ORIGINAL ARTICLE

Morphological Patterns of Renal Disease in Systemic Lupus Erythematosus (SLE)

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ABSTRACT

Aim: To observe the various morphological presentations of SLE on renal biopsy in terms of ISN / RPS classification.
Settings and Design: Simple descriptive study, conducted in the Morbid Anatomy & Histopathology Department, University of Health Sciences, Lahore.
Methods: We studied 30 biopsy samples of patients diagnosed as Systemic Lupus Erythematosus according to American Rheumatism Association (ARA) criteria. Histolopathological examination of samples was carried out using light microscopy. Samples were classified using the ISN/RPS Classes of lupus nephritis. The data was entered and analysed using SPSS 20.0 (Statistical Package for Social Sciences). Mean±SD was calculated for quantitative variables. Frequencies and percentages were calculated for qualitative variables.
Results: Among these 30 patients, 25(83%) were females and 5(17%) were males; minimum age being 5 years and maximum being 62 years (mean+S.D = 22.77+13.76). A total of 13 cases (43%) fell in ISN/RPS Class IV, 6 cases (20%) in ISN/RPS Class V, 5 cases (17%) in ISN/RPS Class III & 3 cases (10%) each in ISN/RPS Classes II & VI.
Conclusions: Morphological patterns of renal disease in study population closely matches the patterns observed in neighbouring regions with ISN/RPS Class IV being the commonest finding. Renal biopsy is critical in establishing the ISN/RPS Class and consequently in clinical management of patient with lupus nephritis.
Keywords: SLE, ISN/RPS classification, renal morphology

INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that can affect any part of the body. As occurs in other autoimmune diseases, the immune system attacks the body's cells and tissue, resulting in inflammation and tissue damage[1].

Worldwide, the prevalence of SLE varies. The reported prevalence of systemic lupus erythematosus (SLE) in United States is 20 to 150 cases per 100,000[2] and[3]. Europe has a higher prevalence of lupus erythematosus than USA, with Italy and Spain having the highest prevalence of disease. Martinique and the Afro-Caribbean population of United Kingdom also have a very high prevalence rate [4.] In women, prevalence rates are much higher and generally vary from 164 (white) to 406 (African American) per 100,000[5]. Patients with lupus erythematosus are subject to varied symptoms & complaints that can affect practically any organ of the body; consequently, the clinical presentations can be quite diverse[6]. Renal involvement is also quite common in systemic lupus erythematosus (SLE). An abnormal urinalysis with or without deranged serum creatinine is generally seen in a substantial proportion of patients at the time of diagnosis or later on[7]. It occurs in approximately 60 percent patients and is a major source of morbidity[8].

American College of Rheumatology (ACR) proposed diagnostic criteria in 1982[9]. These were further revised in 1997. ACR criteria are used worldwide for making a diagnosis of SLE and are appended below (Hochberg, 1997)[10].In order to accommodate the insights into pathogenesis of SLE that have been gathered since 1995, ISN/RPS (International Society of Nephrology/Renal Pathology Society) proposed a new classification in 2004 (Fig1) (Weening et al., 2004)[11].

Fig. 1: International Society of Nephrology / Renal Pathology Society 2003 Classification of Lupus Nephritis

I	Minimal mesangial lupus glomerulonephritis (LGN)
II	Mesangial proliferative LGN
III	Focal LGN (<50% of the total number of glomeruli)
	III (A) Purely active: focal proliferative LGN
	III (A/C) Active and chronic
	III (C) Chronic: focal sclerosing LGN
IV	Diffuse segmental (IV-S) or global (IV-G) LGN (50% or more of the total number of glomeruli)
	IV-S (A) or IV-G (A): diffuse segmental or global proliferative LGN
	IV-S (A/C) or IV-G (A/C)
	IV-S (C) or IV-G (C): diffuse segmental or global sclerosing LGN
V	Membranous LGN
VI	Advanced sclerotic LGN (>90% of glomeruli globally sclerosed without residual activity): end stage LGN

