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Case Report

Minimal change disease: a variant of lupus nephritis

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Abstract

Some patients with systemic lupus erythematosus (SLE) present with nephrotic syndrome due to minimal change disease (MCD). Histopathological diagnosis of patients with SLE and nephrotic-range proteinuria has shown that these patients present with diffuse proliferative glomerulonephritis and membranous glomerulonephritis, World Health Organization (WHO) classes IV and V, respectively, more frequently than the other classes. In the present study, we reported a case of nephrotic syndrome and renal biopsy-proven MCD associated with SLE. A complete remission occurred after steroid treatment, which was followed by a relapse 15 months later with a concomitant reactivation of SLE. A second biopsy showed WHO class IIb lupus nephritis. Prednisone treatment was restarted, and the patient went into complete remission again. The association of MCD and SLE may not be a coincidence, and MCD should be considered as an associated SLE nephropathy.

Keywords: lupus nephritis; minimal change disease; prednisone

Introduction

Histopathological diagnosis of patients with systemic lupus erythematosus (SLE) and nephrotic-range proteinuria has shown that these patients present with diffuse proliferative glomerulonephritis and membranous glomerulonephritis, World Health Organization (WHO) classes IV and V, respectively, more frequently than other classes [1]. Most of the cases with focal proliferative glomerulonephritis (WHO class III) have shown non-nephrotic proteinuria [1]. Among patients with lupus nephritis and mesangial hypercellularity (WHO class II), however, proteinuria either is absent or occurs within a range below 1 g/24 h [2].

Interestingly, some patients with SLE present with nephrotic syndrome due to minimal change disease (MCD) [3–13]. Remarkably, this histological finding (MCD), which has typically been encountered in idiopathic MCD, has not been described in the histologic classification of the WHO [1] or in the recent classification proposed by the International Society of Nephrology [14].

In the present study, we reported a case of nephrotic syndrome and renal biopsy-proven MCD associated with SLE and discussed treatment options and possible outcomes.

Case report

A 41-year-old female was referred because of generalized oedema, which had persisted for 5 months, and mild arthralgia in her hands and knees. She had only been treated with sodium levothyroxine because of hypothyroidism, and she denied using any non-steroidal anti-inflammatory drugs. Physical examination revealed normal blood pressure and generalized oedema. Heart and lung functions were normal, and we did not detect any liver, spleen or lymph node enlargement. Urinary microscopic examination showed 4–6 white blood cells and 15–20 red blood cells per high-power field. Proteinuria was 6 g/24 h, serum creatinine was 1 g/dL (88 μmol/L), albumin was 1 g/dL (10 g/L) and total cholesterol was 420 mg/dL (10.8 mmol/L). The blood cell profile showed that her haemoglobin was 8.8 g/dL (88 mmol/L), her white blood cell count was 4000/μL and her platelet count was 228 000/μL. Her C3 was 0.8 g/L [reference values (RV): 0.9–1.8 g/L], C4 was 0.1 g/L (RV: 0.1–0.4 g/L) and anti-Sm antibody titre was 21 U/mL (RV: <20 U/mL). Serology was reactive for antinuclear cytoplasmic antibody and negative for anti-DNA antibodies, HIV, hepatitis B and hepatitis C. The antinuclear factor was 1:400 (speckled pattern).

A percutaneous renal biopsy revealed 36 glomeruli with a mild focal (20%), segmental increase in mesangial cellularity. The tubulointerstitium and blood vessels showed a normal pattern. Immunofluorescence showed segmental mesangial staining of 1+ intensity for IgA, IgM and C3 (with areas of capillary extension also showing staining for C3). Staining with antisera for IgG, fibrinogen and C1q was negative. Electron microscopy revealed that the thickness of the glomerular capillary membrane was normal, and podocytes exhibited diffuse effacement of foot processes (Figure 1). Rare intracellular tubuloreticular inclusions were only found in glomerular endothelial cells. A

