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Rapidly progressive glomerulonephritis in adult Nigerians: A report of 4 cases

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Summary
The clinicopathological features of rapidly progressive glomerulonephritis (RPGN) were studied in 4 young adult Nigerians who presented with acute GN. There was a predilection for males with a male to female ratio of 3:1. Hypertension, nephrotic-range albuminuria, haematuria granular and cellular urinary casts, and a rapid progression to severe renal failure or death were the findings in all four patients. Renal biopsy revealed histological features compatible with findings in RPGN in all the patients, including the presence of crescents and epithelial cellular proliferation. The study shows that the early development of hypertension and deterioration of renal function in patients with features of acute glomerulonephritis should arouse suspicion of a rapidly progressive GN whose course could be altered by appropriate therapeutic measures, some of which are highlighted.

Keywords: *Rapidly progressive; glomerulonephritis; Nigerians.*

Résumé
Les traits clricopathologiques de la progrssion rapide de glomerulonephritis (RPGN) ont ete etudes chez 4 jeunes adultes Nigeriana qui se sont pesentes avec une propotion homme-femme de 3:1. L'hematuria, l'intervalle rephrotique d'albuminuria, l'hematuria granulaire et les platre cellulaires urinaires, e t une progression rapide a un defaut renat severe ou la mort ont ete les conclusions chez tous nos patients. La biopsie renale revelait les traits histologiques compatibles aux conclusions chez tous nos patients. La biopsie renale revelait les trits histologiques compatibles aux conclusion dans RPGN chez tous les maladies, complenent la presence croisante de la proliferation cellulaire epithelial. L'etude montre que le development le plus to possible de l'hypertension et la deterioration de la fonction renale chez les patients avec les traits de glomerulonephritis aigu doit eveiller des surpicious d'une progression rapide de GN don't le cheminement peut etre altere par des measures therapentiques approroprees don't certains sont souligries.

Introduction

Rapidly progressive glomerulonephritis (GN) has been described as the clinical presentation of crescentic glomerulonephritis, an aggressive glomerular disease resulting in a rapid loss of renal function, often developing abruptly and showing little tendency towards spontaneous or complete recovery [1,2].

Various forms of glomerular diseases have been described in the adult African, the commoner histologic types in the nephrotic syndrome being the membranous and the messangio-capillary forms [3,4]. However, some adult patients with acute GN occasionally present with a rapid downhill course towards terminal renal failure, often being taken for granted to be an acute or acute on chronic renal failure [1], a situation further compounded in the environment of a developing country like Nigeria by the scarcity of immuno-histopathological diagnostic facilities. In some cases however,When renal biopsy has been possible, the presence of epithelial crescents has been demonstrated in the glomeruli of a few such patients. This study is therefore a report of four patients with a rapidly progressive form of GN in whom the clinical and histopathological characteristics closely match that of crescentic GN. As early recognition and treatment can prevent the development of end-stage renal failure, our aim is to create an increased awareness and a higher level of suspicion among our physicians by reporting this potentially treatable condition.

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Case 1

O.M. is a 15 year old male student who presented at the Renal Clinic of the University College Hospital, Ibadan having been referred from the General Outpatient Clinic with a two-week history of facial and pedal edema following a 'weeping' skin rash involving the feet two weeks previously. There was associated history of 'Coca-Cola coloured urine but no reduction in urine output, pains or fever. On examination he was found to have bilateral pitting pedal edema with a blood pressure of 130/90mmHg but not in heart failure. The urine showed 3+ albuminuria, with microscopic haematuria and numerous granular casts. Blood biochemistry revealed urea of 35mg/dl, creatinine of 0.9mg/dl, total serum protein 4.6g/dl, albumin of 2.0g/dl, creatinine clearance 72ml/min, and 24-hour urine protein of 7.6g/day. Renal ultrasound revealed bipolar diameters of 9.9cm and 10.2cm for the right and left kidneys, respectively. Histological examination of needle biopsy specimen of the kidney showed 20 glomeruli with varying degrees of proliferation of the mesangium and endothelium, one of which was completely sclerosed. There was increased lobulation of the glomerular capillaries with thickening of the basement membranes. In two glomeruli, there was epithelial proliferation with crescent formation. The patient was discharged on oral furosemide therapy, but he became progressively hypertensive and azotemic on follow-up until he was last seen thirteen weeks after discharge.

Case 2

O.O. a 24 year-old male apprentice tailor was referred with a history of generalized body swelling for 2 months. There was no history of sore throat or skin lesion, and no oliguria or change in urine colour. On examination he was generally bloated with marked ascites. His blood pressure was 150/80mm/Hg, and urine showed 3+ albuminuria with microscopic haematuria and granular casts +++. Blood urea was 67mg/dl and creatinine 1.8mg/dl, creatinine clearance 45mls/min, and total serum protein, 3.7g/dl with albumin of 1.4g/dl, and 24-hour urine protein, 3.7g/24 hour. His right and left renal bipolar diameters by ultrasound measurement were 11.0cm and 11.9cm, respectively. He was admitted and placed on furosemide diuretics, while percutaneous renal biopsy was performed four weeks after admission and patient discharged for follow-up. Histopathological examination of the renal biopsy specimen showed eleven glomeruli. There were mesangial and epithelial cell proliferation with increased mesangial matrix. The glomerular tuft and its interstitium showed moderate amount of

eosinophilic material. There was also capillary membrane thickening.

