Lupus: Open Access

Martens et al., Lupus Open Access 2017, 2:2

Case Report Open Access

Re-Occurring Proteinuria in a SLE Patient: Always Lupus Nephritis?

Henk A. Martens[1*], **Marc Bijl**[2], **Marius C. Van den Heuvel**[3] **and Cees G.M. Kallenberg**[4]

[1]*Department of Rheumatology, Sint Maartenskliniek Nijmegen, Netherlands*

[2]*Department of Rheumatology and Clinical Immunology, Martini Hospital Groningen, Netherlands*

[3]*Department of Pathology, Medisch Centrum Leeuwarden, Netherlands*

[4]*Department of Rheumatology and Clinical Immunology, University Medical Center Groningen, University of Groningen, Netherlands*

[*]**Corresponding author:** Henk A. Martens, Department of Rheumatology, Sint Maartenskliniek, 6500 GM Nijmegen, Netherlands, Tel: + 0031-24-3659278; Fax: + 0031 50 3619308; E-mail: h.martens@maartenskliniek.nl

Received date: April 17, 2017; **Accepted date:** May 25, 2017; **Published date:** June 05, 2017

Abstract

Introduction: Renal disease, designated as lupus nephritis (LN), is one of the severe manifestations of Systemic Lupus Erythematosus (SLE). The proliferative forms require aggressive treatment with corticosteroids and cytotoxic drugs. In a substantial number of patients, renal disease relapses after treatment.

Case report: In this case report, we present a 27-year old woman, who had been treated for a membranoproliferative LN in the past. Seventeen years later she presented with chest pain and nephrotic-range proteinuria and severe hypoalbuminemia. The diagnosis of pulmonary embolism was made. Renal biopsy revealed only minimal abnormalities, confined to the mesangium. There was no glomerulonephritis. Based on this finding and the nephrotic-range proteinuria, the diagnosis of minimal-change disease was made. The patient was treated with prednisolone, after which the proteinuria diminished, but did not disappear. After the addition of azathioprine, the proteinuria resolved completely.

Conclusion: This case illustrates that, although the diagnosis of LN has been made in the past, this does not exclude the occurrence of renal pathology caused by other diseases than SLE. Therefore, a renal biopsy is mandatory in every SLE patient with occurrence of renal abnormality es, even when a history of LN is present.

Keywords: SLE; Lupus nephritis; Proteinuria; Minimal-change disease; Renal biopsy

Introduction

One of the most severe manifestations of SLE is renal disease, designated as lupus nephritis (LN). The proliferative forms of LN (ISN/RPS class III and IV) [1] are often characterized by proteinuria, and, at microscopic examination of the urine, presence of dysmorphic erythrocytes and/or cellular casts. Nephrotic syndrome or loss of renal function is common. These proliferative forms require aggressive treatment with corticosteroids and cytotoxic drugs. In a substantial number of patients, renal disease relapses after treatment. [2] In this case-report we present a patient with SLE who had been treated for proliferative LN in the past, who presented with severe hypoalbuminemia and nephrotic-range proteinuria several years later.

Case Report

A 27-year old woman was admitted to our hospital because of chest pain and a sub-febrile temperature. Seventeen years before SLE had been diagnosed, based on cutaneous lesions, proteinuria, anti-nuclear antibodies and antibodies to double stranded DNA. At that time, renal biopsy revealed a diffuse membranoproliferative glomerulonephritis, WHO class IV (Figure 1). She was subsequently treated with prednisolone and azathioprine, after which remission was achieved and proteinuria resolved (Table 1A).

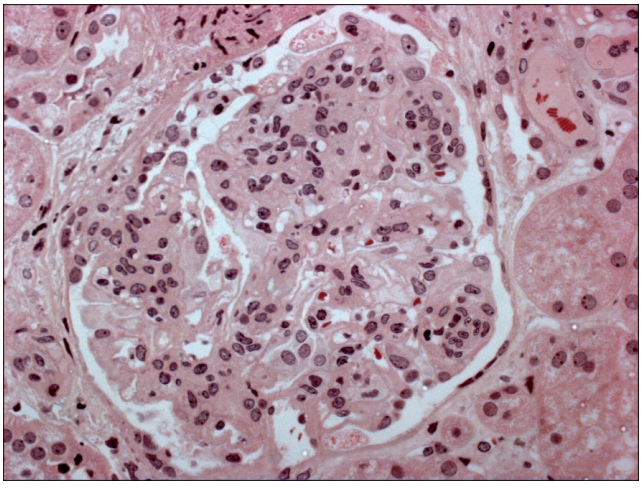

Figure 1: Glomerulus showing an uneven proliferation of mesangial en endothelial cells. H & E staining, 40 X.

