Research Article

Role of Renal Biopsy in Systemic Lupus Erythematosis (SLE)

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Abstract

Aims and Objectives: 1)To evaluate histopathological findings in Lupus Nephritis and to classify it according to the International Society of Nephrology/Renal Pathology Society (ISN/RPS 2003) classification system for Lupus Nephritis. 2) To correlate the histological findings with the disease process. **Materials and Methods:** Renal biopsy performed at a tertiary care centre and Hospital in South India, for duration of 2 years was collected along with relevant clinical data. Ultrasound guided renal biopsy was performed and tissue were processed routinely and the slides were stained with Hematoxylin and Eosin. Special stains that is per iodic acid Schiff (PAS) and Methanamine silver (PASM) were performed for all cases. All the cases were correlated with Immunofluroscence (IF) study. 30 Renal biopsies were performed, 21 cases were of Primary Glomerulonephritis and 9 cases were Secondary Glomerulonephritis out of which 6 were cases of Systemic Lupus Erythematosus. Renal Biopsy of all the cases of SLE was classified according to ISN/RPS classification system. **Results:** Out of 30 cases (n=30), Primary glomerulonephritis (GN) accounted for 70% and secondary GN accounted for 30%. Among secondary glomerulonephritis predominant lesion were systemic lupus nephritis (66.7%) followed by diabetes mellitus (22.2%) and Amyloidosis (11.1%). In secondary GN the predominant lesion was Systemic Lupus Nephritis, Out of 6 (100%) cases of Lupus Nephritis, 4 (66.7%) cases were class IV, 1(16.7%) case was class II and 1(16.7%) case was class V. **Conclusion:** Management goals in patients with Lupus Nephritis include early diagnosis and appropriate therapy whilst preserving overall Kidney function without undue side effects and prevent irreversible damage. ISN/RPS 2003 classification tends to correlate with clinical syndrome and provide valuable information regarding prognosis and guideline for treatment. ISN/RPS classification system also intends to facilitate a higher degree of reproducibility, resulting in a better patient care. A renal biopsy examined by routine light microscopy, Immunofluroscence and electron microscopy contributes toward diagnosis, prognostic information, and appropriate management.

Keywords: Renal Biopsy, Systemic Lupus erythematosis, lupus Nephritis

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INTRODUCTION

SLE is an autoimmune disease with protean clinical and pathological manifestations involving almost all the organs in the body. There is high incidence of renal involvement during the course of the disease, with varied renal pathological lesions and diverse clinical features. Renal involvement is observed in most SLE patients at some point during the natural history of the disease, with a significant proportion having an adverse outcome. Nearly 50% of SLE patient develop renal disease in the first year of diagnosis. Approximately 20% of SLE patients with renal disease include children and older adults. The diagnosis of Lupus Nephritis cannot be based on clinical features alone like proteinuria, rising serum creatinine, active sediment, since the clinical features do not permit a reliable prediction of the type of SLE Nephritis. The correlation of clinical renal and serological features with underlying renal pathologic findings is not absolute, having poor predictive value in nearly 30% to 50% of cases.[1,2,3] Renal biopsy is an essential diagnostic tool in histopathological diagnosis of renal disorders. Renal biopsy remains gold standard in establishing the

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diagnosis, evaluating the acuteness, severity of the disease process (grade of the disease) and the degree of reversibility (stage of the disease). A renal biopsy is a pivotal step in determining the nature of renal involvement in patients with Lupus Nephritis. Renal involvement (Lupus nephritis) is a major complication of SLE and is a strong determinant of morbidity and mortality. Six classes of LN are distinguished in the current classification of the International Society (ISN/RPS). Classification and treatment decisions strongly depend on the findings on renal biopsy.[4,5,6,7]

MATERIALS AND METHODS

The material for this study was obtained from 30 patients who underwent renal biopsy at a tertiary care centre and Hospital in Mangalore. The relevant data obtained in each case were name, age, sex, clinical features, laboratory findings and clinical diagnosis. In each case ultrasound guided renal biopsy was performed, 2 samples were collected. One sample was immediately put into Bouin's fluid and transported to laboratory for processing and other sample was put in Mitchell's media for IF. All samples were processed and stained with Hematoxylin and Eosin (Hand E). Special stains that are PAS and PASM were performed, to see for any basement membrane thickness and sclerosis. All the cases were correlated with IF. Clinical presentation was divided into nephritic syndrome, nephrotic syndrome, asymptomatic hematuria, asymptomatic proteinuria, acute renal failure and chronic renal failure. On microscopic examination, the renal biopsies were classified into VI classes. Abbreviated International society of Nephrology / Renal Pathology Society classification of Lupus Nephritis (2003)

