Dear Sir,

Several pieces of evidence suggest that plasma fibronectin (FN) has an important role in removal from circulation and processing of immune complexes (IC). Specific FN membrane receptors able to enhance IC inter-nalization via Fc receptors have been shown on mononuclear phagocyte system cells [1]. FN binding accelerates IC clearance from circulation and inhibits IC deposition in the mesangial area [2]. It was recently shown that IgA antibodies from patients with primary IgA nephropathy (IgAN) binds to collagen via a collagen-binding site of FN [3]. We observed that circulating IgA-FN aggregate (IgAFN-Ag) levels were related to the rate of removal from circulation of a recently proposed test probe for IgA-containing IC kinetic studies, i.e. an aggregated mixture of IgA1 and IgG [4]. Moreover 93.3% of 30 patients with IgAN were found to have IgAFN-Ag compared to 11.7% of 103 patients with other types of glomerulonephritis (GN) [5]. It was concluded that IgAFN-Ag is a useful serological marker for IgAN and may be involved in the pathogenesis of this disease [5].

We examined 100 sera from 58 adult patients with IgAN [idiopathic in 51, associated with Henoch-Schönlein purpura (HSP) in 7]. Control groups included 14 lupus GN patients, 9 patients with membranous GN and 9 patients with alcoholic cirrhosis without urinary abnormalities. The Bio-Carb Diagnos-
tics (Lund, Sweden) enzyme-linked immuno-sorbent assay was used. Results were calculated by subtracting absorbance at time 0 from absorbance at time 60 min for each well. Controls included three dilutions of a positive standard serum and a normal serum sample provided by the manufacturer, 4 sera (2 positive and 2 negative in previous assays) collected form the personal case report and a pool of 33 sera from 15 healthy subjects. Assay-to-assay variations were corrected by multiplying the OD value of the test specimen by the quotient obtained by dividing the mean OD in 20 healthy controls by the pool value of the daily protocol. Values exceeding the
upper 95% confidence limit of healthy people ranging in age from 19 to 47 years ( > 0.25 OD) were considered as positive.
The mean value of IgAFN-Ag in IgAN patients (0.30 ± 0.26, OD 400 nm) was found to be significantly higher (p < 0.001) than normal (0.09 ± 0.04) and control disease groups: 0.18 ± 0.9 in lupus GN (p < 0.05) and 0.15 ± 0.6 in membranous GN (p < 0.01). Patients with alcoholic liver cirrhosis without urinary abnormalities had levels of IgAFN-Ag (0.22 ± 0.16) similar to IgAN patients.
Positive values were obtained at the first determination in 26 out of 51 idiopathic IgAN patients (50.9%), 2 out of 7 HSP (28.5%), 2 out of 14 lupus GN (14.2%), 0 out of 9 membranous GN and 3 out of 9 cirrhosis patients.
Sequential evaluation of sera slightly increases the possibility of detecting positive results (54.6% of 86 sera from IgAN patients). Considering the entire GN patient population and assuming as ‘true positive subjects’ the patients with IgAN or HSP nephritis, sensitivity of the assay was 58%, specificity 86.9% an accuracy 71.6%. In this selected biopsy-proven GN population predictive value of positive and negative results were 90.3 and 40.0%, respectively.
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IgAFN-Ag values were significantly correlated with IgA levels (measured by laser nephelometry) both in the patient population considered as a whole (R = 0.27; p < 0.01) as well as the IgAN sample (R = 0.27; p < 0.02). Conversely, no significant correlation could be established between FN serum concentration (detected by nephelometry) and IgAFN-Ag levels, whatever the group of patients considered.
Linear regression analysis failed to reveal relationships with the mean erythrocyte number of three urine samples collected in 1 week, with protein urine excretion, or with serum creatinine in IgAN patients. However, by arbitrarily assuming as criteria of ‘urinary activity’ proteinuria levels > 1.5 g/24 h and/or
hematuria > 25 erythrocytes/high power (×400) microscopic field, contingency tables indicated a significant prevalence of positive IgAFN-Ag values in the ‘active’ group (χ² = 23.2; p < 0.0001). These data confirm, although with the percentage of positive values considerably lower than those previously reported by other authors [5], that the detection of supranormal levels of IgAFN-Ag in a patient with urinary abnormalities is highly suggestive of IgAN, but does not allow an accurate immunological monitoring of IgAN patients.
In vitro experiments showed that interaction between IgA and FN is a normal process enhanced in IgAN [6]. This enhancement was reported to relate with plasma levels of IgAFN-Ag [6], which is in agreement with our observation of a significant relationship between IgAFN-Ag and total IgA levels. Presently, however, the pathogenetic relevance of circulating IgAFN-Ag remains doubtful.

References


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