On admission the patient complained of chest pain. She used an oral contraceptive and doxasozine because of hypertension. Two months before she had temporarily used an NSAID because of arthralgias. At physical examination, besides a temperature of 37.9°C and a sinustachycardia of 110/min., no apparent abnormalities were

present. Blood pressure was normal (140/80). Laboratory tests revealed a serum creatinine of 89 µmol/l (normal 50-90 µmol/l), serum albumin of 13 g/l (35-50 g/l), complement C3 of 1.19 g/l (0.90-1.80), a slightly decreased complement C4 level of 0.09 g/l (0.10-0.40), an ANA titer>1:640 and an anti-double-stranded DNA antibody titer of 23 E/ml (Farr assay, normal<10). The latter had remained stable compared with the values during the last year before admission. Urine analysis showed 20-25 non-dysmorphic erythrocytes/HPF without casts, 24 h urine contained 12.8 g proteinuria. Proteinuria was selective (selectivity-index 13%). Pulmonary embolism was present on spiral CT. Renal vein thrombosis and malignancies were not found.

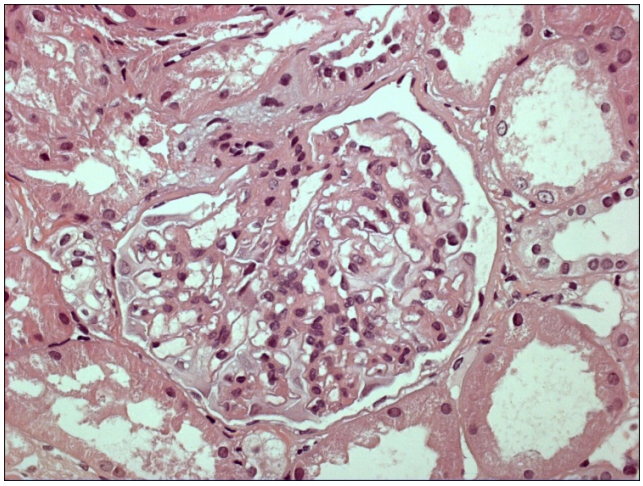

Figure 2: Glomerulus with only minimal focal expansion of mesangial matrix and minimal increase in cellularity, without signs of glomerulonephritis. H & E staining, 40 X.

Parameter	Dec'85	Feb'86	Apr'86	May'86	Nov'86
Proteinuria (g/24 h)	0.2	1.7	4.3	2.5	0.3
Complement C3 (g/l)	n.a.	n.a.	n.a.	n.a.	1.11
Complement C4 (g/l)	n.a.	n.a.	n.a.	n.a.	0.13
Anti-ds DNA (critidia)	neg	1:40	1:160	neg	neg
Erythrocyturia (cells/HPF)	n.a.	0-5	20-25	5-10	
Dysmorphic erythrocytes or			none	none	
Casts			↑ p+a)		

Table 1A: biochemical characteristics of the two episodes of renal disease in our patient, Lupus-nephritis episode.

A renal biopsy was performed, see (Figure 2). This showed glomeruli with only focally minimal expansion of mesangial matrix and a minimal increase in cellularity, without signs of glomerulonephritis. The glomerular basement membrane was normal. No abnormalities of the tubulo-interstitium or arteries were present. Immunofluorescence staining showed only minimal mesangial deposition of IgM and C3. Based on the histopathological findings and the nephrotic-range proteinuria, a diagnosis of minimal-change nephropathy was made.

Prednisolone 60 mg once daily was started. The patient was treated with anticoagulant therapy because of pulmonary embolism. After 3 months of treatment, proteinuria had diminished to a level of 4.3 g/24 h. Proteinuria gradually resolved to 0.0 g/24 h after azathioprine was added. 3.5 years after start of treatment, the patient was still in remission, and immunosuppressive drugs could be withdrawn (Table 1B).

Parameter	Oct'02	Jan'03	Feb'03	Mar'03	May'03	Jan'05
Proteinuria (g/24 h)	0	5.8	12.8	4.3	4.3	0
Complement C3 (g/l)	0.93	1.13	1.36	1.04	1.18	1.02
Complement C4 (g/l)	0.09	0.12	0.18	0.1	0.16	0.17
Anti-ds DNA (Farr, E/ml)	16	20	50	20	4	6
Erythrocyturia (cells/HPF)	0	15-20	20-25	0-5	5-10	0-5
Dysmorphic erythrocytes or			none	none		
Casts			↑ p)		↑ a)	
p+a) start of prednisolone and azathioprine treatment; p) start of prednisolone treatment; a) azathioprine added to treatment; n.a.= not available						

Table 1B: Biochemical characteristics of the two episodes of renal disease in our patient, Minimal-change episode.

