No Pathogenic Role of Enhanced Plasma IgA Binding Capacity to Fibronectin and IgA-Fibronectin Aggregates in Henoch-Schönlein Purpura

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Dear Sir,

Numerous clinical and histological observations suggest that the pathogenesis of Henoch-Schönlein purpura (HSP) nephritis is related to the deposition of circulating complexes containing IgA in the glomerular mesangium [1]. Several authors [2-4] have demonstrated the presence of circulating aggregates containing IgA and fibronectin (FN) in HSP nephritis and IgA nephropathy (IgAN) as well. Some authors [2, 3] postulate that these aggregates bind to glomerular collagen and induce renal lesions, while our previous work [4] strongly suggests that IgA-FN complexes do not play any pathogenic role in IgAN and result from an enhancement of IgA physiological binding to FN, related to increased polymeric IgA plasma concentrations [4]. As HSP in children is often observed without any renal symptoms [5], this illness represents an ideal clinical model for clarifying the pathogenic role of circulating IgA-FN complexes and of the FN-binding capacity of IgA.

We have, therefore, measured by previously described enzyme-linked immuno-sorbent assay methods [4] the amount of circulating IgA-FN aggregates and the FN-binding capacity of plasma IgA in 15 children (10 males and 5 females, 3-18 years of age) presenting with HSP. Five of them presented with no renal signs (no urinary abnormalities, no reduced creatinine clearance) at the time of testing, whereas the remaining 10 displayed hematuria, associated with proteinuria in 2 of them. Besides typical cutaneous and gastrointestinal signs, the diagnosis of HSP was also ascertained by the demonstration of either significant IgA glomerular mesangial deposits (5 cases) or a leukocytoclastic vasculitis with granular dermal IgA deposits (10 cases). The control group consisted of 15 age-matched children undergoing blood examination for the purpose of surgical procedures (orchidopexy, hernia, phimosis, etc.).

The FN-binding capacity (optical density; mean $\pm$ SD) of plasma IgA measured in patients with HSP was significantly ($p < 0.05$) higher (0.70 ± 0.40) than that observed in controls (0.43 ± 0.23). However, an increased FN-binding capacity of plasma IgA was not more frequently found in patients with renal symptoms (4 of 10) than in the others (3 of 5). The

circulating IgA-FN aggregate levels (optical density; mean $\pm$ SD), as determined by the gelatin-binding capacity of plasma IgA, were also significantly ($p < 0.05$) higher in HSP patients (0.57 ± 0.40) as compared with controls (0.32 ± 0.17). However, the percentage of increased values was not higher in patients with renal symptoms (5 of 10) than in the others (3 of 5). To provide information on the size of IgA preferentially interacting with FN, as well as on the features of this interaction, plasma from 2 patients with HSP and from 2 controls was transferred to an Ultrogel AcA 22 molecular sieve column as described [4] before, being tested by enzyme-linked immunosorbent assay for the FN-binding capacity of IgA in the presence (500 mM) or absence of various monosaccharide solutions (α -methyl mannose, Z-galactose, or N-acetyl-glucosamine). By this method, it was demonstrated that the absolute amount of macro-molecular IgA was markedly increased in HSP. Moreover, IgA fractions of normal or pathological plasma presenting with a molecular weight > 450 kD exhibited a much higher FN-binding capacity than monomeric IgA fractions. In addition, when the results were expressed for 100 μ g IgA, FN-binding capacity of the 'macromolecular' IgA fraction was comparable in patients and controls. Finally, the FN-binding capacity was not inhibited in the presence of monosaccharide solutions. In conclusion, the results of the present study support the concept that the ability of macromolecular IgA to directly bind to FN is involved in the formation of circulating IgA-FN complexes, that this normal binding, although enhanced in HSP, is probably not responsible for kidney injury, at least in the patients studied, and that this binding represents a protective mechanism limiting, as in normal subjects, the accumulation of some FN-binding polymeric IgA molecules in the glomerular mesangium. This is in agreement with the difficulty to induce renal IgA deposits and glomerular lesions after parenteral injection of polymeric IgA in experimental animals [6]. Besides, the results of our experiments also suggest that the FN-binding capacity of plasma IgA is probably not mediated by lectin-like bonds.

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