HYPERTENSION IN MESANGIAL IgA GLOMERULONEPHRITIS

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Summary

Blood pressure in 75 patients with IgA nephropathy (IgA-GN), confirmed by renal biopsy, was related to clinical, immunological and morphological findings. The findings were compared with an age-matched control group of patients with non-IgA-GN. Overall prevalence of hypertension (HT) was similar in IgA-GN and non-IgA-GN (38.7% vs 38.2%). The presence of HT in IgA-GN was related to age, renal function, immunohistological pattern and degree of glomerular sclerosis or vascular lesions respectively. No correlation was found between HT and elevated serum IgA, circulating IgA immune complexes and IgA skin deposits. The current observations underline the value of hypertension for predicting development of renal failure. Vascular lesions are not only strongly correlated with, but may even precede development of, hypertension as confirmed by longitudinal observations.

Introduction

Mesangial IgA glomerulonephritis (IgA-GN) is the most common form of GN (25%). In contrast to previous more optimistic reports [1,2] about one-third of such patients will ultimately develop chronic renal insufficiency. Despite much recent progress with respect to understanding the pathogenesis of this condition, information on the genesis of hypertension and its role in progression of renal failure is still controversial. In the present study, blood pressure was related to clinical, immunological and histological findings in patients with biopsy-confirmed IgA-GN.

Dedicated to Professor Dr Drs.h.c. W Doerr, Heidelberg on the occasion of his 70th birthday.
Patients and methods

Between 1976 and 1983 we observed 75 patients with biopsy-confirmed idiopathic mesangial IgA-GN. Patients with alcoholic liver disease, liver cirrhosis and systemic diseases (Henoch-Schönlein purpura, SLE) were excluded. Median age was 32 years (range 16–62 years). Some pertinent clinical findings were reported previously [3,4]. Patients with IgA-GN were compared with an age matched control group consisting of 110 cases with biopsy-confirmed GN other than IgA-GN (in the following non-IgA-GN) i.e. minor glomerular abnormalities (n = 43): idiopathic nephrotic syndrome with focal-segmental sclerosis (n = 15); membranous GN (n = 15); mesangial-proliferative GN (n = 26); membrano-proliferative GN (n = 11). Skin biopsies were performed of clinically normal skin from the median aspect of the thigh by surgical excision in 58 patients with IgA-GN. For details of light and immunofluorescence techniques see Reference 3. The data analysed refer to the time of renal biopsy. Hypertension was defined as blood pressure >140/90mmHg measured on three independent occasions. Statistical evaluation was by Fisher’s exact test.

Results

Prevalence of HT was similar in IgA-GN and non-IgA-GN. Thirty-eight point seven per cent (29/75) of patients with IgA-GN and 38.2 per cent (42/110) with non-IgA-GN were hypertensive at the time of renal biopsy. The incidence of HT increased with declining renal function (serum creatinine <1.5mg/100ml: 22.4 per cent in IgA-GN, 31.7 per cent in non-IgA-GN; serum creatinine >1.5mg/100ml: 94 per cent in IgA-GN, 57.1 per cent in non-IgA-GN).

In both IgA-GN and non-IgA-GN there was a close relationship between HT and age (hypertensive patients <30 years IgA-GN 17.2 per cent, non-IgA-GN 33 per cent; >30 years IgA-GN 82.8 per cent; non-IgA-GN 66.7 per cent). In IgA-GN episodes of macrohaematuria were associated with significantly lower incidence of HT (HT without macrohaematuria: 65.5 per cent; HT with macrohaematuria: 34.5 per cent, p<0.01); however, age and macrohaematuria could not be dissociated from the confounding variables of renal function.

There was no relation of HT to serum IgA or the presence of circulating IgA immune-complexes. Furthermore, the presence or absence of IgA deposits in skin biopsies were not related to blood pressure. IgA deposits in skin biopsies were demonstrable in 25.9 per cent of all patients, more specifically in 23.8 per cent of HT and 27 per cent of non-HT patients.