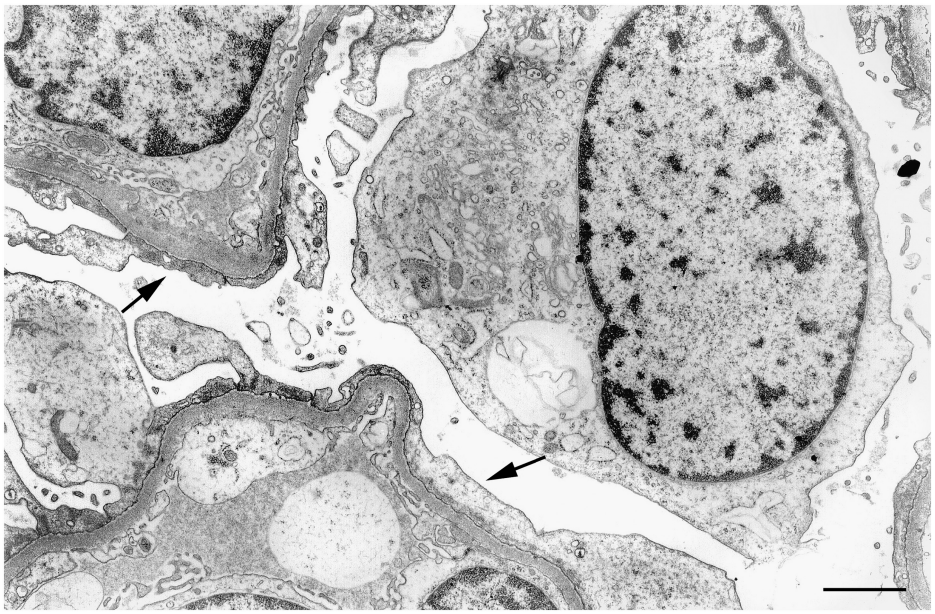

Fig. 1. Electron micrograph shows effacement of the visceral epithelial cell foot processes (arrows). Bar = 1.7 μm.

diagnosis of SLE, WHO class IIb lupus nephritis and MCD-induced nephrotic syndrome was established.

The patient was started on prednisone therapy, which resulted in a complete remission of the nephrotic syndrome. One month after complete cessation of prednisone treatment, the patient presented with arthralgia in her hands, wrists and knees. Seven months later, there was a relapse of the nephrotic syndrome. At the time of relapse, her blood pressure was around 200/120 mmHg, albumin was 1.1 g/dL (11 g/L), creatinine was 1.5 mg/dL (132 μmol/L), total cholesterol was 338 mg/dL (8.7 mmol/L), antinuclear factor antibody was 1:800 (speckled pattern), anti-Sm antibody was 140 U/mL, C3 was 0.4 g/L and C4 was <0.1 g/L. The blood cell profile showed that her haemoglobin was 8.4 g/dL (84 mmol/L), her white blood cell count was 3700/μL and her platelet count was 160 000/μL.

A second percutaneous renal biopsy revealed 28 glomeruli. Two of the glomeruli showed mild focal mesangial hypercellularity, and the remaining glomeruli showed a normal pattern. The interstitium showed mild fibrosis, and the tubuli showed mild atrophy. Immunofluorescence showed focal and segmental mesangial staining of 1+ intensity for IgM and diffuse and global mesangial staining of 3+ intensity for C3. Staining with antisera for IgA, fibrinogen and C1q was negative, and electron microscopy was not available. The histopathologic diagnosis was compatible with WHO class IIb lupus nephritis [1].