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Sada KE, Makino H. Usefulness of ISN/RPS Classification of Lupus Nephritis. J Korean Med Sci. 2009 Jan;24(Suppl 1):S7-S10. http://dx.doi.org/ 10.3346/jkms. 2009.24. S1.S7

In lupus patients who have clinical or laboratory evidence of renal disease (e.g., proteinuria, active urine sediment, raised serum creatinine or decreased glomerular filtration rate); renal biopsy is performed to determine the histological subtype of lupus nephritis (LN) and to guide treatment[12].

SUBJECTS AND METHODS

The study was conducted in the Department of Morbid Anatomy &Histopathology, University of Health Sciences, Lahore. The subjects were selected from Departments of Nephrology in Sheikh Zayed Hospital, Services Hospital, Children Hospital, Jinnah Hospital & Fatima Memorial Hospital, Lahore. In all cases complete medical history was obtained and reviewed with the respective consultant nephrologist. Patients were thoroughly explained and informed consent for renal biopsy was obtained from all patients. Renal biopsies were obtained from each patient under real-time ultrasound guidance, using a needle biopsy gun. The core for light microscopy was sent in 10% formol saline& paraffin embedded blocks were prepared in the laboratory. A total of 140 renal biopsies was procured & based on inclusion criteria, 30 cases were included. Biopsy samples were evaluated according to ISN/RPS (International Society of Nephrology/Renal Pathology Society) classification using light microscopy techniques. Haemotoxylin /eosin stain, PAS stain, Gomori's Trichrome stain & Jones Methanamine Silver staining techniques were used. The data was entered and analysed using SPSS 20.0 (Statistical Package for Social Sciences). Mean±SD was calculated for quantitative variables. Frequencies and percentages were calculated for qualitative variables.

RESULTS

Among these 30 patients, 25 (83%) were females and 5 (17%) were males. The ratio being 5:1; meaning that for every 5 females, there was one male patient (Table 1).

Table 1: Gender distribution among 30 patients

Gender	Frequency	Relative frequency	Ratio
Female	25	83%	5:6
Male	5	17%	1:6

At the time of taking a renal biopsy, the minimum age was 5 years and maximum was 62 years with a mean+S.D age being 22.77+13.76. Despite the apparent variation in age, majority (73%) of the patients were young (10-35 years). Upon detailed morphological examination 13 cases (43%) fell in ISN/RPS class IV, 6 cases (20%) in ISN/RPS class V, 5 cases (17%) in ISN/RPS class III & 3 cases (10%) each in ISN/RPS classes II & VI (Fig. 1).

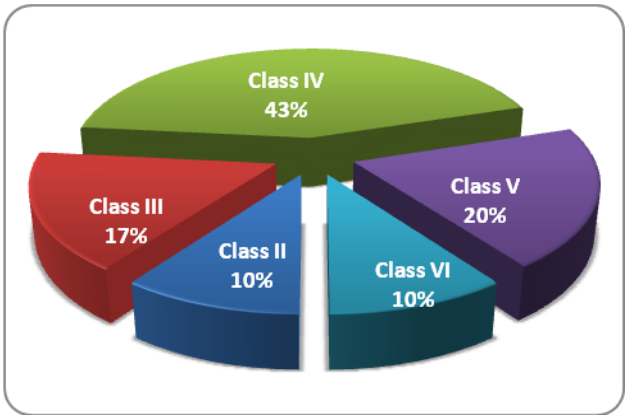

Fig. 1. Morphological Patterns (ISN/RPS Class wise)

Mesangial Nephritis (International Society of Nephrology/Renal Pathology Society Class II)

A total of 3 patients (10%) showed histological findings consistent with focal lupus nephritis (ISN/RPS class II).The histological examination showed normal thickness blood vessels& interstitial tissue showed occasional lymphocytes. Mesangial hypercellularity was observed in all the 3 cases (100%). Glomerular capillary basement membrane did not show thickening in any of the cases in this group. Hyaline deposits were observed in 2 cases (67%). Tubular dilatation was seen in 1 case (33%). In 2 cases (67%) hyaline casts were observed; whereas in 1 case (33%) both hyaline & granular casts were present. Interstitial oedema, interstitial inflammation & evidence of fibrosis were present in one case (33%). Extra-glomerular blood vessels were normal in all the 3 cases (100%).