In contrast to the above immunological findings, HT was clearly related to findings of renal light and immunofluorescence microscopy. In hypertensive patients glomerular deposits containing both IgM and IgA were more frequently found than in normotensive patients (80% vs 20%). A purely mesangial pattern of immune deposits was less frequently associated with hypertension than a mesangial and capillary pattern (35% vs 65%). Extensive capillary wall involvement was uniformly associated with HT and a more severe clinical course. A highly significant relation was observed between HT and extent of glomerular
TABLE I. Blood pressure and glomerular sclerosis or vascular lesions

<table>
<thead>
<tr>
<th></th>
<th>Normal blood pressure</th>
<th>Elevated blood pressure</th>
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<tbody>
<tr>
<td></td>
<td>&lt;140/90mmHg (n = 46)</td>
<td>&gt;140/90mmHg (n = 29)</td>
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<tr>
<td>Glomerular sclerosis*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20%</td>
<td>39 (85%)</td>
<td>10 (34%)</td>
</tr>
<tr>
<td>&gt;20%</td>
<td>7 (15%)</td>
<td>19 (66%)*</td>
</tr>
<tr>
<td>Vascular lesions**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>21 (46%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>present</td>
<td>25 (54%)</td>
<td>28 (97%)+</td>
</tr>
</tbody>
</table>

* percentage of total glomeruli with segmental and/or global sclerosis  
** arteriolar hyalinosis and/or arterial sclerosis  
+ p<0.01

sclerosis or presence of vascular lesions respectively (Table I). Severe arteriolosclerosis was uniformly accompanied by segmental or global glomerulosclerosis comprising more than 20 per cent of glomeruli. No IgA-deposits were seen in arterioles except occasionally in the short segment of vas afferens contiguous with the vascular pole. Of particular interest is the later development after a median follow-up of six years of HT and chronic renal failure in five of 25 initially normotensive patients who had arteriolar hyalinosis in their initial renal biopsies.

The median rate of progression of renal failure (creatinine mg/dl per 12 months) was significantly (p<0.05) greater in IgA-GN patients with renal failure (creatinine 1.5mg/dl) who had persistent hypertension (n=11), i.e. 140/90mmHg on all occasions irrespective of medication [0.1mg/dl/12 months; range (-0.7)–(+8.6)] as compared with those who had intermittent hypertension (n=14), i.e. at times above and at times below 140/90mmHg [0.4mg/dl/12 months; range (-1.0)–(+0.9)]. The median follow-up was 30 months, range 7–84; median age 42 years (range 24–61) in the patients with intermittent hypertension; in the patients with persistent hypertension the median follow-up was 25 months, range 7–42, median age was 44 years (range 31–61).

Discussion

The above data demonstrate that the incidence of HT in IgA-GN is comparable to that in other forms of GN and clearly related to age, renal function and type of renal lesions. The incidence of HT is higher than in historical reports but in line with recent observations of other authors[5,6]. The present demonstration of a relation between blood pressure status and course of renal failure is in good agreement with a previous retrospective analysis of D’Amico[7] who noted hypertension as one important factor differentiating patients with a benign and malignant course.
The demonstration of a correlation between hypertension and severity of renal lesions does not solve the problem of whether renal lesions are the cause or the consequence of HT. It is therefore of note that arteriolar hyalinosis may precede the development of HT, as noted by us in several longitudinal observations. These observations are in agreement with previous results of Finer [8]. This raises the issue of whether intrarenal and glomerular hypertension precedes the development of systemic hypertension. Such glomerular hypertension has been demonstrated in animal models of glomerulonephritis [9] and other models of glomerular damage [10].

These concepts may provide a rationale for thorough antihypertensive intervention in such patients.

References

2 McCoy RC, Abramowsky CR, Tisher CC. Am J Pathol 1974; 76: 123
5 Droz D. Contr Nephrol 1976; 2: 150

Open Discussion

DAVISON (Chairman) Thank you Dr Rambausek for that excellent presentation. Could I perhaps start the discussion by asking you why you feel the presence of IgM in addition to the IgA should have such an important role?

RAMBAUSEK We could not find any pathogenetic role for the IgM. We think it is a finding that we cannot explain up to now. It is mainly found in the sclerotic lesions.

ZUCCHELLI (Bologna) Regarding the identical frequency of hypertension between IgA and other glomerulonephropathies, it is our opinion that in membranous nephropathy there is not the same incidence as in IgA nephropathy. We think that the mesangial lesion probably is more related to the hypertension than in general glomerulonephropathy. Secondly, about the importance of vascular lesions in the genesis of hypertension. We have studied many patients with vascular lesions without hypertension. In this patient we have an activation of intrarenal beta receptors and we think that probably the stimulation of these receptors may be the cause of secondary arterial lesions and secondary hypertension. Do you agree with this hypothesis?
RAMBAUSEK  We agree completely with your last hypothesis. The incidence of hypertension in IgA nephritis is much higher than in membranous nephropathy. Maybe because you have more subjects with a nephrotic syndrome in this population group. Did you compare that?

ZUCCCELLI  Yes, without nephrotic syndromes.