

## IgA Nephropathy in the Caribbean Case Reports

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### ABSTRACT

*IgA nephropathy can be considered the most common cause of primary glomerulopathy in developed countries. There has been no report of cases of IgA nephropathy from Caribbean countries. The authors report five cases of IgA nephropathy from Trinidad and Tobago, and Guyana, diagnosed from biopsy studies. No cases were of African origin and some did not have the typical presentation associated with IgA nephropathy. Caribbean nephrologists are reminded that this entity can be seen in Caribbean patients and can only be diagnosed through immunofluorescence staining of renal biopsy specimen. This diagnosis is required for the proper management of patients with glomerular disease, particularly when there may be progression to end stage renal failure as can occur in up to twenty per cent of patients with IgA nephropathy. Accurate diagnosis is important, since disease recurrence can be seen in the transplanted kidney, but this does not often lead to graft failure.*

## La Nefropatía IgA en el Caribe Reportes de Casos

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### RESUMEN

*La nefropatía IgA puede considerarse la causa más común de glomerulopatía primaria en los países desarrollados. No ha habido reportes de casos de nefropatía IgA de los países del Caribe. Los autores reportan cinco casos de nefropatía IgA de Trinidad y Tobago, y Guyana, diagnosticados a partir de estudios de biopsia. Ninguno de los casos fue de origen africano y algunos no presentaron las características típicas asociadas con la nefropatía IgA. Se les recuerda a los nefrólogos del Caribe que esta entidad puede ser observada en pacientes del Caribe y puede ser diagnosticada sólo mediante tinción por inmunofluorescencia de un espécimen de biopsia renal. Este diagnóstico es un requisito para el tratamiento adecuado de pacientes con la enfermedad glomerular, en particular cuando puede haber progresión al fallo renal en etapa terminal, como puede ocurrir hasta en el veinte por ciento de los casos con nefropatía IgA. El diagnóstico exacto es importante, ya que la recurrencia de la enfermedad puede verse en el riñón trasplantado, pero esto no conduce a menudo al fallo del injerto.*

West Indian Med J 2009; 58 (1): 72

### INTRODUCTION

IgA nephropathy is the most common cause of primary glomerulonephritis in developed countries. The prevalence of IgA nephropathy varies in different geographic areas, 40% in Asia, 20% in Europe and 10% in North America (1, 2). The clinical presentation of IgA nephropathy is heterogeneous. Two major clinical presentations are seen: mild proteinuria

with microhaematuria occurring more commonly in adults and Asians and macroscopic haematuria seen more frequently in children and Americans (3).

The diagnosis of IgA nephropathy can only be confirmed by examination of renal biopsy tissue by light microscopy as well as immunofluorescence. Electron microscopic examination is less contributory.

Reports of renal biopsy studies from two of the larger Caribbean countries (4, 5) revealed that the most common primary glomerulopathies were Focal and Segmental Glomerulosclerosis (FSGS), Minimal Change Disease (MCD) and Membranoproliferative Glomerulonephritis (MPGN). Mesangial Proliferative Glomerulonephritis was found in only 11% of cases in the Trinidad study (4). No comment

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was made about the absence of IgA Nephropathy, possibly because immunofluorescence was not performed in the Trinidad study, but more importantly because this disease was considered rare in blacks (6, 7).

Since September 2007, immunofluorescence examination of renal biopsy specimens has been performed at the Eric Williams Medical Sciences Complex (EWMSC). We report five cases of IgA nephropathy. Out of twenty-one primary glomerulopathies diagnosed at EWMSC from September 2007 to March 2008, four were IgA nephropathy. The fifth case was confirmed extra-regionally.

### Case Reports

1) Mr D is a 19 year old Indo-Trinidadian who had been on dialysis for three months. He was known to be hypertensive for six months and presented with a three-month history of nephrotic syndrome/microscopic haematuria. A 24-hour urine sample revealed 5.3 g of protein. Blood investigations showed abnormal renal function tests: blood urea nitrogen, 19 mmol/L and serum creatinine, 575  $\mu$ mol/L. Immunological studies revealed that ANA, C3, C4, C-ANCA, P-ANCA, and Anti GBM were within the normal ranges. The patient was seronegative for human immunodeficiency virus (HIV), hepatitis B and hepatitis C. Renal ultrasound revealed increased echogenicity with right and left kidneys measuring about 12 cm.

