IGA NEPHROPATHY: A MALAYSIAN EXPERIENCE

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SUMMARY

A total of 45 patients with IgA nephropathy were seen at the Department of Nephrology, General Hospital, Kuala Lumpur and the Department of Medicine, Universiti Kebangsaan Malaysia (National University of Malaysia) between January 1982 to June 1985. This represents an incidence of 10.7% of all primary glomerulopathies. There does not appear to be any racial predilection and the clinicopathological features generally conforms with those reported elsewhere. However it seems to be as common in females as in males but the latter have a worse prognosis. The high incidence of renal failure and hypertension in our patients within the short follow-up period is noteworthy.

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INTRODUCTION

IgA nephropathy is a sub-group of chronic glomerulonephritides of unknown aetiology. It has well-established clinical and pathological features and is characterised by mesangial deposition of IgA in renal glomeruli as detected by immunofluorescent examination.[1] The disease appears to have a worldwide distribution and its incidence varies from 11 – 42% of biopsies performed for primary glomerular disease in series from France,[2] Australia,[1] Singapore,[3] Japan[4] and North America.[5] Currently, there is no satisfactory explanation for the disparity.

IgA nephropathy was initially considered a benign disease but recent experience shows that it is a progressive glomerulopathy and it has been estimated that 2 – 3% of patients will develop renal failure every year.[1] The purpose of this communication is to present our experience with IgA nephropathy in Malaysia.

MATERIALS AND METHODS

From January 1982 to June 1985, a total of 419 patients suffering from primary glomerular diseases were seen and biopsied at the Department of Nephrology, General Hospital, Kuala Lumpur and the Department of Medicine, Universiti Kebangsaan Malaysia. All renal tissues were subjected to light-microscopy and immunofluorescent examination using antisera against IgG, IgA, IgM, C_3, C_4 and fibrin.

The diagnosis of IgA nephropathy was based on clinical data and immunofluorescent staining of predominantly IgA within the mesangium of the glomeruli. The presence of liver disease, malignancies, systemic lupus erythematosus were excluded. Patients with clinical features of anaphylactoid purpura were also excluded. For light-microscopy only those biopsies with four or more glomeruli were included.

RESULTS

Clinical Features

45 patients met the diagnosis criteria for IgA nephropathy. This represents an incidence of 10.7%. Their ages ranged from 10 – 53 years but 27 (60%) were less than 30-years-old. There were 27 males and 18 females; 17 were Malays, 24 Chinese and four Indians. The mode of presentation is shown in Table I.

Two patients presented during pregnancy. Two patients had thyrotoxicosis, one patient had chronic rheumatic heart disease with aortic incompetence and another had rheumatoid arthritis.

TABLE I

MODE OF PRESENTATION IN IgA NEPHROPATHY

Presentation		No.	(%)
Nephrotic syndrome		15	(34)
Asymptomatic – proteinuria	8)		
– haematuria	1)	18	(41)
– proteinuria & haematuria	9)		
Macroscopic haematuria		8	(17)
Stress haematuria		1	(2)
Chronic renal failure		1	(2)
Acute oliguri renal failure		2	(4)
Total		45	(100)

All patients were seen between one week to 13 years from the onset of the disease. However 25 cases (56%) were seen within six months.

Hypertension (defined as blood pressure more than 130/90 mmHg) was detected in seven patients at presentation and another five developed it during follow-up.

Urine analysis showed that 31 patients (69%) had both albuminuria and haematuria. 13 patients (29%) had only albuminuria and one (2%) had isolated haematuria. The urinary findings remained essentially the same during follow-up. Bouts of macroscopic haematuria were reported in five patients following symptoms of an upper respiratory tract infection.

Fifteen patients developed renal failure (defined as serum creatinine of 125 μmol/l or more) at presentation or during follow-up. There were 14 males and one females. Their serum creatinine ranged from 128 μmol/l to 1,650 μmol/l. Of these, nine patients had nephrotic syndrome and three had asymptomatic proteinuria and haematuria. Nine of these patients with renal failure were less than 30-years-old. Since then, one patient was lost to follow-up and four progressed to end-stage renal failure requiring dialysis or transplantation.

Pathological Features

Light-Microscopy. The histopathological diagnosis correlated to clinical presentation is shown in Table II.

The most common lesion was diffuse proliferative glomerulonephritis. It was frequently associated with axial enlargement of the mesangium with deposits at the mesangial and paramesangial areas. Focal proliferative glomerulonephritis was seen in only six patients, minimal change in one and chronic sclerosing glomerulonephritis in two. Epithelial crescents involving 25–50% of the glomeruli were seen in eight patients and one other, who presented with acute oliguric renal failure, had 100% crescents.

