Collapsing glomerulopathy in systemic autoimmune disorders: a case occurring in the course of full blown systemic lupus erythematosus

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Collapsing glomerulopathy (CG) is a recently described form of glomerular injury. Characteristic histopathological changes of CG consist of segmental and global collapse of the glomerular capillaries, wrinkling and retraction of the glomerular basement membrane, and marked hypertrophy and hyperplasia of podocytes. The most common cause is HIV associated nephropathy, but a few other causes were found recently.¹ CG has been reported during infections by parvovirus B19 (PVB19), cytomegalovirus, filariasis or tuberculosis and treatment with pamidronate.¹ CG has been also reported in systemic autoimmune disorders.

We report a case of CG occurring as the initial manifestation of a well defined systemic lupus erythematosus (SLE). A 17 year old young African woman was referred in September 2003 to our Internal Medicine Department for fatigue and fever (40°C). Physical examination showed alopecia, typical discoid lupus, and non-deforming polyarthritis evolving for 2 months. Antinuclear antibodies (ANA, 1/1280 speckled and homogeneous), anti-DNA, anti-SSA, anti-SSB, and anti-Sm antibodies were positive, the C3 fraction was low (0.69 g/l, normal >0.85). Red and white cell counts displayed lymphopenia ($1.2 \times 10^9/l$) and anaemia (haemoglobin 98 g/l) with 122 000 reticulocytes and a positive direct IgG Coombs test. Anticardiolipin antibodies and a search for lupus anticoagulant were negative. A lupus nephritis was suspected because of a nephrotic syndrome with hypoalbuminaemia (30 g/l), proteinuria (9 g/day; 70% albumin), and microscopic haematuria. The serum creatinine level was normal (75 µmol/l). SLE was diagnosed and a renal biopsy was performed. Renal biopsy found focal segmental collapse of glomerular capillaries. Immunofluorescence staining was negative for IgG, IgA, IgM, C1q, C3, fibrin, albumin, κ and λ chains. A diagnosis of CG was considered and lupus nephritis was ruled out.

Extensive searches for the main causes of CG were negative. PVB19 serology found IgG but no IgM, whereas PVB19 DNA polymerase chain reaction was negative in peripheral blood. The following serologies were negative: HIV, cytomegalovirus (CMV), hepatitis C virus, hepatitis B virus, *Treponema pallidum* haemagglutination-Venereal Disease Research Laboratory assay, Lyme borreliosis, Leishmania, and Loa loa. Blood HIV DNA polymerase chain reaction was negative at the time of diagnosis and 6 months later. The patient was not a drug misuser and had never received pamidronate, lithium, or interferon α before. The patient was treated with steroids (prednisone 0.5 mg/kg/day) and hydroxychloroquine (400 mg/day). Joint pain disappeared within 2 weeks. Three months later, her daily proteinuria had dropped to 0.6 g, albuminaemia was raised at 34 g/l, and there was no haematuria. One year later, there was no proteinuria, serum creatinine was 82 µmol/l. Prednisone was tapered to 15 mg/day.

We found 162 reported cases of HIV negative CG, at times called “idiopathic”.^{2–9} Among these, 18 (11%) were associated with either a connective tissue disease (CTD) or positive ANA. CTD associated with CG were: SLE-like disorders (<4 SLE American College of Rheumatology criteria; n = 8),^{4–5} primary Sjögren’s syndrome (n = 1),⁶ mixed CTD (n = 1).⁴ Additionally, CG was reported in patients without clinical features of CTD but with positive ANA (n = 8)^{3–6} and/or positive anti-DNA test (n = 1)⁶ and/or hypocomplementaemia (n = 1).⁶ CG associated with autoimmune conditions in 69% of patients evolved to end stage renal disease, an outcome, similar to that reported for patients with idiopathic CG, ranging from 50% to 100% in most series.⁵

Our patient with full blown SLE was promptly treated with steroids and hydroxychloroquine, and her renal disease improved with treatment. Because CG may relapse after an initial spontaneous remission,^{1–6} early improvement must be interpreted cautiously. Although there are no prospective treatment trials in CG, retrospective studies suggest that the best results have been obtained when treatment with steroids is started shortly after diagnosis.¹ Association of CG with CTD is not restricted to systemic autoimmune disorders. Recently, two cases of CG occurring during adult’s Still’s disease were reported.¹⁰ This newly recognised entity should be considered when patients with SLE or SLE related disorders develop a severe nephrotic syndrome without SLE pathological changes on renal biopsy, especially negative immunofluorescence staining.

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REFERENCES

- Schwimmer JA**, Markowitz GS, Valeri A, Appel GB. Collapsing glomerulopathy. *Semin Nephrol* 2003;**23**:209–18.
- Weiss MA**, Daquiaoag E, Margolin EG, Pollak VE. Nephrotic syndrome, progressive irreversible renal failure, and glomerular “collapse”: a new clinicopathologic entity? *Am J Kidney Dis* 1986;**7**:20–8.
- Detwiler RK**, Falk RJ, Hogan SL, Jennette JC. Collapsing glomerulopathy: a clinically and pathologically distinct variant of focal segmental glomerulosclerosis. *Kidney Int* 1994;**45**:1416–24.