The histology of the renal biopsy showed variable sclerosis of the glomeruli, increased mesangial cellularity and mild GBM thickening. Periglomerular fibrosis was present. Blood vessels showed hyperplastic arteriolar walls. Vasculitis was not evident. Immunofluorescence revealed peripheral and mesangial positivity for IgA and C3. IgM was positive, and IgG and C1q were negative.

2) Mr C is a 34-year old Chinese – Trinidadian who had features of intermittent proteinuria (1.5 gm in 24 hr) and microscopic haematuria for 3 years but no gross haematuria. There was no significant medical, family and drug history related to renal disease. Examination revealed a normotensive patient with just mild leg oedema. Urinalysis revealed intermittent microscopic haematuria and proteinuria. Significant blood investigations at the time of biopsy showed: normal complete blood count, serum creatinine 124  $\mu$ mol/L, normal serum albumin and 24-hour urine protein of 1.38 g. Abdominal ultrasound demonstrated kidneys of normal sizes with good cortico-medullary thickness.

Histology showed mild enlargement of glomeruli with variable mesangial expansion. There was no glomerular basement membrane (GBM) thickening. Tubules showed mild atrophy with casts and few red blood cells in the lumen. Patchy fibrosis of the interstitium was present. Blood vessels showed no vasculitis. Immunofluorescence revealed mesangial IgA and C3 positivity and IgM positivity. IgG, C1q and fibrinogen were negative.

3) M is a 12-year old Indo-Trinidadian who had a history of persistent microscopic haematuria and occasional

macroscopic haematuria for the last two years. There was no family history of kidney disease. Physical examination was normal. Investigations, which included renal function tests, 24-hour urine for protein, calcium and phosphate and coagulation studies were all normal. Intravenous urogram and renal ultrasound were normal.

Histology showed variation in cellularity amongst different segments with slight prominence of the mesangium but no areas of necrosis or crescent formation. Focally, the glomeruli showed segmental sclerosis. Vessels showed no vasculitis. Immunofluorescence showed mesangial deposition of IgA (3+) in all glomeruli with a similar deposition of C3 (2+) and deposition of IgM (1+). IgG and fibrinogen were negative.

4) Mr B is a 30-year old Guyanese East Indian who developed nephrotic syndrome four years ago and was treated with steroids. He subsequently developed hypertension one year ago and polycythaemia for which no cause was found. Family history was unremarkable. His physical examination, apart from cushingoid facies, was unremarkable. His investigations included: creatinine, 88.4  $\mu$ mol/L-, serum albumin, 28g/L; white blood cell count, 11.7 x 10<sup>9</sup>/L; platelet, 367 x 10<sup>9</sup>/L; haemoglobin (Hb) 171g/L, C3 and C4- were normal, ANA-negative, 24-hour urine collection contained 1.2 g of protein. Renal U/S showed the right and left kidney each measuring 10 cm.

Histology revealed glomeruli that showed mild increase in mesangium with no features of endocapillary proliferation. Glomerular basement membrane appeared normal. Tubular atrophy, fibrosis and vasculitis were not evident. Immunofluorescence (IF) examination showed moderate to strong mesangial positivity for C3 and IgA but negative for IgG, IgM and C1q.

5) B is a four-year old, East Indian girl from Guyana with a three-month history of a nephrotic/nephritic clinical picture that was unresponsive to steroids. There was no significant family history of renal disease. Blood investigations were: creatinine, 53  $\mu$ mol/L; serum albumin, 18 g/L; serum cholesterol, 8.2 mmol/L; haemoglobin 110 g/L, normal WBC count and platelets. Immunology showed slightly elevated C3, normal C4 negative ANA and rheumatoid factor and antineutrophilic cytoplasmic antibody was negative. Renal ultrasound revealed bilaterally enlarged kidneys with hyperechoic areas. Serum protein electrophoresis revealed elevated IgA

Histology revealed glomeruli that showed a variety of changes including diffuse mesangial hypercellularity and widening, focal segmental glomerular sclerosis with several healed crescents (Fig. 1).