The patient's blood pressure remained stabilised at a diastolic of 90mmHg until four months later when he was readmitted with left ventricular failure and severe hypertension with blood pressure of 180/120 mmHg. In spite of aggressive treatment for hypertension and pulmonary edema, the patient died the following day. A post-mortem examination was refused by the relations.

Case 3

O.Y., a 45 year-old trader, was first seen at the Renal Clinic with reduced urinary output and generalized body swelling of 6 weeks duration. There was a history of Coca-Cola coloured urine. His presenting blood pressure was 140/90mmHg and had moderate ascites. His blood chemistry revealed urea of 55mg/dl, creatinine of 1.9g/dl with creatinine clearance of 59ml/min, total serum protein 4.3g/dl and albumin of 1.49g/dl. Urine examination showed a 4+ albuminuria with 24-hour urine protein of 9.8g/24 hours numerous waxy and granular casts, and ultrasound measured renal bipolar diameters of 10.9cm and 12.8cm for the right and left kidneys, respectively. A percutaneous renal biopsy was done two weeks later while the patient continued treatment with diuretics. The renal biopsy showed 32 glomeruli which were moderately enlarged, with 10 showing moderate epithelial cell proliferation with capsular adhesion. There was glomerular mesangial matrix increase and cellular proliferation with thickening and mild crescent formation. There was occasional duplication of the capillary basement membrane with eosinophilic deposits in the Bownman's space.

The blood pressure rose progressively to 170/110mmHg while still on the ward with urea rising to 155mg/dl. Patient however developed uraemic symptoms with pulmonary and generalised edema, and in spite of diuretic and anti-hypertensive treatments, the patient died on the ward six weeks after presentation. Post mortem examination was refused.

Case 4

A.A., a 17 year old school girl was first seen at the Renal Clinic on referral with a 2-month history of facial and leg swelling, progressive tiredness on mild exertion and diminution in urine output. She had been receiving treatment for nephrotic syndrome at a peripheral hospital with 'Lasix' and 'aldactone' before being referred. On examination the blood pressure was 180/110mmHg, with marked ascites and peripheral edema. Blood chemistry done 4 weeks previously at the referral hospital revealed an initial blood urea of 34mg/dl, but on admission to our Unit was 106mg/dl with creatinine 8.8mg/dl. Total plasma protein was 4.0g/dl with albumin of 2.1g/dl, and 24 hour urinary protein was 4.1g/24 hours. Urine examination revealed microscopic haematuria and numerous granular and waxy casts, and renal ultrasound showed renal bipolar diameter of 10.1cm and 10.4cm on the right and left sides, respectively. Anti-hypertensive and diuretic drugs were commenced and patient managed conservatively as acute renal failure. The blood pressure remained difficult to control in spite of anti-hypertensive drugs fluctuating between 160/100 and 180/130mmHg. She became progressively uraemic with blood urea rising to 300mg/dl. She was hemo-dialysed thrice, and a percutaneous renal biopsy done immediately afterwards, 5 weeks after admission showed 40 glomeruli, all of which were globally or focally sclerosed, with some focally sclerosed glomeruli containing crescents. There was moderate fibrinoid deposit with mononuclear infiltration.

The blood pressure became better controlled after dialysis and patient was discharged for follow-up. She remained uraemic until she was lost to follow-up 6 weeks later.

Discussion

Rapidly progressive GN is a renal condition that results in a rapid loss of renal function, even though it has been shown to be potentially treatable [1,2]. Early recognition becomes desirable if its progression to end-stage renal failure (ESRF) is to be prevented [5]. Many glomerular and systemic diseases may present with a rapidly progressive form of GN notable examples of which are Goodpasture's disease, Wegener's granulomatosis, systemic lupus erythematosus, mixed essential cryoglobulinaemia, and post-infectious glomerulonephritis [2]. The renal manifestation of these conditions is usually with glomerular epithelial crescents formation giving rise to its description by many authors as crescentic rapidly progressive GN [8,9]. It is noteworthy that data is scanty on the prevalence of crescentic GN per se as a disease entity from available studies on glomerulonephritids in this environment, probably due to technical and material constraints at making specific diagnosis. However, our interest was stirred on encountering these cases who presented with clinical features closely resembling those described in crescentic rapidly progressive GN with subsequent support by histopathology.

