Case Report

IgA Nephropathy Presenting as Hypertensive Emergency and End-Stage Renal Disease in a Child

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Abstract

IgA nephropathy (IgAN) is the most common noninfectious glomerulonephritis worldwide. Most of the children and young adults with IgAN present with macroscopic hematuria during an upper respiratory or gastrointestinal illness. However, various atypical presentations including overt nephrotic syndrome and rapidly progressive renal injury have been reported. Here, we present a case of IgAN that presented with hypertensive encephalopathy with features of end-stage renal disease as the initial presentation.

Key words: Children, end-stage renal disease, hypertension, IgA nephropathy

INTRODUCTION

IgA nephropathy (IgAN) is the most common noninfectious glomerulonephritis (GN) worldwide. The range of clinical manifestations of IgAN varies from asymptomatic microscopic hematuria to rapidly progressive GN. The typical mode of presentation varies according to age group and biopsy patterns. By far the two most common clinical presentations are asymptomatic hematuria and progressive kidney disease. IgAN with rapidly progressive course is rare and most frequently associated with a pathologic finding of >50% of glomeruli exhibiting crescents.[1] Here, we report a case of IgAN that presented with hypertensive emergency with tubulointerstitial chronicity on renal biopsy as the initial presentation without any significant history.

CASE REPORT

A 13-year-old male child presented with 5 days' history of multiple episodes of vomiting along with 3 episodes of abnormal body movements. There was gradually increasing pallor of 15 days' duration. There was no history of hypertension, hematuria, oliguria, poor urinary stream, joint pain, rash, polyuria, or recurrent urinary tract infection. At admission, he was drowsy and disoriented, but there was no obvious focal neurological deficit. His vitas were pulse 120/min (with no radiofemoral delay), blood pressure (BP) 180/110 mm of Hg (with no significant difference between upper and lower extremities), respiratory rate 18/min, and SpO_2 of 98% on room air. He was provisionally diagnosed as a case of hypertensive encephalopathy and was started on sodium nitroprusside continuous infusion and intravenous phenytoin. Sodium nitroprusside was gradually titrated with a target BP <95th centile in next 48 h. Routine hematological evaluations resulted as hemoglobin 9.5 g/dL, total lymphocyte count 11,540/mm^3 (58% polymorphs and 36% lymphocytes), and platelet 1.88 lakh/mm^3. Peripheral blood smear was suggestive of normocytic normochromic anemia with no evidence of schistocytes. Urinalysis revealed 3+ protein, 80–100 red blood cell (RBC)/hpf, and 15–20

