

MALIGNANT ESSENTIAL HYPERTENSION: COMPARISON WITH MALIGNANT HYPERTENSION IN IgA NEPHROPATHY

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Summary

In the last 12 years, 10 patients with biopsy proven IgA nephropathy presented with malignant hypertension. Their clinical course was compared with that of 10 patients with essential malignant hypertension who underwent renal biopsy. There were no differences in the known duration of hypertension, history of gross haematuria or proteinuria, but patients with malignant essential hypertension had higher blood pressures and more severe degrees of renal failure on admission. Despite this, patients with malignant essential hypertension had a better prognosis for recovery of renal function.

Malignant hypertension in IgA nephropathy is commoner than previously reported. In spite of some clinical differences it presents in a fashion similar to that of malignant essential hypertension, and therefore, given a case of malignant hypertension, it is difficult to rule out IgA nephropathy if a renal biopsy is not performed.

Introduction

Although hypertension is common in IgA nephropathy [1], malignant hypertension has been infrequently reported as the presenting feature of this glomerular disorder [2].

This article describes a subset of patients with IgA nephropathy and malignant hypertension, and compares them with a series of patients with documented essential hypertension who underwent renal biopsy, to determine if there are any clinical differences that might allow distinction between the groups.

Methods

From January, 1972 to January, 1985, 10 patients with malignant hypertension were diagnosed as having IgA nephropathy at our institution. They were compared

with a series of 10 consecutive patients with a diagnosis of malignant essential hypertension seen over a similar period of time and in whom a renal biopsy specimen was available.

Renal biopsies

After fixation in Bouin's fluid and paraffin inclusion, 3μ sections were stained with haematoxylin-eosin, PAS, Masson's trichrome and silver methenamine. Cryostat sections were treated with fluorescein labelled specific antisera to human IgA, IgG, IgM, C₃, C_{1q} and C₄ (Behringwerke Laboratories). All biopsies were studied by light microscopy and immunofluorescence. Particular attention was paid to glomerular cellularity, percentage of sclerosed glomeruli and to the degree of interstitial fibrosis or infiltrates and of tubular atrophy. In addition, renal vessels were evaluated for the presence or absence of hyaline arteriosclerosis, proliferative endarteritis or arteriolar fibrinoid necrosis.

Criteria for diagnosis Malignant hypertension was defined as a diastolic blood pressure equal or higher than 140mmHg, grade III or IV hypertensive retinopathy and renal failure (serum creatinine of 2mg/100ml or more).

IgA nephropathy was diagnosed on the basis of the immunofluorescence demonstration of pure or predominant diffuse IgA deposits in the glomerular mesangium and the absence of liver disease, Henoch-Schönlein purpura or systemic lupus erythematosus.

Essential hypertension was diagnosed when 1) a renal biopsy was available and there was no evidence of primary glomerular disease; 2) a renal angiogram ruled out renovascular hypertension, and 3) there were no clinical or laboratory findings suggesting other forms of secondary hypertension.

Student's 't' test or the χ^2 test were employed for statistical analysis, as appropriate.

Results

There was no significant difference between patients with malignant essential hypertension or malignant hypertension in IgA nephropathy in terms of sex (9 males in each group), age (38.5 ± 3.7 , \pm SEM versus 36.4 ± 3 years, respectively), or known duration of hypertension (11.2 ± 8.2 versus 23.3 ± 9.6 months, $p=NS$). Five of the 10 patients with IgA nephropathy gave a history of gross haematuria, but this symptom was also recorded in two of 10 patients with essential malignant hypertension ($p=NS$). Moreover, both groups had similar degrees of proteinuria at onset ($2.4\pm 0.7g/24hr$ in essential hypertension versus $3.3\pm 0.7g/24hr$ in IgA nephropathy, $p=NS$).

Patients with malignant essential hypertension had significantly higher mean arterial blood pressures and peak serum creatinines on admission than patients with IgA nephropathy (177.7 ± 4.7 versus $164\pm 3.2mmHg$, $p=0.026$ and 8.9 ± 1.2 versus $4.6\pm 0.9mg/100ml$, $p=0.012$ respectively).

After a mean follow-up of 32.4 ± 11.3 months for patients with essential

hypertension, and of 11.3 ± 2.4 months for patients with IgA nephropathy ($p=NS$), four of 10 of the former and six of 10 of the latter required dialysis. In the remaining, serum creatinine had changed at an average -5.4 ± 1.8 mg/100ml in patients with essential hypertension and -0.4 ± 0.3 mg/100ml in patients with IgA nephropathy ($p=0.037$).

TABLE I. Semi-quantitative study of the main histological findings (excluding specific glomerular lesions)

	IgA nephropathy	Malignant Essential hypertension	p
% Sclerosed glomeruli (\pm SD)	28.4 ± 12.4	17.5 ± 13.9	NS
Interstitial fibrosis	3/10	2/10	NS
Interstitial infiltrates	7/10	3/10	NS
Tubular atrophy	5/10	0/10	<0.05
Arteriolar fibrinoid necrosis	3/10	7/10	NS
Proliferative endarteritis	3/10	8/10	<0.025
Hyaline arteriosclerosis	7/10	1/10	<0.025

Vascular and tubulointerstitial lesions were evaluated as absent if 0 to + and present if ++ or +++

Table I summarizes the main histological features. Figure 1 illustrates the histopathological findings in a patient with IgA nephropathy and malignant hypertension.

