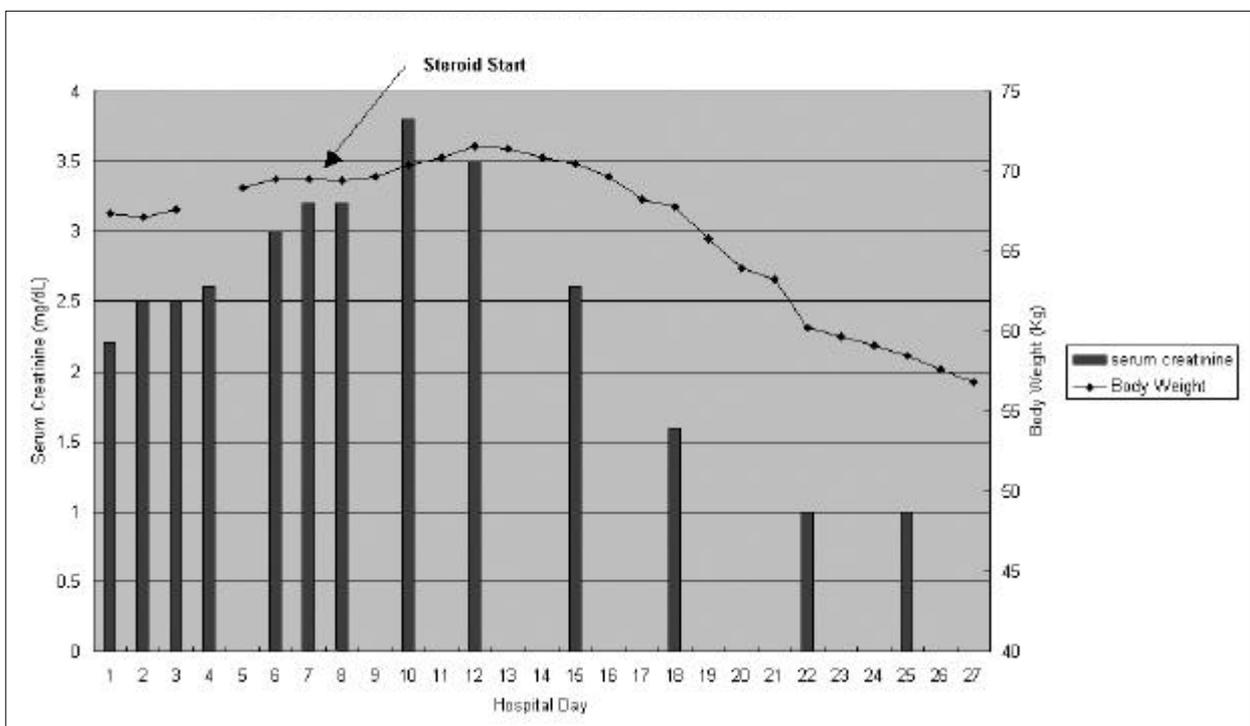


Fig. 1. Changes of serum creatinine and body weight during admission.

while by the 19th day of steroid therapy the serum albumin, total protein and creatinine had reached 2.5 g/dl, 4.2 g/dl and 1.0 mg/dl, respectively. She was discharged with improved symptoms and signs. She has been taking a tapering dosage of oral steroids and shows improved symptoms and signs in the outpatients department (Table 1).

DISCUSSION

Lupus nephritis been categorized into types WHO I-V on the basis of morphological-histological criteria, which generally correspond to the severity of the clinical picture, course and the prognosis of the renal lesion.^{4,5} The nephrotic

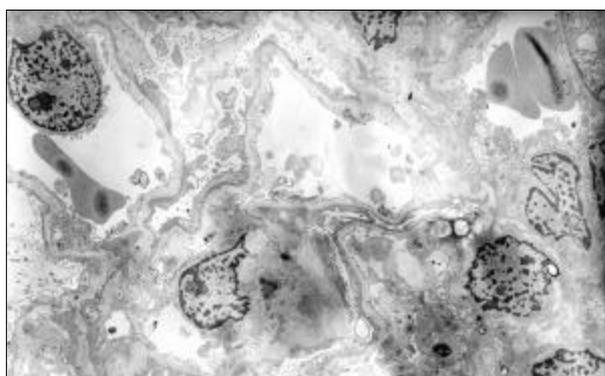


Fig. 3. The section shows a marked effacement of the foot processes of visceral epithelial cells as well as a microvillous transformation. The mesangial area is unremarkable. The basement membrane is irregularly wrinkled. The capillary lumina are patent. There are no electron deposits on electron microscopy.

syndrome is commonly associated with mesangial lupus nephritis which develops to the nephrotic syndrome.⁶ Our patient fulfilled four of The American college of Rheumatology criteria for classification of SLE (Positive antinuclear antibody, leukopenia, positive anti-ds DNA, malar rash). However, her biopsy findings and clinical course were typical of MCNS: there was a prompt remission of the nephrotic syndrome and ARF after administration of prednisolone. The absence of immunoglobulin deposits in the glomeruli by immunofluorescent staining, absence of definite abnormalities on light microscopy and diffuse foot process effacement and no electron-dense deposits on electron microscopy were important diagnostic clues. ARF may be encountered in association with NS caused by non-steroidal anti-inflammatory drugs (NSAIDs), or it may accompany a diuretic-induced hypersensitivity acute interstitial nephritis or bilateral acute renal thrombosis, but our patient did not have these disorders. Her past history shows that she refused a recent intake of NSAID but there was no evidence of an acute interstitial nephritis on renal biopsy. Furthermore, the renal blood flow was normal and there was no evidence of an intravascular thrombosis on ultrasonography. Possible causes of reversible ARF in this case were a diminished circulating plasma volume, a severe disturbance in visceral epithelial cells so as to result in a nearly total obliteration of the slit pores and a severe reduction in hydraulic conductivity.⁷ Alternatively, a severe proteinuria could result in the occlusion of the distal nephron lumens caused