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pus cells/hpf. His renal functions (serum urea 257 mg/dL and serum creatinine 12.1 mg/dL) and serum electrolytes (Na 129 mmol/L, K 6.0 mmol/L) were severely deranged. Serum calcium (8.2 mg/dL) was normal while serum phosphorus (6.2 mg/dL) and serum PTH (282 pg/dL) were on higher side. Ultrasonography of kidney and urinary bladder was unremarkable with a normal kidney size. Cortical thickness was preserved, but there was increased echogenicity and moderate loss of corticomedullary differentiation. The child was immediately put on hemodialysis, and sodium nitroprusside infusion was continued for 72 h. Slow, gradual control of BP led to improved sensorium and cessation of seizure activity. Negative history related to the current illness was further confirmed once his higher functions normalized. Later, he was maintained on oral antihypertensives (amlodipine, labetalol, frusemide, and clonidine). As there was grossly deranged renal function and active urinary sediments in urine, diagnosis was modified to acute GN. Antistreptolysin titer was 50 IU/mL (Normal reference range <200 IU/mL) and serum C3 was found to be 116.2 mg/dL (reference range of 90–180 mg/dL). Viral markers (hepatitis B surface antigen, HIV and IgM anti-hepatitis C virus) were nonreactive. Antinuclear antibody, anti-double-stranded DNA antibody, and anti-neutrophil cytoplasmic antibody were negative. He remained dialysis dependent and after 3 sessions of alternate day hemodialysis, there was persistent microscopic hematuria (urinalysis: Protein 3+, RBC 50–80/hpf), oliguria and deranged renal function (urea-118 mg/dL, Cr-6.1 mg/dL). Percutaneous renal biopsy was done under real-time ultrasound guidance, and tissues were sent for light microscopy and immunofluorescence. As final biopsy report was expected about a week later, immunosuppression was started empirically for crescentic GN. Intravenous methylprednisolone pulses were given for 3 doses and were followed by oral prednisolone. Renal biopsy results were suggestive of IgAN with tubulointerstitial chronicity. Light microscopy [Figure 1] findings were: IgAN associated with global tuft sclerosis in 4/8 (50%) glomeruli, secondary segmental sclerosis in 3/8 (37.5%) capillary tufts and mild increase in mesangial cellularity in viable glomerular areas. The crescent formation was seen in 3/8 (37.5%) glomeruli (2 fibrocellular and 1 fibrous). Patchy acute tubular injury involving viable cortical tubules and multifocal chronic tubulointerstitial inflammation were noted. Significant areas of tubular atrophy and interstitial fibrosis was observed in the sampled cortex, although Oxford MEST score quantification of chronicity was not feasible due to the small cortical area and marginal number of glomeruli sampled.[2] Vascular hypertensive changes in the form of arteriolar wall thickening and prominent hyalinosis were also noted. Direct immunofluorescence study [Figure 2] revealed: IgA 2+ mesangial (granular/confluent), IgG negative, IgM/C3 segmental entrapment, C1q-negative, kappa 1+ mesangial (granular/confluent), and lambda 1+ mesangial (granular/confluent). As there were few cellular crescents 1 pulse of cyclophosphamide was also given, but there was no satisfactory improvement. He remained dialysis dependent, oliguric (urine output 0.5–0.7 mL/kg/h) and hypertensive (required amlodipine and labetalol). No further immunosuppression was considered in view of too much chronicity on biopsy. Prednisolone was also gradually tapered and stopped. Supportive management for chronic kidney disease was started. The family was counseled for a long-term requirement of renal replacement therapy and renal transplantation in future. He was discharged on alternate day maintenance hemodialysis, 2 antihypertensives and end-stage renal disease (ESRD) supportive medications with a regular follow-up plan.

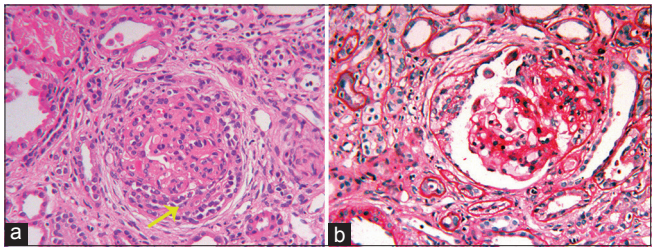

Figure 1: Light microscopy H and E (a) and PAS (b) image showing a glomerulus with increased mesangial matrix and cellularity with a fibrocellular crescent (arrow) (H and E, PAS ×250)

DISCUSSION

IgAN occurs at all ages but is most common during the second and third decade of life. Males are affected more commonly and male: female ratio has varied from 2:1 to 6:1 in different studies.[3] The diagnostic hallmark of IgAN is the predominance of IgA deposits, either alone or with IgG, IgM, or both, in the glomerular mesangium. The frequency

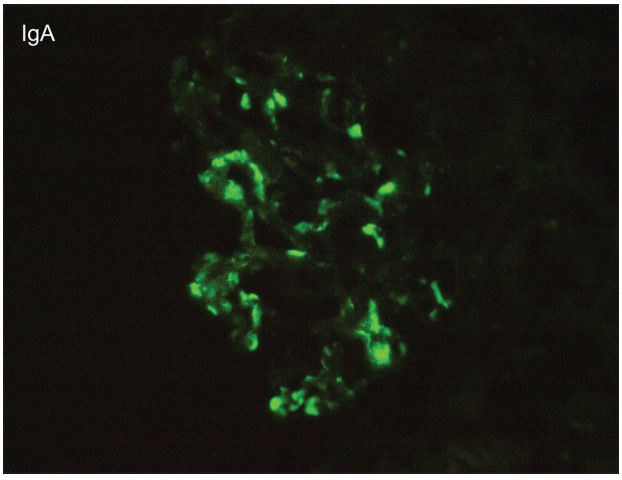

Figure 2: Direct immunofluorescence image showing mesangial IgA staining (FITC, ×400)