Immunofluorescence revealed moderate to strong mesangial positivity for IgA. There was C3 positivity in the mesangium and in the tubular basement membrane. IgG, IgM and C1q were negative (Fig. 2).

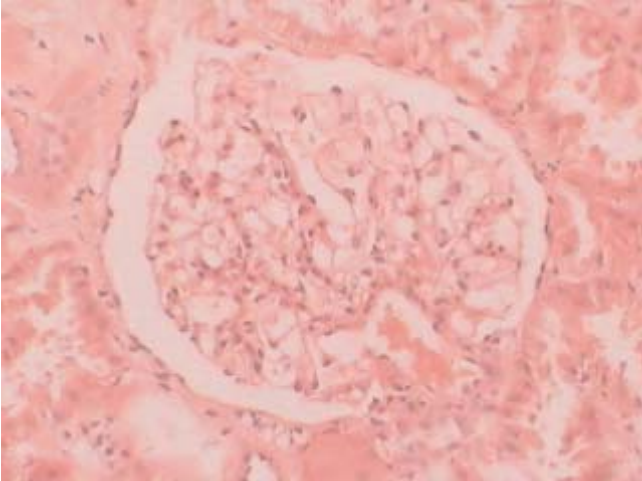


Fig. 1: Light microscopy of a glomerulus from a patient with immunoglobulin A nephropathy showing increased mesangial matrix and cellularity.

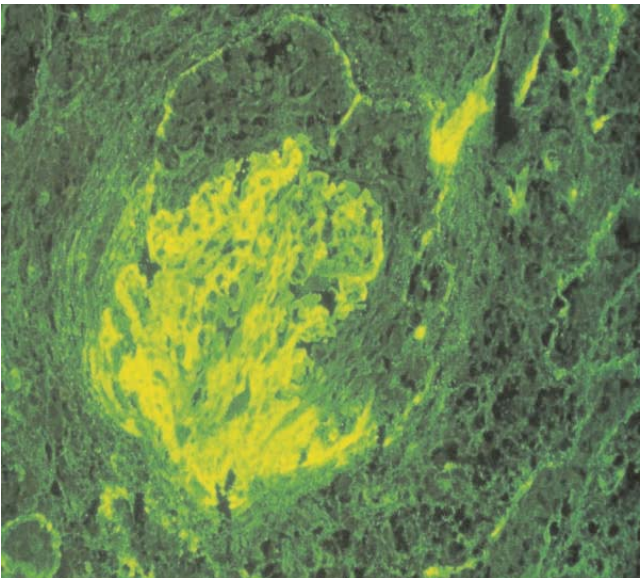


Fig. 2: Immunofluorescence microscopy demonstrating large mesangial immunoglobulin A (IgA) deposits diagnostic of IgA nephropathy.

## DISCUSSION

There are no reports of IgA nephropathy in the Caribbean. A report from the Caribbean Renal Registry does not list IgA nephropathy as one of the reported aetiologies of end stage renal disease [ESRD] (8). However, these five cases illustrate that IgA nephropathy is present in renal cases in Trinidad and Guyana and as seen in one case, can be a cause of ESRD. The cases all showed the hallmark positivity of IgA staining. It is quite possible that there may have been some cases of IgA nephropathy in the 190 cases of ESRD from Trinidad and Tobago due to either chronic glomerulonephritis or unknown causes as reported in the Caribbean Renal Registry, if biopsies with immunofluorescence examination had been performed. More so, if they were of non-African descent as four of the five cases in this report were of

East Indian descent and one was of Chinese stock.

The incidence of IgA nephropathy is rare in Indian adults (9) and Afro-Americans (6, 7). The presence of certain Caucasian alleles IgA2 allotypes did not confer an increased risk of IgA nephropathy on the black population who presented with IgA nephropathy (10). Further studies are required to elucidate if there is any ethnic predilection for IgA nephropathy in Trinidad and Tobago and Guyana.

Routine histology is not diagnostic as a wide range of changes not specific to IgA nephropathy can be seen. These include MCD, FSGS, diffuse and focal proliferation with sclerosis and even crescent formation. Immunofluorescence should be performed on all biopsy specimens, particularly from cases with minimal urinary findings where there is a suspicion of a primary glomerulopathy and in patients of non-African ethnicity.