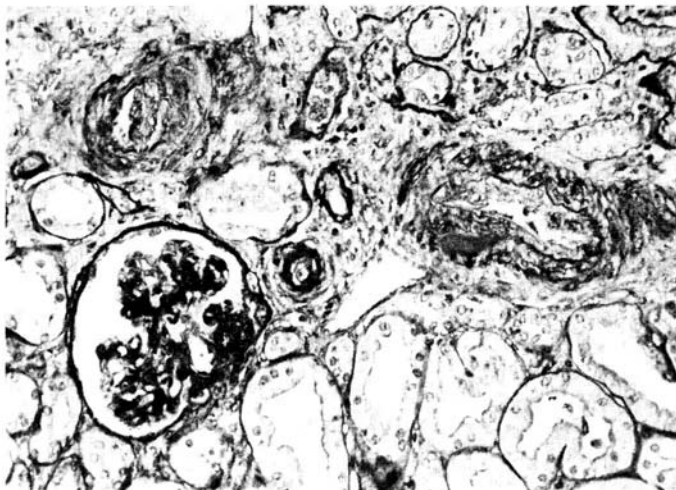


Figure 1. Renal biopsy fragment in a patient with IgA nephropathy and malignant hypertension showing glomerular mesangial expansion, proliferative endarteritis and arteriolar fibrinoid necrosis (PAS x 315 – reduced for publication)

There was no correlation between the percentage of sclerosed glomeruli, or the degree of tubular atrophy, interstitial fibrosis or infiltrates with the severity of renal failure, need for dialysis or subsequent course.

Discussion

The results of this study indicate that malignant hypertension is a complication of IgA nephropathy that occurs more commonly than previously reported. Patients presenting with malignant hypertension represent approximately 15 per cent of our total series of IgA nephropathy. Despite the fact that patients with IgA nephropathy had higher blood pressures and serum creatinines on admission than patients with essential malignant hypertension, there was considerable overlap in clinical features between both groups, so that given an individual case of malignant hypertension it is difficult to rule out IgA nephropathy unless a renal biopsy is performed. The question arises as to whether it is necessary to biopsy all patients with malignant hypertension. Present day anti-hypertensive therapy permits blood pressure control in almost all patients with severe hypertension before performing the renal biopsy, thereby lessening the risk of subsequent haemorrhage.

We do not advocate performing renal biopsies in all patients with malignant hypertension, because our data are limited to a relatively small number of patients. Nevertheless we believe that a liberal interpretation of the indications for renal biopsy in malignant hypertension would lead to the discovery of a sizeable number of patients with underlying glomerular disease, and particularly of IgA nephropathy. This is of more than academic interest since it carries prognostic implications. Six of our 10 patients with IgA nephropathy and malignant hypertension progressed to dialysis in less than a year. Therefore the development of malignant hypertension worsens considerably the prognosis of IgA nephropathy. In the patients who did not require dialysis at the end of follow-up there were clear cut differences between the two groups: whereas in the patients with IgA nephropathy renal function remained essentially unchanged, in the patients with malignant essential hypertension there was an average decrease of 5.4mg/100ml in serum creatinine. This occurred with acceptable blood pressure control in both groups. The long-term improvement in renal function when patients with malignant hypertension have their blood pressures controlled is well known [3].

From the histological point of view, it is of note that only three patients with IgA nephropathy had arteriolar fibrinoid necrosis. In this work, we have defined malignant hypertension primarily on clinical grounds, and it is not mandatory to have correlation between clinical malignant hypertension and the histological demonstration of fibrinoid necrosis [4]. In fact, arteriolar fibrinoid necrosis is found less frequently than proliferative endarteritis in malignant hypertension [4].

The reasons for the high prevalence of malignant hypertension in IgA nephropathy are unknown, but recent evidence suggests the possibility of alterations in the renal microvasculature. It has been found that some patients with IgA

nephropathy have demonstrable intra-renal vascular sclerosis long before they develop hypertension [5] and this has been found in up to one-third of initial renal biopsies [6]. Moreover, extraglomerular electron dense deposits probably representing immune complexes have been reported in the renal arterioles of a significant number of patients with IgA nephropathy [7]. The latter observation is supported by the immunofluorescent demonstration of IgA, C₃ and fibrin in segments of the wall of intestinal submucosal arteries in patients with IgA nephropathy and abdominal pain [8].

These observations indicate that alterations in the peripheral arterioles, probably immune-complex mediated, are common in IgA nephropathy and that severe hypertension could result from them.

Regardless of the exact pathogenetic mechanism involved, IgA nephropathy should be included in the differential diagnosis of malignant hypertension, and renal biopsy should be considered in the diagnostic work-up of such patients.

References

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