Serum Laminin Level and Disease Activity in Primary Membranous and Membranoproliferative Gomerulonephritis: A Prospective Follow-Up

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Dear Sir,

In a previous cross-sectional study, we showed that in patients with primary chronic glomerular disease, the serum levels of laminin PI were related only to the kind of histological lesion, being significantly higher in chronic nephropathies characterized by either a diffuse thickening of the glomerular basement membrane or by mesangial proliferation and matrix expansion [1]. In the present study, we prospectively determined the serum levels of laminin PI, a pepsin-resistant fragment of laminin, by a competitive RIA in 11 patients, 7 males and 4 females, mean age 43 years (range 31-65), with biopsy-proven primary membranous (n = 8) or membranoproliferative (n = 3) glomerulonephritis. No patient suffered from chronic hepatic disease. The mean initial serum creatinine and proteinuria were 1.87 mg/dl (1.5-2.5) and 3.5 g/day (2-6), respectively. Patients were followed every 4 months for a 29-month period from diagnosis. In every control, we determined the serum creatinine, the endogenous clearance of creatinine, the systolic and diastolic blood pressure and the 24-hour urinary protein excretion. In all patients we determined serum laminin levels at the moment of diagnosis and after 12 and 24 months’ follow-up. Likewise, serum laminin levels were determined at the moment that patients achieved complete or partial remission or suffered a relapse. During follow-up, renal function did not change significantly (GFR: 48 ± 16 ml/min/m2 at kidney biopsy vs. 43 ± 21 ml/min/m2 at 29 months, NS).

The mean serum laminin levels at kidney biopsy (2.1, range 1.6-2.8 U/ml) were comparable to those we observed in a previous study [1]. Serum laminin did not correlate with renal function nor with 24-hour protein excretion.

Two patients with membranous nephropathy achieved complete remission within the 1st year of follow-up either spontaneously (n = 1) or after a 6-month course therapy with cyclophosphamide and glucocorticoids (n = 1). Two additional patients with
membranous nephropathy achieved also spontaneous remission at 14 and 18 months, respectively. In all patients with complete remission, serum laminin levels, decreased significantly (mean 2.2, range 1.8-2.5 U/ml vs. 1.76, 1.4-1.8 U/ml, p = 0.002). In 3 out of the 7 remaining patients (2 patients with membranous and 1 patient with membranoproliferative glomerulonephritis), proteinuria decreased significantly (mean 2.9, range 2.5-2.8 g/day at kidney biopsy vs. 1.7, 0.9-2.3 g/day at 29 months, p < 0.01) but serum laminin levels remained high (mean 2.1, range 1.85-2.3 U/ml). In the remaining 4 patients (2 patients with membranous and 2 patients with membranoproliferative glomerulonephritis), proteinuria did not change during follow-up and the serum levels of laminin remained high at the end of follow-up (mean 2.08, range 1.9-2.4 U/ml vs. 2.1, 1.85-2.75 U/ml, Wilcoxon test, p = 0.5). In 1 patient in whom complete remission was achieved after cyclophosphamide and prednisone therapy, membranous nephropathy relapsed at 18 months and, coinciding with this relapse, serum laminin increased (1.4 U/ml prior to vs. 2.12 U/ml coinciding with relapse). After a second cyclophosphamide trial, proteinuria decreased significantly (4.2 vs. 1.8 g/day) but no complete remission was achieved and serum laminin level remained high (2 U/ml).

Although a number of authors have provided evidence for increased serum laminin levels in some forms of chronic renal disease, at present little is known about the clinical relevance and the factors leading to this increase [2, 3].

In this study, we showed that serum laminin level was increased in most but not all patients with either membranous or membranoproliferative glomerulonephritis but we could not find a relationship between serum laminin and proteinuria at the moment of diagnosis. Although our data, for the first time provide evidence for a relationship between serum laminin levels and disease activity in primary membranous nephropathy, the clinical relevance of this fact is unclear, because during follow-up serum laminin only underwent significant changes in patients achieving a complete remission and correlated weakly with variations in urinary protein excretion in patients on partial remission. Moreover, since serum laminin was determined at the same time that patients achieved remission or experimented a relapse, we could not determine whether laminin changes preceded changes in urinary protein excretion. In our opinion, further studies are required in order to assess whether persistently elevated serum laminin levels may be an indicator of poor prognosis in the long-term and whether serum laminin may be an early marker of the disease activity in patients with membranous nephropathy.

References