Clinically the disease has been described as having a predilection for males, and can occur at any age [1]. Our report tends to be in agreement as three out of four of our patients are males, and their ages ranged widely between 15 and 45 years. Hypertension is also one key clinical feature that frequently early accompanies rapidly progressive GN, and quite often to dangerously high levels [16]. Therefore the presence of hypertension (especially when severe) or an early development of it in a patient with the nephrotic syndrome should arouse suspicion of rapidly progressive GN. In all our patients (except case 4) the presenting blood pressure was only mildly elevated at presentation, becoming evidently accelerated early in the course of the disease.

Another important clinical finding in RPGN is the presence of active urinary sediments in the form of microscopic haematuria, and either one or both of red blood cells and granular casts [1,2], both of which indicate severe glomerular inflammation. All our four patients presented with active urinary sediments as seen in Table 1.

Table 1: Clinical and laboratory features on presentation

	Case 1	Case 2	Case 3	Case 4
Presenting BP	130/90	160/115	160/110	180/110
Ultrasound Renal size(cm)	9.9:10.2	11.0:11.0	10.9:12.8	10.1 10.4
Blood Urea (mg/dl)	35	67	144	106
Creatinine (mg/dl)	0.9	1.8	4.3	8.8
Creatinine clearance (ml/min)	72	52	59	-
24 Hr urine protein g/24 hr	7.6	3.7	9.8	4.1
Urine microscopy				
Red blood cells	+++	+++	+++	+++
Granular casts	+++	+++	+++	+++
Serum protein g/dl				
Globulin	2.6	3.3	4.3	4.0
Albumin	2.0	1.5	1.4	2.1
Duration of follow-up	13 weeks	16 weeks	6 weeks	8 weeks

Table 2: Histopathological findings on renal biopsy specimens patients

Recognised glomerular Histopathological characteristics (6)	Patients 1	2	3	4
1. Thickening of GBM	Present	Present	Present	absent
2. Increased mesangia matrix	Present	present	presnt	absent
3. Notable mesangial lobulation	present	present	present	absent
4. Mesengial hypercellularity	present	present	present	absent
5. Capsular adhesions	absent	present	absent	absent
6. Epithelial cresent formation/cellular proliferation	presnt	present	absent	present
7. Leukocytes infiltration	present	absent	absent	present
8 Eosinopphilic fibrun deposit	present	present	present	present
9 Segmental/global sclerosis	absent	absent	present	present

The early development of azotemia and renal failure is the clinical hallmark of RPGN [1,2,5,6]. All our patients presented with a rapidly developing azotemia within a short period (with the exception of case 2 who died before a second assessment of renal function could be made).

Although serological tests are important in making specific diagnosis, renal biopsy with immunofluorescence and electron microscopy is the ultimate in diagnosing crescentic rapidly progressive GN, the presence of crescents being pathognomonic[1,6]. Towards this end and barring contraindications, a renal biopsy should always be performed to confirm suspected cases [2,5]. Serological diagnostic tests could not be performed on our patients due to technical and reagent constraints. However, renal biopsy was done in all the four patients although the histopathology reports came in too late to influence the management of these patients. It is worth noting that these are highlights of some of the drawbacks of proper renal care in the developing world, and should attract greater attention by health planners. In addition, the fact that the renal histopathology reports might not be readily available further emphasizes the need for an increased physician awareness of this disease based on recognized clinical features. In an attempt to strengthen the diagnosis of crescentic RPGN in our patients, we have tried to match the histopathological findings in the glomeruli of each patient with the classical histopathological features of crescentic RPGN as described by Darmady and MacIver[6] (Tables 1 and 2). The presence of epithelial crescents (which develop from extensive extra-capillary proliferation of cells, and fibrin-related structures within the glomeruli are the most constant histopathological features in all our patients. Other features like thickening of the glomerular basement membrane, mesangial hyper-cellularity and increased mesangial matrix were found in three out of the four patients.

Early appropriate treatment has been established by several workers to improve the outlook in patiesnts with RPGN [2,5]. Treatment is directed towards initiating an arrest and inducing a remission of the glomerular cellular proliferation process. Several regimens of treatment have been tried although the overall patient survival varies and is in particular dependent on the underlying initiating disease [1,2,7,8,9].High dose prednisolone with or without the addition of cyclophosphamide has been used as first line standard treatment with varying results [2]. Plasma exchange has been used as adjunctive therapy [8]; and maintenance therapy usually with tapering doses of prednisolone and azathioprine [2]. The accompanying hypertension would require aggressive treatment to prevent the development of heart failure, which might hasten the demise of the patient. Dialysis treatment might be indicated when renal failure is severe, as well as to improve blood pressure control [10].

In conclusion, these case presentations have shown that RPGN might not be a rarely encountered glomerulopathy in the Nigerian patient and that there is the need for increased awareness of this potentially treatable cause of end-stage renal failure by physicians in this environment. Improved renal biopsy and histopathology facilites remain indispensable in the management and should therefore not be abandoned in our renal centers.

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