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Research Article

Clinicopathological Spectrum of Two Common Conditions Encountered in Renal Biopsies: Acute Diffuse Proliferative Glomerulonephritis and Lupus Nephritis.

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Abstract

Background: Acute diffuse proliferative glomerulonephritis (ADPGN) and lupus nephritis (LN) are commonly encountered conditions in renal biopsies. ADPGN is usually a self-limiting childhood disease occurring commonly after streptococcal infection. LN is a common complication of systemic lupus erythematosus (SLE) with diverse clinical and histological features.

Objectives: The objective of this study is to describe the clinico-pathological spectrum of ADPGN and LN in renal biopsies.

Method: A retrospective-descriptive study was done by retrieving all renal biopsies (1225) received in the year 2018 at the Department of Pathology, Faculty of Medicine, University of Peradeniya. Biopsies diagnosed as ADPGN and LN were selected.

Results: Out of all renal biopsies (1225), 63(5.1%) were diagnosed as ADPGN and 92(7.5%) as LN. ADPGN was seen in an age range of 3-78 years. 24(38.1%) were children and 39(61.9%) were adults. Nephritic syndrome (NS) was the commonest presentation in both children and adults (n=23,36.5%) while 13(20.6%) showed nephrotic-nephritic mixed picture (NNMP).

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Cellular crescents were seen in 11 patients (17.4%) and most were adults with NNMP. Tubular injury was seen in 19 (30.1%) and most were children with NNMP. 34 (53.9%) patients showed classic uncomplicated ADPGN. Immunofluorescence showed IgG-positivity in 9(14.2%). C3 was positive in 27(42.8%).

In LN cases, 47(51.09%) patients were women with Class IV lesions, which was the commonest group. Of the class IV patients (n=56) most presented with non-nephrotic range proteinuria (NNRP), while 35 (62.5%) had microscopic haematuria (MH) and 26(46.4%) showed elevated serum creatinine. All class II patients(n=15) were women (100%). 9 (60%) patients showed NNRP, 9 (60%) MH and 4(26.7%) elevated SC. All class III patients(n=5) were also women who had NNRP and MH. SC was elevated in 1(20%) patient.

Conclusions: Most children and adults who underwent renal biopsy for ADPGN had presented with NS while a lesser number had NNMP. A study done by Wijewickrama et al. in 2015 also revealed that NS was the commonest presentation of ADPGN in adults. Common complications detected in our study were cellular crescents and tubular injury which were found more in patients with NNMP than NS. C3-positivity was commoner than IgG possibly because biopsies were performed during the latter phase of the disease. Common classes of LN were class IV, II and III. Most of these patients had NNRP

and MH while a lesser number showed elevated serum creatinine.

Keywords; acute diffuse proliferative glomerulonephritis, lupus nephritis, nephritic syndrome, nephrotic-nephritic mixed picture, non-nephrotic range proteinuria

Introduction:

ADPGN and lupus nephritis are commonly encountered conditions in renal biopsies. ADPGN is a common childhood disease seen between the ages 5-15 years and follows various infections of which the commonest is streptococcal infection. However, it can follow other bacterial, viral or parasitic infections as well. Patients usually present with nephritic syndrome characterized by gross haematuria, oedema and hypertension. Proteinuria and impaired renal function can also be seen [1,2]. ADPGN is characterized histologically by diffuse endocapillary proliferation, showing endothelial and mesangial proliferation with infiltration of leukocytes in the glomerular tuft with capillary narrowing [1,3]. Immunofluorescence shows granular deposits of IgG and C3 along the capillary loops. Since this condition is usually self-limiting, most childhood patients with a typical clinical picture do not require biopsy. Biopsies are performed when there is an atypical picture including nephrotic syndrome, acute renal failure, anuria, persistent hypertension or if there is no evidence of recovery after 6 weeks [1.2].

Adult cases with post infectious ADPGN is an emerging entity and most reported cases are seen in the elderly with immunocompromised status including diabetes and cancers. Streptococcus species and staphylococcus aureus are commonly recognized causative organisms. The diagnosis in these cases may be delayed due to overlapping clinical features and low degree of clinical suspicion [3].

LN is a common complication of SLE leading to end stage renal disease in 10-30% of patients [4]. LN shows a wide clinical spectrum including acute nephritic syndrome, nephrotic syndrome and acute or chronic renal failure. Renal biopsy is indicated in all SLE patients with urine sediment abnormalities or impaired renal function. Histological features are diverse and are divided into six different classes [1]. The clinical management of the patient depends on the severity of the disease mainly assessed by histopathology [1,4].

Objectives:

The objective of this study was to describe the clinicopathological features of the patients diagnosed as ADPGN and LN in their renal biopsies, which were reported in our center.