Prednisone treatment was restarted, and the patient had complete remission of her nephrotic syndrome. Azathioprine was also administered because of systemic manifestations of SLE. One year later, the patient was asymptomatic with normal urinalysis; serum creatinine was 0.9 mg/dL

Table 1. Cases of minimal change disease associated with SLE

	Number of patients and gender	Age (years)	Clinical features	Treatment	Outcome	Relapses
Matsumura *et al*. [3]	3 (F)	11, 23 and 30	NS—3	CT and IS	CR	Yes—2 cases
Okai *et al*. [4]	1 (M)	22	NS	PSL	CR	No
Makino *et al*. [5]	1 (F)	41	NS	PSL	CR	Yes
Nishihara *et al*. [6]	1 (F)	17	NS	PSL	CR	Yes
Guery *et al*. [7]	1 (F)	27	NS + ARF	Pred + PSL pulse + CP-IV	CR	No
Horita *et al*. [8]	1 (F)	25	NS	PSL	CR	No
Sugimoto *et al*. [9]	1 (F)	51	NS + ARF	CT	CR	No
Dube *et al*. [10]	6 (F)1 (M)	18–58 (mean = 32.7)	NS—7ARF—4	Pred	CR	Yes—3 cases
Seo *et al*. [11]	1 (F)	41	NS + ARF	PSL	CR	No
Hertig *et al*. [12]	4 (F)		NS—4ARF—1	Pred	CR	Yes—2 cases; No—2 cases
Horino *et al*. [13]	1 (F)	29	NS	PSL	CR	No

F, female; M, male; NS, nephrotic syndrome; ARF, acute renal failure; CT, corticotherapy not specified; PSL, prednisolone; Pred, prednisone; CR, complete remission; CP, cyclophosphamide; IS, immunosuppression not specified.

(79.2 μmol/L), haemoglobin was 12.7 g/dL (127 mmol/L), blood leucocytes were 6300/μL, C3 was 1 g/L and antinuclear factor antibody was 1:800 (speckled pattern).

Discussion

In the present study, we reported a case of a concomitant occurrence of minimal change nephrotic syndrome and WHO class IIb lupus nephritis. The patient had a complete remission after steroid treatment and showed a relapse 15 months later at the same time as SLE reactivation. Because the second biopsy was not studied by electron microscopy, the effacement of the podocytes could not be demonstrated.

There are only a few reports describing MCD in patients with SLE, especially in patients with class II lupus nephritis (WHO classification). According to the literature, up to 22 cases have been described (Table 1) [3–13]. In the study by Dube *et al*. [10], seven cases of patients with MCD and SLE were reported; however, an association with non-steroidal anti-inflammatory drugs (NSAIDS) could not be ruled out in at least two of the patients. In the majority of the cases described in the literature, patients showed a complete remission of the nephrotic syndrome after corticotherapy (sometimes an immunosuppressant drug was added to the treatment). In addition, SLE symptoms completely disappeared after treatment. Interestingly, patients who relapsed tended to have concomitant SLE reactivation along with the nephrotic syndrome [6,12].

In some cases, the diagnosis of SLE did not fulfil the WHO criteria in the initial presentation of the nephrotic syndrome [6]. Similar to the case described in the present study, most of the cases in the literature have been classified as WHO class II lupus nephritis during follow-up.

In addition to nephrotic syndrome, 8 patients out of the 22 cases described in the literature (Table 1) also presented with renal failure (common in adult-onset MCD), which resolved following treatment with corticotherapy [7,9–12].

Similar to previous cases [3–13], the patient in the present study showed a good response to steroid therapy as the single treatment in the first episode of MCD. In addition, she also responded to the combination of steroids and azathioprine, which was used in the relapse episode 15 months later.

Interestingly, the amount of foot process effacement is the only factor that has been identified to be involved with nephrotic proteinuria in patients with lupus nephritis class II or lupus-associated MCD. Indeed, foot process effacement has been shown to be >80% in these patients compared with <20% in patients with non-nephrotic proteinuria, even though the histological lesions are the same [15].

This present case supported other researchers who have suggested that the rare association of SLE and MCD is not a coincidence. In our opinion, MCD should be considered as an associated SLE nephropathy.

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Conflict of interest statement. None declared.

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