Class I Minimal mesangial lupus nephritis
Class II Mesangial Proliferative Lupus nephritis
Class III Focal lupus nephritis
Class IV Diffuse segmental Lupus nephritis (IV-S) or global (IV- G) Lupus nephritis
Class V Membranous nephritis
Class VI Advanced sclerosing lupus nephritis

RESULTS AND ANALYSIS

Out of 30 cases (n=30), Primary glomerulonephritis (GN) accounted for 70% and secondary GN accounted for 30% (table 1 and figure 1). Among secondary glomerulonephritis predominant lesion were systemic lupus nephritis (66.7%) followed by diabetes mellitus (22.2%) and Amyloidosis (11.1%) (Table 2 and Figure 2). Most of the cases were seen in the age group of 20-40 yrs with female preponderance (Table 3 and table 4).Out of 6 (100%) cases of Lupus nephritis, 4 (66.7%) cases were class IV, 1 (16.7%) case was class II and 1 (16.7%) case was class V. Crescent was noted in 1 (16.7%) case and wire loop lesion was noted in 1 (16.7%) case. Out of 4 (66.7%) cases of lupus nephritis, 1 (16.7%) case showed immunofluorescence of IgG, IgA, C_3 coarse granular positivity in mesangium and capillary wall, 1 (16.7%) case showed full house immunofluorescence with C_3 positivity, 1 (16.7%) case showed IgA, M and C_3 positivity and 1(16.7%) case showed no deposits. 1 (16.7%) case of class II Lupus nephritis on immunofluorescence showed IgG and C_3 coarse granular positivity in mesangium and peripheral capillary wall. 1 (16.7%) case of class V lupus nephritis showed IgG, M and C_3 granular positivity in mesangium and capillary wall (Table 5)

Table 1: Occurrence of Various Lesions

Lesion	n = 30	Percentage
Primary Glomerulonephritis	21	70%
Secondary Glomerulonephritis	9	30%
Total	30	100%

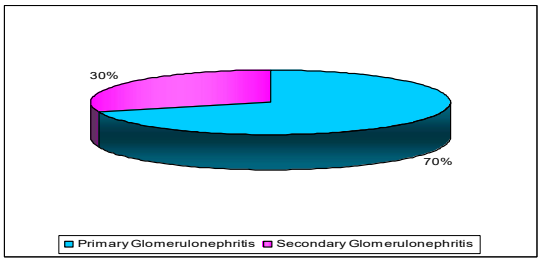

Figure 1: Occurrence of Lesions

Table 2: Occurrence of Secondary Glomerulonephritis

Sr. No.	Lesion	No. of Cases	Percentage
1	Systemic lupus erythematosus (SLE)	6	66.7%
2	Diabetes Mellitus (DM)	2	22.2%
3	Amyloidosis	1	11.1%
	Total	9	100%

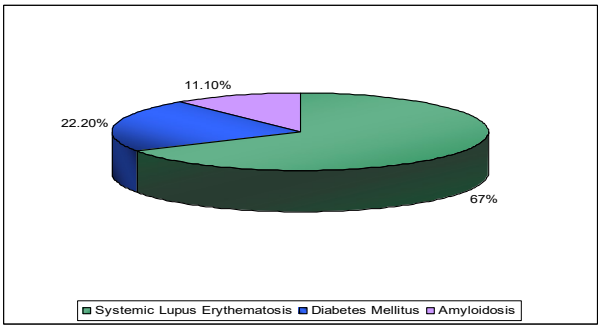

Figure 2: Occurrence of Secondary Glomerulonephritis

Table 3: Age Distribution in Secondary Glomerulonephritis

Lesions	< 20 yrs	20–40 yrs	> 40 yrs	Total
Systemic lupus erythematosis (SLE)	1 (11.1%)	5 (55.6%)	-	6 (66.7%)
Diabetes Mellitus (DM)	-	-	2 (22.2%)	2 (22.2%)
Amyloidosis	-	-	1 (11.1%)	1 (11.1%)
Total	1 (11.1%)	5 (55.6%)	3 (33.3%)	9 (100%)

Table 4: Sex Distribution in Secondary Glomerulonephritis

Lesion	Male	Female	Total
Systemic lupus erythematosis (SLE)	1 (11.1%)	5 (55.5%)	6 (66.7%)
Diabetes Mellitus (DM)	2 (22.2%)	-	2 (22.2%)
Amyloidosis	-	1 (11.1%)	1 (11.1%)
Total	3 (32.2%)	6 (66.7%)	9 (100%)