of IgA without IgG or IgM varies greatly, from 0 to more than 85% across centers. Complement C3 and properdin are almost always present. C4 or C4d, mannose-binding lectin, and terminal complement complex (C5b–C9) are frequently detected, whereas C1q is usually absent. These findings suggest involvement of the alternative and lectin pathways of complement activation.[4] Coincidental discovery of minor urinary abnormalities is the most common clinical scenario encountered in IgAN. Atypical manifestations including overt nephrotic syndrome, acute or rapidly progressive kidney injury, secondary forms of IgAN and recurrent IgAN after renal transplantation have been reported in literature.[5] By far the two most common clinical presentations are asymptomatic hematuria and progressive kidney disease. About 75% of children and young adults with IgAN present with recurrent macroscopic hematuria during an upper respiratory or gastrointestinal illness.[4] Asymptomatic microscopic hematuria can be found in 60% of subjects.[6] Although nephrotic-range proteinuria is not uncommon in IgAN, coexistence of the nephrotic syndrome is rare. IgAN with rapidly progressive course is rare and most frequently associated with a pathologic finding of >50% of glomeruli exhibiting crescents.[1] Hypertension is infrequently present at disease onset and when present, is usually mild to moderate in severity and relatively easy to control. Likewise, decreased renal function rarely presents at disease onset.[7] Our patient presented with features of hypertensive emergency with severely deranged renal function at admission. Numerous studies have addressed the predictive value of pathology findings. The recent Oxford Classification of IgAN has demonstrated the importance of mesangial hypercellularity, segmental glomerulosclerosis, endocapillary hypercellularity, and tubular atrophy/interstitial fibrosis; as independent pathological variables predicting kidney outcome.[8] Control of proteinuria and BP by suppression of angiotensin II with an ACE inhibitor or angiotensin II–receptor blocker (ARB) has been the recommended management for most of the cases of IgAN. For urinary protein excretion that is persistently more than 1 g/day despite 3–6 months of proper supportive care (ACE inhibitor, ARB, or both and blood pressure control) and an estimated GFR of more than 50 mL/min/1.73 m^2; the KDIGO guidelines suggest adding fish oil or a 6-month course of glucocorticoids or both. Intensive immunosuppression (glucocorticoids with cyclophosphamide or azathioprine) is reserved for patients with crescents in more than half the glomeruli and a rapid decline in renal function. Patients with fewer crescents and stable renal function should be treated with an ACE inhibitor or ARB. The KDIGO guidelines do not support the use of mycophenolate mofetil or antiplatelet drugs. Tonsillectomy has been recommended by some centers, particularly in Japan, but this approach was not included in the KDIGO guidelines because of the lack of data from randomized controlled trials.[8]

CONCLUSION

IgAN is a common glomerular disease and an important cause of renal failure in children. Most commonly it presents with recurrent macroscopic hematuria and has favorable prognosis. Antihypertensive and antiproteinuric measures have been the mainstay of management in most of the published literature. However, a subset of patients with IgAN with extensive crescents on biopsy, have a rapidly progressive course. Moreover, very rarely it may present with hypertensive emergency with features of ESRD at the outset only. Advances in understanding the molecular basis of its pathogenesis may lead to earlier diagnosis, better monitoring of the clinical course or response to treatment, and ultimately targeted therapy. Children with IgAN should therefore be regularly followed up for early detection of hypertensive changes and proteinuria. Timely management of hypertension and proteinuria would definitely prevent such life-threatening emergencies and progression to end-stage renal disease in a long run.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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