Clinical Profile and Outcome of IgA Nephropathy from a Tertiary Care Hospital in North India

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Abstract

Aim: To study the clinical profile and outcome of the patients with kidney biopsy diagnosis of IgA Nephropathy (IgAN).

Methods: A retrospective study of the patients diagnosed IgAN over a period of three and half years.

Results: Sixty (13.5%) had a diagnosis of IgAN. Twenty four (40%) had a clinical diagnosis of rapidly progressive glomerulonephritis (RPGN), 20 (33.3%) chronic kidney disease (CKD), 11 (18.3%) nephrotic syndrome, three (5%) acute glomerulonephritis and two (3.3%) asymptomatic urinary abnormalities. Fifty-six (93.4%) patients had hypertension; 15 (25%) patients were presenting as a hypertensive crisis with malignant hypertension in two. Fifteen of the RPGN patients presented with the hypertensive crisis, and all of them had evidence of thrombotic microangiopathy (TMA) on biopsy. Three (5%) patients had secondary IgAN. Patients with the nephrotic syndrome responded to treatment and had a significantly higher renal survival. Patients with interstitial fibrosis and tubular atrophy (IFTA) ≥25% and mesangial hypercellularity score of >0.5 did not respond to treatment.

Conclusion: RPGN, CKD, and nephrotic syndrome were the typical manifestation of IgAN. Hypertension and hypertensive crisis were common. Response to treatment was seen in nephrotic syndrome whereas those with IFTA ≥25% and mesangial hypercellularity score of > 0.5 did not respond to treatment.

Introduction

IgA nephropathy (IgAN) is one of the commonest glomerulonephrites worldwide, with variable prevalence across different races and geographic regions. As a primary glomerulonephritis, it is also the most common cause of end stage renal disease.1,2 It is also called as Berger’s disease since its initial description by the pathologist Jean Berger.3 It has varied prevalence, prognosis, and clinical features. Some of this variance in the clinical spectrum can be explained due to variability in the source of data. However, there is still evidence of a higher burden of IgAN in countries of East and Pacific Asian region.1 IgAN can present as primary glomerulonephritis (idiopathic) or as secondary glomerulonephritis (associated with systemic disease or IgA vasculitis). Clinical feature varies from asymptomatic urinary abnormalities, nephrotic syndrome, nephritic syndrome, crescentic glomerulonephritis, gross haematuria, chronic kidney disease (CKD) to end stage renal disease (ESRD). There is limited data on IgAN from India, but due to the availability of immunofluorescence (IF) in recent years, it is being recognized more frequently in kidney biopsies. We did a retrospective analysis of patients with the biopsy diagnosis of IgAN at our center to elucidate its clinical features.

Material and Methods

A retrospective analysis of all the patients who underwent kidney biopsy at Indira Gandhi Medical College Shimla, Himachal Pradesh, India, a tertiary care institute, over a period of three and half years from June 2014 to Nov 2017 and had a biopsy diagnosis of IgAN was done. All the patients of ≥18 years of age were included in the study. The record was retrieved for presenting complaints, clinical diagnosis, urine analysis, serum creatinine, serum albumin, 24-hour urine protein, viral markers and biopsy findings on light microscopy and immunofluorescence and subsequently urine analysis, 24-hour urine protein, serum creatinine, and serum albumin were determined at follow up. All patients were treated as per Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, with optimal blood pressure control with ACEI/ARB and immunosuppression as per indication.5 Nephrotic syndrome, CKD, complete and partial remission were defined as per KDIGO guidelines.5 Kidney biopsy was scored using the Oxford classification of IgAN.1

Results

A total of 444 native kidney biopsies were done in three and half year period from June 2014 to Nov 2017. Among these 60 (13.5%) had a diagnosis of IgA N. Table 1 shows the baseline demographic, clinical and histopathological characteristics of IgAN patients. Among patients with IgAN 24 (40%) had clinical diagnosis of rapidly progressive glomerulonephritis (RPGN), 20 (33.3%) CKD, 11 (18.3%) nephrotic syndrome, 3 (5%) acute glomerulonephritis, 2 (3.3%) asymptomatic urinary abnormalities. Among 24 patients of RPGN 15 (62.5%) presented with the hypertensive crisis. Overall 56 (93.4%) patients had blood pressure >140/90 mm of Hg, with 15 (25%) presenting as a hypertensive crisis and two among 15 had malignant hypertension.

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purpura (HSP) and one scrub typhus.

Table 2 shows the follow-up and response to treatment. The mean duration of follow up was 17.6±12.2 (range 2-53) months. 58.3% of patients showed complete or partial remission (responders). The rate of complete or partial response was significantly higher in patients with nephrotic syndrome (p=0.020). The patients with biopsy evidence of interstitial fibrosis/and tubular atrophy of ≥25% and mesangial hypercellularity score of >0.5 as per Oxford classification of IgAN were significantly less likely to respond. Even the proportion of TMA on kidney biopsy was higher among non-responders (p=0.075). Kaplan-Meier survival analysis with the end point of reaching ESRD did not show any statistically significant difference among responders (CR+PR) and non-responders group (Figure 1); however, patients who were able to achieve complete remission had statistically significant higher survival versus other subgroups (p=0.037).