TABLE II

CORRELATION BETWEEN HISTOPATHOLOGICAL DIAGNOSIS AND CLINICAL PRESENTATION IN IgA NEPHROPATHY

	Minimal Change	Focal Pro. GN	Diffuse Pro. GN	Chronic Sclerosing GN	Total
Nephrotic syndrome	1	5	8	1	15
Asymptomatic proteinuria and/or haematuria		1	16	1	18
Macroscopic haematuria			8		8
Stress haematuria			1		1
Chronic renal failure			1		1
Acute renal failure			2		2
Total	1(2.2%)	6(13.4%)	36(80%)	2(4.4%)	45

In order to assess the severity and chronicity of each biopsy, we calculated the chronicity index by the following method:

Glomerular: Sclerosis	)	1	—	up to 25%
	)	2	—	up to 50%
	)	3	—	up to 75%
Glomerular: Crescents	)	4	—	above 75%
Interstitial Fibrosis	)	1	—	mild
	)	2	—	moderate
Hypertensive vascular changes	)	3	—	severe

Thirty-seven patients had a chronicity index score from 0 — 5; five from 6 — 10; and 3 from 11 — 14. As expected, those patients who developed hypertension and renal failure had the higher scores.

Immunofluorescent Examination. Results of immunofluorescent examination (IF) correlated to the light-microscopy diagnosis are shown in Table III.

Thirty-three biopsies had IgA alone or in combination with IgG. 10 biopsies had IgA and IgM and only two had all IgA, IgG and IgM. 25 cases had complement C_3 and seven had fibrin demonstrated in the glomeruli.

DISCUSSION

Malaysia is a multiracial country with an approximate population of 15 million people. Malays constitute about 50% of the population, Chinese 40% and Indians 10%.

The 45 patients in our study represent an incidence of 10.7% of primary glomerulopathies

TABLE III

CORRELATIONSHIP BETWEEN LIGHT-MICROSCOPY DIAGNOSIS AND IMMUNOFLUORESCENT STAINING IN IgA NEPHROPATHY

	Minimal Change	Focal Pro. GN	Diffuse Prof. GN	Chronic Sclerosing GN	Total
IgA		3	20		23
IgA + IgG		1	9		10
IgA + IgM	1	1	7	1	10
IgA + IgM + IgG		1		1	2
Total	1	6	36	2	45

seen at the two centres. This finding concurs with a report from Britain[6] but differs from that in Singapore[3] which reports an incidence of 33.7% and from Japan which ranged from 35 – 40%.[4,7] Although Singapore is our immediate neighbour and has a population structure somewhat similar to ours, the difference in incidence is probably explained by differences in patient selection method. A large number of the cases from the Singapore report were young healthy men detected to have urinary abnormalities prior to national service, whereas our series cover the whole spectrum of the local population representing different social, cultural and economical backgrounds.

IgA nephropathy affects all three major races in Malaysia and the incidence appears to reflect the population structure. However, contrary to most reports, females here seem to be almost as commonly affected when compared to males. Although there was a wide variation at the age of onset, it is disturbing to note that about 60% of our cases were less than 30-years-old. As IgA nephropathy is less 'benign' than once reported, we can expect substantial number of patients requiring replacement therapy for end-stage renal failure with time.

The commonest mode of presentation in this series and in others[1,3] was asymptomatic proteinuria and/or haematuria. However about 34% of our cases presented with the nephrotic syndrome and of these nine developed renal failure. Singapore[3] reported a similar experience but in a series from Australia[8] this mode of presentation was uncommon. This may suggest that IgA nephropathy is a more severe disease in this region but a more likely explanation is that we see our patients at a much later stage of the disease. Contrary to classical description of the disease, only eight patients (17%) presented with painless macroscopic haematuria. To our knowledge stress haematuria has not been reported before. The patients who also had thyrotoxicosis, chronic rheumatic heart disease and rheumatoid arthritis were probably not related to the nephropathy as all four diseases are common in our community.

Twelve patients (27%) developed hypertension either from the onset or during follow-up. Renal failure developed in 15 patients (33%) and of these, four progressed to end-stage renal failure. This group of patients had hypertension, greater urine protein level and higher chronicity index at biopsy. We often attribute the renal failure to late consultation by our patients and it was surprising

to note that 25 patients (56%) were seen within six months of the onset of symptoms. Our series also shows that renal failure was commoner in males and this concurs with the experience in Australia.[8]

The light-microscopy findings showed that most of our patients had diffuse proliferative or focal segmental proliferative glomerulonephritis. Epithelial crescents were not uncommon. Similar findings were reported from Australia[8] where crescents were seen in 33% of their biopsies. The presence of crescents correlated very well with the development of renal failure both at presentation and on follow-up.

Immunofluorescent findings concurs with most reports.[3,4,8] There was no correlationship between the amount of IgA deposited and the histology, haematuria of proteinuria. Complement C_3 was present in 55% of biopsies suggesting that activation is via the alternative pathway.

CONCLUSION

In conclusion, IgA nephropathy is a common glomerulopathy in Malaysia. It does not appear to have any racial predilection. The clinicopathological features of this disease generally conforms with those reported elsewhere. In contrast, it seems to be as common in females as in males but the latter have a worse prognosis. Nephrotic syndrome as a presenting feature is not uncommon. The high incidence of renal failure in our patients within the short follow-up period is noteworthy.

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