- 4 Laurinavicius A, Hurwitz S, Rennke HG. Collapsing glomerulopathy in HIV and non HIV patients: a clinicopathologic and follow-up study. *Kidney Int* 1999;**56**:2203–13.
- 5 Avila-Casado MC, Vargas-Alarcon G, Soto ME, Hernandez G, Reyes PA, Herrera-Acosta J. Familial collapsing glomerulopathy: clinical, pathological and immunogenetic features. *Kidney Int* 2003;**63**:233–9.
- 6 Valeri A, Barisoni L, Appel GB, Seigle R, D'Agati V. Idiopathic collapsing focal segmental glomerulosclerosis: a clinicopathologic study. *Kidney Int* 1996;**50**:1734–46.
- 7 Bariety J, Nochy D, Mandet C, Jacquot C, Glotz D, Meyrier A. Podocytes undergo phenotypic changes and express macrophagic-associated markers in idiopathic collapsing glomerulopathy. *Kidney Int* 1998;**53**:918–25.
- 8 Grcevska L, Polenakovik M. Collapsing glomerulopathy: clinical characteristics and follow-up. *Am J Kidney Dis* 1999;**33**:652–7.
- 9 Singh HK, Baldree LA, McKenney DW, Hogan SL, Jennette JC. Idiopathic collapsing glomerulopathy in children. *Pediatr Nephrol* 2000;**14**:132–7.
- 10 Kumar S, Sheaff M, Yaqoob M. Collapsing glomerulopathy in adult: Still disease. *Am J Kidney Dis* 2004;**43**:4–10.

Lack of association of mannose binding lectin variant alleles with systemic lupus erythematosus

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Mannose binding lectin (MBL) is a member of the collectin family, is structurally related to the complement component C1q, and is involved in the innate immune response.¹ So far, three mutations of MBL have been described in codons 54, 57, and 52 (termed variant alleles B, C, and D or 0 alleles) that are associated with dysfunctional formation of the molecule.^{2–3} Homozygous combinations of variant alleles of MBL have been found in about 1–10% of Europeans and are associated with increased incidence of infections in childhood, subsets of adults, and possibly those with systemic lupus erythematosus (SLE).⁴

In a recent prospective study of 91 patients with SLE, MBL deficiency was a risk factor for “arterial thrombosis”, in particular, with myocardial infarction.⁵ We have now examined in a multicentre study 287 white German patients with SLE for MBL deficiency as a risk factor for myocardial and cerebral infarction.

DNA of these patients has been collected since 1999 in a German multicentre study on the genetics of connective tissue diseases⁶ after receiving written consent. All patients were white German subjects and fulfilled the American College of Rheumatology criteria for the classification of SLE.⁷ Of the patients with SLE, 263/287 (91.6%) were female, with a mean (SD) age at inclusion of 48 (14.5) years, and median duration of SLE at the time of inclusion of 15 years. DNA from 120 white German blood donors and from 61 patients with Sjögren's syndrome (classified according to ESG criteria⁸) was obtained as control.

MBL alleles were defined using a restriction fragment length polymorphism analysis as described previously.⁹ To control the quality of the method, 50 samples were analysed twice and gave identical results on retesting.

Homozygous combinations of 0 alleles of MBL were present in 20/287 (7%) and heterozygous 0 alleles in 103/

287 (36%) patients with SLE, in 6/61 (10%) and 16/61 (26%) patients with Sjögren's syndrome, and in 12/120 (10%) and 60/120 (50%) controls, respectively (not shown). The homozygous combination of 0 alleles was not associated with SLE.

Data on the prevalence of previous myocardial or cerebral infarction was reviewed from the charts of all patients with SLE, where possible, and could be collected from 14/20 patients with and 160/267 patients without homozygous MBL 0 alleles. Myocardial infarction had occurred in 1/14 (7.1%) and cerebral infarction in 0/14 (0%) patients with homozygous MBL 0 alleles compared with 13/160 (8.1%) and 12/160 (7.5%) patients without homozygous MBL 0 alleles (table 1).

Since then, 8/20 patients with SLE with homozygous MBL 0 alleles have been followed up for 4 years and myocardial and cerebral infarction have not occurred (not shown).

Inconsistent results were obtained from several studies, as to whether MBL is a risk factor for coronary artery disease. In a recent publication on 91 Danish white patients with SLE, 4/7 patients with homozygous MBL variant alleles developed myocardial infarction.⁵ Those patients have been followed up prospectively for up to 8 years. In our retrospective study on white German patients with SLE there was, however, no association of the prevalence of arterial thrombosis, myocardial or cerebral infarction, or leg embolus with MBL variant alleles.

Patients in our study were significantly older than those in the Danish study. The possibility cannot be ruled out that patients with homozygous MBL 0 alleles die at a younger age of arterial thrombosis or infections, the most common causes of death in patients with SLE¹⁰ and may be underrepresented in our study.

However, reports of MBL alleles as risk factors for myocardial infarction in SLE cannot be confirmed at present.

Table 1 Prevalence of previous myocardial and cerebral infarction and leg embolus in patients with SLE typed for MBL alleles

	A/A	A/O	O/O
Myocardial infarction	7/102 (7)	6/58 (10)	1/14 (7)
Cerebral infarction	8/102 (8)	4/58 (7)	0/14 (0)
Leg embolus	3/102 (3)	0/58 (0)	0/14 (0)

Results are shown as No (%).

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