Table 1. Changes in Multiple Factors During Oral Prednisolone Administration

Day	3	8*	17	33	61	76	93	124	139	148	162	178	192
PDS (mg)		60	60	60	50	40	30	20	15	12.5	10	7.5	5
Urine protein	3+	3+	3+	2+	1+	-	1+	trace	trace	trace	1+	trace	1+
Anti-DNA Ab	1:320 (+) [†]		1:10 (+)	(-) [‡]			(-)				(-)		
ANA	1:320 homogenous		1:80 homogenous	1:40 homogenous			(-)				(-)		
C3 (mg/dL)	78			76			92				69		
C4 (mg/dL)	25			16			14				13		
Serum albumin (g/dL)	1.6	1.7	2.1	3			3.5						

*starting of oral prednisolone administration; [†]positive; [‡]negative.

by cast formation or an extratubule compression caused by interstitial edema. Interstitial edema or intratubular obstruction may produce a form of intranephron obstructive uropathy. Thus, the ARF was believed to have resulted from a progression of MCNS in our patient. In the literature, 9 cases have been reported on the association between SLE and MCNS (Matsumura et al. 1989, Okai et al. 1992, Makino et al. 1995, Horita et al. 1997, Nishihara et al. 1997, Guery et al. 1998, Perakis et al. 1998).⁸⁻¹⁴ Among these, SLE developed simultaneously with the onset of MCNS in 4 cases and developed when MCNS relapsed in 3 cases, and MCNS developed during a course of SLE in 2 patients (Table 2). The development of proteinuria, hematuria and edema in SLE patients leads clinicians to positively consider the presence of renal involvement (lupus nephritis) without suspicion. Coexistence of ARF, MCNS and SLE as in this case is extremely rare. Some physicians argue that the clinical diagnosis of lupus nephritis is easy and that the prognosis and treatment may be assessed without the support of a histological analysis.¹⁵ Unless renal biopsy is performed, administration of a cytotoxic agent is unavoidable.

SLE is an autoimmune disease that is characterized by an overproduction of autoantibodies. On the other hand, the pathogenesis of the MCNS is as yet unknown. Although SLE and MCNS are independent of each other and are caused by unrelated disease processes, immune abnormalities are considered to be the cause of SLE and

MCNS. A T cell dysfunction is present in both disorders, and there might be abnormalities associated with SLE and MCNS.^{10,12} In SLE, an increase in helper T cell function and a lack of T cell suppression lead to an excess antibody production. SLE patients who have a multisystem involvement, but without a renal disease, have a high helper/suppressor T cell ratio due to a decrease in the number of circulating suppressor cell.¹⁶ In contrast, patients with SLE that is manifested by a severe renal disease have a low helper/suppressor T cell ratio.¹⁷ In MCNS, a glomerular permeability factor¹⁸ from T cells, circulating lymphokines, is known to increase the glomerular permeability by loss of glomerular polyanion.¹⁹ Several investigators²⁰⁻²² reported altered numbers of circulating T cells as well as depressed or enhanced T cell functions. Fiser et al.²¹ reported an increase in the number of suppressor T cells and a decrease in helper T cells, while Ozaki²² found just the opposite. There may be another pathogenic link, which is known to be associated with genes coded within the major histocompatibility complex between two diseases. However, unlike SLE, there is no clear evidence to suggest that complement and the immune complexes play a role in the pathogenesis of MCNS. The question remains whether SLE is a simple coincidence with MCNS or a precipitating agent of MCNS.

In summary, we reported a case of ARF that is associated with MCNS in SLE. After experiencing

Table 2. Literature Review of SLE Associated with MCNS

Author	Year	Sex	Age	Serum Creatinine (mg/dl)	Clinical course
Matsumura et al. ⁷	1989	F	37	NS	SLE developed when MCNS relapsed
		F	21	NS	SLE developed when MCNS relapsed
Okai et al. ⁸	1992	F	22	NS	SLE developed simultaneously with an onset of MCNS
		M	22	NS	SLE developed simultaneously with an onset of MCNS
Makino et al. ⁹	1995	F	41	1.51	MCNS developed during a course of SLE
Horita et al. ¹⁰	1997	F	25	NS	SLE developed simultaneously with an onset of MCNS
Nishihara et al. ¹¹	1997	F	17	0.5	SLE developed with remitting MCNS
Guery et al. ¹²	1998	F	27	3.41	SLE developed simultaneously with an onset of MCNS
Perakis et al. ¹³	1998	F	45	1.1	MCNS developed with remitting SLE nephritis
Our Case	2000	F	41	2.2	SLE developed simultaneously with an onset of MCNS

NS, not subscribed.

this case; we suggest the following; first, a renal biopsy should be performed in SLE patients to exclude other glomerular diseases. secondly, there may be a immunological association between SLE and MCNS

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