High Level of Protein C and Protein S in Nephrotic Syndrome

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Dear Sir,

As thromboembolic complications remain one of the most serious problems in adult patients with nephrotic syndrome (NS), the protein C-protein S natural anticoagulant system was evaluated in 32 adult patients with glomerular disease, 11 without and 21 with NS of different types (table I). The control group consisted of 20 healthy adult volunteers; protein C antigen level was measured in plasma and concentrated urine by an ELISA method (Asserachrom Protein C® from D. Stago, Paris); plasma protein S was assayed by the Laurell technique; factor II, VII, X and antithrombin III biological activities were assayed by routine techniques. Plasma protein C antigen level was not statistically different between control group and groups I, II, III but differed significantly between the control group and severe NS (group IV). In all proteinuric patients, plasma concentration of protein C antigen was positively correlated with the degree of proteinuria ($r = 0.67$, $p < 0.001$), cholesterol level ($r = 0.45$, $p < 0.02$) and the triglyceride

level ($r = 0.38$, $p < 0.05$) and inversely correlated with serum albumin concentration ($r = -0.50$, $p < 0.001$). No correlation could be demonstrated between plasma protein C antigen level and the other vitamin-K-dependent proteins, proteins S, factors II, VII, X. All the patients tested for protein C urinary loss ($n = 17$) exhibited protein C antigen in the urine (mean excretion rate, 16.77 U/24 h with extremes ranging from 0.08 to 80.6 U/24 h). The degree of protein C excretion in urine was positively correlated with the degree of proteinuria ($r = 0.520$, $p < 0.001$) but neither with proteinuria selectivity index nor plasma protein C level.

Plasma protein S antigen was measured in only 11 patients with NS and was found statistically significantly higher than in the control group ($p < 0.001$). Plasma protein S antigen level was inversely correlated with serum albumin concentration ($r = -0.73$, $p < 0.01$).

From our data we can conclude that despite the urinary loss of protein C, also reported by Mannuci et al. [3] and Salla et al. [5], an increased liver synthesis leads to normal or high plasma protein C antigen. Similar results

Table I. Protein C, protein S and AT III levels in glomerulopathy and NS (mean $\pm$ SD)

Protein C U/ml

Protein S U/ml

AT^{III}

U/ml

Group I

Glomerulopathy; p < 3 g/24 h; SA > 30 g/l

1.2 ± 0.21

0.99 ± 0.14

Group II

Mild NS; 3 < p < 5 g/24 h; SA < 30 g/l

1.36 ± 0.30

0.98 ± 0.20

Group III

Moderate NS; 5 < p < 10 g/24 h; SA < 30 g/l

1.45 ± 0.43

1.91 ± 0.02*

1 ± 0.06

Group IV

Severe NS; p > 10 g/24 h; SA < 30 g/l

1.82 ± 0.24*

0.92 ± 0.24

Control group p = 0

1.12 ± 0.26

0.92 ± 0.06

0.97 ± 0.10

*p < 0.001 versus controls.

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have been described by Cosio et al. [2], Mannucci et al. [3], 2 Pabinger-Fashing et al. [4], Sala et al. [5], Sorensen et al. [6]. Thus an acquired quantitative protein C deficiency in NS cannot be

responsible for the thrombotic tendency of 3 these patients. No quantitative deficiency in protein S was observed, but further investigations are needed to evaluate a possible decrease in functional protein S through some shift from free to bound protein S, as suggested by Comp et al. [1].

It is interesting to note that in the same group of 5 patients the concentrations of five vitamin-K-dependent proteins behave differently, which could be related to different liver synthetic rate, or to a difference in the extent to urinary loss, or both.

References