Discussion

IgAN is a distinctive disease, diagnosed solely from IF. Findings of dominant or co-dominant deposits of IgA in glomerular mesangium after excluding lupus nephritis and postinfectious glomerulonephritis.6 There is a variable prevalence of IgAN according to the source of data. Studies from India show a prevalence of IgAN varying from 7-16%.7 In our study, 13.5% of patients who underwent indication based native kidney biopsy were diagnosed to have IgAN. In some parts of the world, around 60% of cases of IgAN are detected during routine medical examination or screening of the general population.8 The clinical presentation of IgAN varies according to biopsy practice patterns, age and practice of routine health screening. Worldwide asymptomatic haematuria and progressive kidney disease are the two most clinical presentations.4 In studies from India nephrotic syndrome, chronic renal failure, acute nephritis and hypertension are some of the most common clinical features at presentation.9,10 In a study by Das et al. hypertension was present in 63.2% of the patients of IgAN.10 Hypertension has many implications for IgAN. It may be present at the onset of disease or its course. It is also a significant predictor of histopathological findings and prognosis of IgAN.11 Some of the patients may even present in hypertensive crisis. Hypertensive crisis is defined as systolic blood pressure (BP) > 180 mm Hg or a diastolic BP > 120 mm Hg and is further categorized as hypertensive emergency or urgency on presence of ongoing end-organ damage in the former.12 In our study 93.4% of the patients had hypertension with 25% presenting in hypertensive crisis. Most common clinical syndrome in our study was RPGN although none of these qualified to have crescentic glomerulonephritis as per biopsy findings, i.e.,>50% glomeruli showing crescents. Crescentic glomerulonephritis is uncommon in IgAN and is seen in less than 5% of cases of IgAN.13 Our study also differs from most other Indian studies with relatively less prevalence of nephrotic syndrome (18.3%) although nephrotic range proteinuria was quite common (55%).

Another salient feature of our study was a high prevalence of TMA in kidney biopsy. 16.7% of our patients had biopsy findings consistent with TMA, and it was conspicuous in the patients who presented in a hypertensive crisis. TMA is a common finding in patients with accelerated hypertension and IgAN is also one of the most frequent secondary cause for accelerated hypertension. Endothelial cell injury and microvascular thrombi characterize TMA. It has usually been described to present with features of non-immune hemolytic anemia with thrombocytopenia and biopsy consistent with the diagnosis of TMA. On the other hand, few patients may present with kidney biopsy findings of TMA, with or without systemic disease likely to cause TMA with no hematological manifestations.14 None of the patients in our study had hematological manifestations of TMA. In one study (total 109 TMA patients) malignant hypertension (56%) was the most prevalent cause of TMA. Out of 61 patients of malignant hypertension in this study 29 had secondary malignant hypertension and majority of patients of secondary malignant hypertension in this cohort had IgAN.15 Initially thought to be a benign disease presenting with synphryngitic haematuria, now it is well known to progress to ESRD. In our study, 22.3% of patients progressed to
ESRD, and 18.3% showed no response or gradual progression. Around 20-30% of patients with IgAN progress to ESRD over the period of 10 to 20 years. However, the rate and time to progression to ESRD may be more rapid in regions like ours where routine urine examination of the general population is not practiced and many people present with reasonably advanced disease. In our study, the rate of complete or partial remission was significantly higher in patients with nephrotic syndrome. Similarly, patients with biopsy evidence of interstitial fibrosis/ tubular atrophy of ≥25% and mesangial hypercellularity score of >0.5 were significantly less likely to respond. Other studies have also highlighted a higher rate of progression to ESRD in patients with kidney biopsy showing segmental glomerulosclerosis and tubular atrophy and interstitial fibrosis.

Conclusions

IgAN was a common cause of glomerulonephritis in our study. RPGN, CKD, and nephrotic syndrome were common clinical features at disease presentation. Hypertension was almost ubiquitous, and many patients were picked up with the initial diagnosis of hypertension, hypertensive crisis and a few even with malignant hypertension. There was a strong correlation between clinical findings of hypertensive crisis and TMA on kidney biopsy. Nephrotic range proteinuria was more common than a classical nephrotic syndrome. Patients with the clinical presentation of the nephrotic syndrome were more likely to achieve remission and those with IFTA ≥25%, and mesangial hypercellularity score of >0.5 on kidney biopsy was less likely to achieve remission. Many of the patients presented with established CKD or uremic complications with the need for dialysis. The renal prognosis in such subgroup of the patients was poor. Routine urine screening of the general population or any opportunity of healthcare contact should be supplemented with urine analysis and by estimation of serum creatinine.

References