Material and Methods:

A retrospective-descriptive study was done on all renal biopsies (1225) received in the year 2018 at the Department of Pathology, Faculty of Medicine, University of Peradeniya by analyzing archived data.

Renal biopsies were routinely processed as formalin-fixed, paraffin embedded tissue and were stained with Haematoxylene and Eosine (H & E). 63 and 92 biopsies reported as ADPGN and LN were selected. Clinicopathological data including immunofluorescence study results (IgG, IgA, IgM and C3) were also extracted from the request forms and the histopathology reports in the archives. Inclusion criteria for ADPGN were diffuse endocapillary proliferation showing endothelial and/or mesangial proliferation, with or without infiltration of leukocytes in the glomerular tuft, with capillary narrowing. LN was classified into different classes according to the International Society of Nephrology/Renal Pathology Society Classification. Class I (minimal mesangial lupus nephritis) should show normal glomeruli on light microscopy but mesangial immune complex deposits by immunofluorescence. Class II (mesangial proliferative lupus nephritis) was diagnosed when glomeruli showed any degree of mesangial hypercellularity and/or mesangial matrix expansion, with demonstration of mesangial immune complex deposits by immunofluorescence. Class III (focal lupus nephritis) was diagnosed when focal segmental and/or global endocapillary, and/or extracapillary glomerulonephritis

affected less than 50% of the glomeruli. In class IV (diffuse lupus nephritis) there was diffuse segmental and/or global endocapillary and/or extracapillary glomerulonephritis affecting 50% or more of the glomeruli. Class V (membranous lupus nephritis) showed presence of diffusely thickened glomerular capillaries and spike and dome pattern on silver methenamine stain. Class VI (advanced sclerosing lupus nephritis) was diagnosed when there was global glomerulosclerosis in more than 90% of the glomeruli without residual activity.

Results:

Out of all renal biopsies (1225), 63 (5.1%) were diagnosed as ADPGN and 92 (7.5%) as LN. There were 36 (57.1%) men and 27 (42.9%) women with the diagnosis of ADPGN. The age of the patients ranged from 3 to 78 years. The mean age was 33.8 years.24 (38.1%) patients were children and 39(61.9%) were adults. NS was the commonest presentation in both children and adults and was seen in 23 patients (36.5%), while 13 (20.6%) patients showed NNMP. 13 children (54.2%) presented with NS while NNMP was seen in 8(33.3%). In adults, NS was seen in 10 (25.6%) patients and NNMP in 5(12.8%). Sore throat and skin sepsis were documented in 5(7.9%) and 15(23.8%) patients respectively. 12 (19%) patients had preceding fever. Elevated serum-creatinine and high ASOT were noted in 51(80.9%) and 11(17.4%) respectively. Active urine sediment was seen in 50 patients (79.3%).

Histology revealed cellular crescents in 11 (17.4%) patients of which 5(45.4%) presented with NNMP. Out of the 11 patients, 6(54.4%) were adults. Tubular injury was seen in 19 (30.1%) patients of which most(n=9,47.4%) presented with NNMP. There were 11(57.9%) children. Tubulitis was seen in 11(17.4%) patients. 15 children and 19 adults(n=34,53.9%) showed classic uncomplicated ADPGN. Immunofluorescence was performed in 30 cases, which showed IgG positivity in 9biopsies (14.2%) while it was negative in 21(33.3%).C3 was positive in 27 (42.8%) cases while C3 was negative in 3(4.8%) biopsies. Both were positive in 8 cases (12.6%) and both were negative in 3(4.8%) cases (Table 1).

Out of 92 renal biopsies diagnosed as LN, 56 (60.8%), 15 (16.3%), 5 (5.4%), 3 (3.3%) and 2 (2.2%) were categorized as class IV, II, III, VI and V respectively.

Table 1: Clinico-pathological features of ADPGN

Clinico-pathological feature		*Results (Total n = 63)*
Gender	Males	n = 36 (57.1%)
	Females	n = 27 (42.9%)
Age		Mean 33.8 years Range 3 to 78 years Children: n= 24 (38.1%) Adults: n= 39 (61.9%)
Commonest presentation	Children	Nephritic syndrome:n= 13 (54.2%)
	Adults	Nephritic syndrome: n = 10 (25.6%)
Histological findings	Cellular crescents	n = 11 (17.4%)
	Tubular injury	n = 19 (30.1%)
	Tubulitis	n = 11 (17.4%)
	Classic uncomplicated ADPGN	n = 34 (53.9%)
Immunofluorescence findings	IgG positivity	n = 9 (14.2%)
	C3 positivity	n = 27 (42.8%)

Four patients (4.3%) showed II+III lesions, 3(3.3%) were II+V, another 3(3.3%) were III+V and 1(1.1%) was IV+V. Class IV LN (n=56) was the commonest with an age range of 11-62 and a mean of 29.9 years. There were 47 (83.9%) women and 9 (16.1%) men diagnosed as class IV. Most (n=37,66.1%) class IV patients presented with NNRP, while 35(62.5%) had MH and 26(46.4%) showed elevated serum creatinine levels. Second commonest class was II (n=15). All patients were women (100%) with a mean age of 27.8years (range 12-42 years). Nine patients (60%) showed NNRP, 9 (60%) MH and 4(26.7%) elevated SC. All class III patients (n=5) were also women (100%) and mean age was 31.5years (range 27-39 years). All had NNRP and MH (100%). Serum creatinine was elevated in 1 patient (20%). (Table 2)

Discussion and conclusions:

Most children and adults who underwent renal biopsy for ADPGN had presented with NS while a lesser number had NNMP.

