LONG TERM FOLLOW UP OF IgA MESANGIAL DEPOSITS GLOMERULONEPHRITIS

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Summary

The clinical course of IgA Mesangial Deposits Glomerulonephritis (MDGN) has been investigated in 178 patients for 1 to 32 years (mean 6 years) from the onset of symptoms. Impairment of renal function occurred in 28 patients, 13 of whom required RDT or died in uraemia. Hypertension was observed in 67 patients. The actuarial survival rate at ten years was 91%. A significant correlation was observed between the occurrence of renal failure and the following features: absence of episodes of gross haematuria, early appearance of hypertension, marked proteinuria and sclerosing glomerular lesions. These data suggest that IgA MDGN has generally a very prolonged course, but in a few cases may evolve, sometimes early, to chronic renal failure.

Introduction

Glomerulonephritis associated with IgA mesangial deposits (MDGN) is considered a well-defined clinicopathological entity, first described by Berger in 1968\(^1\). This condition has been subsequently described by many authors\(^2\)–\(^6\), however a long term follow up has been described in only a few reports\(^7\),\(^8\).

Materials and Methods

MDGN, defined by the immunohistological picture of diffuse and prevalent mesangial deposits of IgA, was observed in 187 adult patients out of 926 with non-systemic glomerular disease. The age ranged from 16 to 69 years, 125 patients were males. Clinical findings at presentation were as follows: 107 patients had one or more episodes of macroscopic haematuria (in 68 cases in association with upper respiratory tract infection), 80 had symptomless microscopic haematuria and/or proteinuria that in 7 cases exceeded 3 g/24 hrs. C\(_3\) serum levels were normal in all 127 tested cases. High serum IgA levels
(> 400 mg/100 ml) were found in 14 out of 61 patients.

Light microscopy specimens were adequate in 143 cases: 13 showed 'minimal' glomerular lesions, 105 focal proliferative changes, 12 a diffuse mesangial proliferative GN and 13 advanced sclerosing lesions.

Results

Follow-up

One hundred and seventy eight patients have been followed for 1–32 years (mean 6) after the onset of GN.

Complete and prolonged clinical remission was observed in 10 patients. Arterial hypertension, present at onset in 15 patients, developed subsequently in 52. Renal insufficiency (plasma creatinine > 2 mg/100 ml) was present at the time of renal biopsy in 6 patients, and appeared subsequently in 22

![Figure 1. Actuarial survival of IgA mesangial GN (178 cases)](image)

Further cases: 13 of them were submitted to haemodialysis or died in uraemia. The appearance of renal failure occurred during the first five years of the disease in 16 patients. The actuarial survival rate is 91% at ten years (Figure 1).

Correlations

The incidence of renal failure has been correlated with the clinical and histological parameters illustrated in Figure 2. A significant correlation with renal failure (unfavourable outcome) was found for:

1) Absence of macroscopic haematuria.
2) Marked proteinuria.
3) Hypertension.
4) High IgA serum levels.
5) Light microscopy finding of advanced sclerosing lesions.

No correlation was found between the clinical course and the age of patients at onset of nephropathy.

Figure 2. Correlations between features of the disease and the appearance of renal insufficiency
Discussion

Many reports have suggested a good prognosis for MDGN, especially in paediatric groups9–11. Nevertheless a few cases of unfavourable outcome have been reported7,12. More recently a long term study showed a surprisingly high incidence of renal failure in adult patients8.

Our data confirm that some patients may evolve towards renal failure, even though to a lesser extent than reported by Droz8. In our experience the course of the nephropathy is more benign than that of other primary GN, such as membranous or membranoproliferative GN.

The clinicopathological correlations in the follow up study show that macroscopic haematuria is a favourable sign, while heavy proteinuria, hypertension, high IgA serum levels and advanced sclerosing lesions are significantly associated with the occurrence of functional impairment.

Some patients develop renal failure early in the course of the disease, while others have a prolonged course without renal insufficiency. This behaviour could suggest that the two groups represent two entities. Alternatively the cases with an early unfavourable evolution may have had a very long asymptomatic period before the apparent onset, as supported by the finding of advanced sclerosing lesions in some of these patients. In addition, the absence of a major clinical sign such as macroscopic haematuria may delay discovery of the nephropathy.

However the mean age at onset and the duration of the disease were not significantly different in patients with or without renal insufficiency.

Acknowledgment

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References

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10 Davies, DR, Tighe, JR, Jones NF and Brown, GW (1973) J. Clin. Pathol., 26, 672
Open Discussion

BROUMAND (Tehran) Berger’s patients had neither renal failure nor hypertension. Lupus nephritis, Henoch Schönlein nephritis and Berger’s disease can all have IgA nephropathy. Did you rule out lupus by testing for anti-nuclear factor, and how did you rule out Henoch Schönlein?

COLASANTI In my opinion we excluded Schönlein nephropathy because of the absence of systemic signs like purpura and hypocomplementaemia.

KLEINKNECHT (Paris) A high percentage of your patients developed chronic renal failure. I think that this has been underestimated in the past and I wonder whether, if you had a longer follow-up, the incidence of this would be higher. In our experience about 20 to 25 per cent of patients with IgA nephropathy develop chronic renal failure and require haemodialysis or renal transplantation, and according to the mean actuarial curve about 50% of patients at 20 years have chronic renal insufficiency. My question is: did some of your patients with a poor prognosis who developed chronic renal failure get transplanted, and did the original disease recur in the renal graft, and was this harmful for the renal graft?

COLASANTI We have transplanted only one patient and after two years the patient showed recurrence of GN in the graft with IgA mesangial deposits: the patient had microscopic haematuria and normal renal function after two years of follow-up.

KNAPP (Nottingham) Do you feel that you are investigating and biopsying most cases of haematuria because of a close relationship with your urologists, because I think that the pattern of clinical features that one is going to see is going to depend on how many of the patients with haematuria in the population get investigated by nephrologists. A second and a quite separate question is: did any of the people who ended up in renal insufficiency have no bad features at presentation?

COLASANTI If you work with surgeons you see a lot of macrohaematuria but we have done biopsies only in patients in whom we could exclude surgical causes of haematuria and in all the patients in whom we suspected glomerulonephritis. We had 6 cases of recurrent macroscopic haematuria without IgA disease and without any reason being found. The second question: we have 20 cases that developed renal insufficiency some time after the renal biopsy. At the time of renal biopsy they had no sign of bad prognosis, no hypertension etc.

KNAPP Have you any idea of the size of the population that your unit looks after?

COLASANTI About two million people.

ZOUWEN (Utrecht) In a small series we thought the degree of interstitial damage you see in the biopsy is rather an important prognostic sign: did you look out for this? Also, did you do skin biopsies to look for IgA?
COLASANTI We have not noted any precise correlation, because it is difficult to quantitate interstitial damage. In general we find the greatest interstitial damage in patients who have the most glomerular damage. We have done only five skin biopsies and they were completely negative.

CAGNA (Vercelli) At what age in your patients was the illness first detected?

COLASANTI The mean age at onset of nephropathy was 29.6 years, 29.8 for patients in renal insufficiency and 29.3 for the others.

EGIDO (Madrid) About 26% of one hundred renal biopsies we did last year showed this type of nephropathy. One question: what was the incidence of high serum IgA levels in your cases? In our series the IgA was elevated in 70% of all patients and in 90% of those who were hypertensive.

COLASANTI Fourteen patients out of 61 — 23% — of our patients had serum IgA levels above our normal range of 350—400 mg/100 ml. I know that in other reports there are higher incidences.