Discussion

LN is a severe and common manifestation of SLE, with a prevalence of 29 to 65% amongst SLE patients [2]. The proliferative forms (ISN/RPS class III and IV) [1], are associated with poorer outcome. After a mean follow-up of 10 years, 20 to 40% of patients with proliferative lupus nephritis who achieved a complete remission will relapse [3,4]. We initially suspected our patient of having a relapse of proliferative LN. Renal biopsy, however, showed only minimal abnormalities without signs of glomerulonephritis. A class I glomerulonephritis could be suspected, but this type of LN is usually not accompanied by proteinuria or urine abnormalities [2-5,6]. Furthermore, the selectivity and the sudden onset of the proteinuria, the lack of change in serological abnormalities (Table 1B) and the absence of other SLE related disease manifestations supported the diagnosis of minimal-change disease. Although our patient had used an NSAID, this seems unlikely to be the cause of the proteinuria, as she had not taken this drug after the last out-patient visit, at which proteinuria was absent.

Recently, Wang et al. reviewed 19 histories of patients with SLE and minimal-change disease [7], none of them having proliferative LN before. To our knowledge, only one other case of minimal-change disease occurring after a biopsy proven proliferative form of LN has been reported [8]. Differentiating these disease entities has implications for the therapeutic management, as a more aggressive (cytotoxic) therapy in proliferative LN is required. Titers of anti-double-stranded DNA antibodies were relatively low and there were

only mild abnormalities in urine analysis (Table 1B), so one can not rely solely on these parameters in differentiating a relapse of LN from other renal pathology.

The question rises whether the occurrence of two renal disease entities in the same patient is totally co-incidental. In the previously mentioned study by Hertig et al., a calculation is made that, based on the prevalence of idiopathic nephrotic syndrome in France, the probability of this occurring in SLE patients is 0.4 to 1 per 10.000, while the actual reported prevalence amongst SLE patients is substantially higher (≈ 1.6 and ≈ 0.5%). Furthermore, the authors state that altered T-cell function is, probably, operative in both idiopathic nephrotic syndrome and SLE, suggesting similarities in the pathogenesis of both diseases [6].

In conclusion, this case report illustrates that, although a diagnosis of LN has been made in the past, this does not exclude the occurrence of renal pathology caused by other diseases than SLE. Therefore, a renal biopsy is mandatory in patients with a history of LN who present with re-occurrence of renal abnormalities with discrepant or atypical laboratory values.

References

1. Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, et al. (2004) The classification of glomerulonephritis in systemic lupus erythematosus revisited. J Am Soc Nephrol 15: 241-250.
2. Wallace DJ, Hahn BH (2002) Dubois' lupus erythematosus.
3. Illei GG, Takada K, Parkin D, Austin HA, Crane M, et al. (2002) Renal flares are common in patients with severe proliferative lupus nephritis treated with pulse immunosuppressive therapy: long-term followup of a cohort of 145 patients participating in randomized controlled studies. Arthritis Rheum 46: 995-1002.
4. Mok CC, Ying KY, Tang S, Leung CY, Lee KW (2004) Predictors and outcome of renal flares after successful cyclophosphamide treatment for diffuse proliferative lupus glomerulonephritis. Arthritis Rheum 50: 2559-2568.
5. Baldwin DS, Gluck MC, Lowenstein J, Gallo GR (1997) Lupus nephritis Clinical course as related to morphologic forms and their transitions. Am J Med 62: 12-30.
6. Hertig A, Droz D, Lesavre P, Grunfeld JP, Rieu P et al. (2002) SLE and idiopathic nephrotic syndrome: coincidence or not?. Am J Kidney Dis 40: 1179-1184.
7. Wang YT, Chou HH, Chen FF, Chen MJ, Chiou YY (2006) A case of minimal-change nephrotic syndrome in pediatric lupus erythematosus: just a coincidence?. Lupus 15: 244-247.
8. Perakis C, Arvanitis A, Sotsiou F, Emmanouel DS (1998) Nephrotic syndrome caused by minimal-change disease in a patient with focal proliferative SLE nephritis (WHO III) in remission. Nephrol Dial Transplant 13: 467-470.