A study done by Wijewickrama et al. in 2015 also revealed that NS was the commonest presentation of ADPGN in a population of adults included in their study and a considerable number had isolated nephrotic syndrome or NNMP [5].

Table 2: Prevalence and clinical manifestations of common histological classes of LN.

Class	*Number of cases*	*Mean age (years)*	*Gender*		*Commonest presentation*
			Male	Female	
IV	56 (60.8%)	29.2	9 (16.1%)	47 (83.9%)	NNRP (66.1%), MH (62.5%)
II	15 (16.3%)	27.8	0	15 (100%)	NNRP (60%), MH (60%)
III	5 (5.4%)	31.5	0	5 (100%)	NNRP (100%), MH (100%)

Common complications detected in histology in our study were cellular crescents and tubular injury. They were found more frequently in patients with NNMP than NS. Cellular crescents were mostly (54.4%) seen in adults while tubular injury was commonly (57.9%) seen in children. Crescent formation is usually indicative of severe glomerular injury. Although some studies have revealed that there is poor outcome for these patients, others have failed to show similar results [6].

IgG staining may not be demonstrable by immunofluorescence when ADPGN resolves and C3 is only seen in mesangial areas later disappearing gradually from the periphery of the tuft [1]. Therefore, C3-positivity was commoner than IgG positivity in this study population possibly because the biopsies were performed during the latter phase of the disease.

Common classes of lupus nephritis in this study population were class IV, II and III respectively. According to published literature biopsies with class III LN show less than 50% of glomeruli affected by focal and/or global endocapillary GN or extracapillary GN. About 50% of patients have proteinuria and in up to one third it is in the nephrotic range. In class IV lesions more than 50% of the glomeruli are affected and the patients have more severe symptoms including nephrotic range proteinuria. They are more prone to progress to renal failure without treatment [1]. Most patients in all groups in our study had non-nephrotic range proteinuria and microscopic haematuria. A lesser percentage had elevated serum creatinine. In a study done by Dumbutuge et al in 2019, it was concluded that most patients who presented with proteinuria showed a proliferative GN and that the commonest type was class IV, which is compatible with our study [7].

In conclusion, most children and adults who underwent renal biopsy for ADPGN had presented with nephritic syndrome while a lesser number had a nephrotic-nephritic mixed picture. Common complications were cellular crescents and tubular injury and they were found more in patients with nephrotic - nephritic mixed picture than nephritic syndrome. Most biopsies diagnosed as lupus nephritis were class IV, II and III. Majority of lupus nephritis patients in all classes in our study presented with non-nephrotic range proteinuria and microscopic haematuria and a lesser number had elevated serum creatinine.

References

1. Rosai J. Rosai and Ackerman's Surgical Pathology.10th edition, Philadelphia: Elsevier Science limited. 2011.
2. Ikhlas M. Anjum F. Diffuse proliferative glomerulonephritis. In. StatPearls(Internet). Treasure Island(FL): StatPearls Publishing. 2021.
3. Sathi S. et al. Postinfectious glomerulonephritis with crescents in an elderly diabetic patient after acute gastroenteritis: Case report 2019. *Case rep Nephrol Dial*; 9:64-71.
4. Rijnink EC et al. Clinical and Histopathologic Characteristics Associated with Renal Outcomes in Lupus Nephritis. *Clin J Am Soc Nephrol*2017; 12: 734-743.
5. Wijewickrama ES et al. Clinical syndromes of acute diffuse

proliferative gomerulonephritis among adults in a tertiary care centre in Sri Lanka. International conference on Gastrointestinal, Bone and Soft Tissue Pathology, 2015.

6. Wu Q., Tanaka H, Hirukawa T, Endoh M, Fukagawa M. Characterization and quantification of proliferating cell patterns in endocapillary proliferation. *Nephrology Dialysis Transplantation* 2012; 27(8): 3234-3241.
7. Dumbutuge DJB et al. clinicopathological spectrum of renal pathology in systemic lupus erythematosus managed at a tertiary care setting in Sri Lanka. International conference on diagnostic challenges and pitfalls in surgical pathology and cytopathology, 2019.