It is important that this diagnosis of IgA nephropathy be made, as there are implications for the treatment, prevention of the development and management of ESRD. Five to twenty per cent of asymptomatic cases do progress to ESRD and thirty-five to fifty per cent of them (1, 11) will have disease recurrence within six years following renal transplantation. However, the risk of graft failure is negligible and thus IgA nephropathy is not a contraindication to transplantation. It is of some concern that in this report a young adult with IgA nephropathy presented on renal replacement therapy at age 19 years. Such an early presentation of ESRD secondary to IgA nephropathy has been noted as a result of the "malignant" nature of this disease in certain ethnic groups (12). However, other issues such as late diagnosis and uncontrolled hypertension in our patient should be considered as other possible reasons for this presentation.

Given the presence of two children in our limited series, consideration for screening urine in school children should be undertaken. This may highlight childhood cases of renal disease earlier. Only one of the cases presented with the macroscopic haematuria for which IgA nephropathy is typically noted. Thus, limiting the performance of immunofluorescence on renal biopsies to patients who present with the typical features will exclude many diagnoses of this condition.

In summary, IgA nephropathy is reported from Trinidad and Tobago, and Guyana. Further studies must be done to determine if there is a predilection for it in certain ethnic groups. Clinical presentations and routine histology are not entirely diagnostic. Therefore, performing immunofluorescence examination on the renal biopsy specimen is essential to detect and confirm cases. This is especially important in developing countries where prevention of ESRD needs to be more vigorously and actively pursued. In Trinidad and Tobago, where renal transplantation is offered in the management of ESRD patients, it is crucial that pre-transplant aetiologies of chronic kidney disease be known. This would impact positively on the management of post-transplant cases.

**ACKNOWLEDGEMENTS**

The authors would like to thank Ms Theresa Murray for her invaluable secretarial support.

**REFERENCES**

1. Donadio JV, Grande J. IgA Nephropathy. *N Engl J Med* 2002; 347; **10**: 738–48.
2. Charles Jennette J, Heptinstall R, Olsen J et al. IgA Nephropathy and Henoch-Schonlein Purpura Nephritis. Heptinstall's Pathology of the Kidney. Lippincott Williams and Wilkins; 2006: 425–82.
3. Schena FP. A retrospective analysis of the natural history of primary IgA nephropathy worldwide. *Am J Medicine* 1990 **89**: 209–15.
4. Roberts LA, Patrick A, Barton EN, Jankey N, Asgarali Z et al. Significant proteinuria – The Port of Spain General Hospital Experience. *West Indian Med J* 1987; **36 (Suppl)**: 52.
5. Soyibo AK, Williams W, Smith R, Shah D, Barton EN. Renal biopsies done in Jamaica in 2006. *West Indian Med J* 2007; **56**: 309–10.
6. Galla JH. IgA Nephropathy. *Kidney Int* 1995; **47**: 377–87.
7. Nair R, Walker PD. Is IgA nephropathy the commonest primary glomerulopathy among young adults in the USA? *Kidney Int* 2006; **69**: 1455–8.
8. Soyibo AK, Barton EN. Report from the Caribbean Renal Registry, 2006. *West Indian Med J* 2007; **56**: 355–62.
9. Narasimhan B, Chacko B, John GT, Korula A, Kirubakaran MG, Jacob CK. Characterization of kidney lesions in Indian adults; towards a renal biopsy registry. *J Nephrol* 2006; **19**: 205–10.
10. Crowley – Nowick PA, Julian BA, Wyatt RJ, Galla JH, Wall BM, Warnock DG et al. IgA Nephropathy in blacks; studies of IgA2 allotypes and clinical course. *Kidney International* 1991 **39**: 1218–24.
11. Floege J, Feehally J. IgA Nephropathy: Recent Developments. *J Am Soc Nephrol* 2000; **11**: 2395–403.
12. Chacko B, John GT, Neelakantan N, Korula A, Balakrishnan N, Kirubakaran MG et al. Presentation, prognosis and outcome of IgA nephropathy in Indian adults. *Nephrology (Carlton)* 2005; **10**: 496–503.

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