Table 4: Microscopy of Lupus Nephritis

Case Number	Capillary proliferation	Mesangial proliferation	Capillary Inflammation	Basement Membrane Thickening	Sclerosis	nterstitium	Tubules	Vessels
1	-	+	-	-	-	Mild Inflammation	Vacuolization	Unremarkable
2	+	+	-	+	-	Unremarkable	Unremarkable	Unremarkable
3	+ C	-	-	+	-	Mild neutrophilic cells	Vacuolization	Thickened
4	+	-	-	+	-	Unremarkable	Unremarkable	Unremarkable
5	+ WLL	+	-	+	-	Unremarkable	Vacuolization	Unremarkable
6	+	+	-	+	-	Sparse lymphocytes	Vacuolization	Unremarkable

*C – Crescent, WLL – Wire loop lesion

DISCUSSION

SLE is the prototype of a multisystem disease of autoimmune origin, characterised by a bewildering array of auto antibodies, particularly antinuclear antibodies (ANAs). Acute or insidious in its onset, it is a chronic, remitting and relapsing, often febrile illness characterised principally by injury to the skin, joints, kidney, and serosal membranes. Virtually every organ in the body however may be affected. The clinical presentation of SLE is so variable that the American College of Rheumatology has established criteria for diagnosis of this disorder. A definitive diagnosis of SLE is usually made when at least 4 of 11 diagnostic criteria put forth by the American Rheumatologic Association are met.SLE is a fairly common disease, with a prevalence that may be as high as 1 in 2500 in certain populations with female – male ratio of 9:1 and is seen in twenties and thirties. Renal involvement is common in SLE and often determines the course of the disease. The glomerular lesions that frequently accompany SLE have been the subject of intense investigation by clinicians and pathologists for nearly a half of century. These efforts have generated numerous attempts to classify and categorize the pathological features of Lupus nephritis. After several revision of WHO classification of Lupus Nephritis, the recent ISN/RPS 2003 classification aims to enhance the quality of communication among renal pathologists and clinical Nephrologist regarding pathologic findings in Lupus Nephritis.[1, 8, 9, 10,11] The frequency of different renal pathology classes of Lupus

nephritis vary in the different series. In our study compared class IV nephritis outnumbers other classes as found in most of the other studies. [12, 13, 14, 15,16,17,18, 19, 20] this class has involvement of 50% or more of all glomeruli with segmental(S) or global (G). Class IV-G has global lesions in 50% or more glomeruli and Class IV-S has segmental lesions in 50% or more of glomeruli. Active lesions have varying degrees of large sub endothelial deposits (wire loop lesions), hyaline thrombi, endocapillary cellular proliferation, inflammatory cell infiltrate, fibrinoid necrosis with disruption of capillary basement membrane and cellular crescents that generally have mesangial proliferation. 1 case of Wire loop and 1 case of crescent was noted in this study. Generally, a full house IF pattern is found in class IV lesions, with occasional case that are pauci-immune , usually class IV –S. The subdivision of class IV-S and class IV-G were included in the in the ISN/RPS classification because of a long term nephritis outcome study (> 10 yrs) that demonstrated a poor prognosis for diffuse segmental LGN. This study and subsequent study by Hill *et al*.[21] also raise the possibility that class IV-G and class IV-S LGN are caused by different pathogenetic mechanisms. This subdivision may facilitate further studies regarding their possible pathogenetic mechanisms, clinical relevance and prognostic significance. Other class of lesions were class II and class V. Class II; Mesangial LGN is a sine qua non of all classes of LGN, and this category denotes glomerular changes confined to mesangial areas of varying degrees by LM. Clinically, nearly 60% of patients with class II lesions present with asymptomatic proteinuria (subnephrotic range), asymptomatic hematuria, or both with normal renal function. Nephrotic range of proteinuria is not common in this class. This may be indicative of minimal change disease. Although these glomerular lesions remain stable in most cases with close clinical monitoring of the systemic disease and supportive therapy, a significant number may progress to class III or class IV LGN. Class V Membranous LGN; this subset of Lupus nephritis is diagnosed when immune deposits are found in the basement membranes under the glomerular visceral epithelial cell, in a global or segmental distribution involving more than 50% of capillary basement membranes. The incidence of this lesion ranges from 10% to 30% in various reports.[1,4,8,13, 14]

CONCLUSION

Management goals in patients with Lupus Nephritis include early diagnosis and appropriate therapy whilst preserving overall Kidney function without undue side effects and prevent irreversible damage. ISN/RPS 2003 classification tends to correlate with clinical syndrome and provide valuable information regarding prognosis and guideline for treatment. ISN/RPS classification system also intends to facilitate a higher degree of reproducibility, resulting in a better patient care. A renal biopsy examined by routine light microscopy, Immunofluroscence and electron microscopy contributes toward diagnosis, prognostic information, and appropriate management.

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