Focal lupus nephritis (International Society of Nephrology / Renal Pathology Society Class III)

A total of 5 patients (17%) showed histological findings consistent with focal lupus nephritis (ISN/RPS class III). Mesangial hypercellularity was seen in all the 5 cases (100%). Glomerular capillary basement membrane was also thickened in all the cases in this group; hyaline deposits were however seen in 1 sample (20%) only. Tubular epithelial cell necrosis & tubular dilatation were seen in 4 cases (80%). In all 5 cases (100%) hyaline casts were observed. Interstitial inflammation & evidence of fibrosis were present in 4 cases (80%). Extra-glomerular blood vessels were thickened in three cases (60%).

Diffuse proliferative glomerulonephritis (International Society of Nephrology /Renal Pathology Society Class IV)

A total of 13 patients (43%) showed histological findings consistent with diffuse proliferative glomerulonephritis (ISN/RPS class IV).The histological examination revealed that mesangium was hypercellular in 12 cases (92%); in 1 case (8%) mesangiolysis was observed. Glomerular capillary basement membrane was thickened in all 13 cases (100%) in this group; hyaline deposits were seen in 4 patients (31%).

Tubular epithelial necrosis & tubular dilatation were seen in 11 cases (85%). In 11 cases (85%) hyaline casts were observed; one case showed granular/RBC casts. Tubular basement membrane was thickened in 3 cases (23%) whereas as vacuolization was seen in 2 cases (15%). Interstitial inflammation was present in 12 cases (92%) & fibrosis was seen in 9 cases (69%). Extra-glomerular small blood vessels were thickened in 6 cases (46%).

Membranous glomerulonephritis (International Society of Nephrology/Renal Pathology Society Class V)

A total of 6 cases (20%) showed histological findings consistent with membranous glomerulonephritis (ISN/RPS class V). The histological examination showed mesangial hypercellularity in all 6 cases (100%). Glomerular capillary basement membrane was also thickened in all the cases (100%) in this group; hyaline deposits were seen in 2 cases (33%). Tubular epithelial cell necrosis & tubular dilatation were seen in 6 patients (100%) & 5 cases (83%) respectively. In 5 cases (83%) hyaline casts were observed; one biopsy (17%) showed granular/RBC casts. Tubular basement membrane was normal in all cases.

Interstitial oedema & inflammation were present in 2 cases (33%) & 4 cases (67%) respectively. Evidence of interstitial fibrosis was present in 3 cases (50%). Extra-glomerular blood vessels were thickened in 3 cases (50%).

Sclerosing Glomerulonephritis (International Society of Nephrology/Renal Pathology Society Class VI)

A total of 3 cases (10%) showed histological findings consistent with sclerosing glomerulonephritis (ISN/RPS class VI).The histological examination of glomeruli showed that there was mesangial hypercellularity in 2 cases (67%). Glomerular capillary basement membrane was thickened in all the cases (100%) among this group. All cases (100%) showed hyaline deposits. Crescents were observed in 2 cases (67%); variable sclerosis was seen in all biopsies (100%).

Tubular epithelial cell necrosis & tubular dilatation were seen in 2 cases (67%) & 3 cases (100%) respectively. Hyaline casts were observed in all patients. Tubular basement membrane was normal in all biopsy samples in this group. Interstitial inflammation & fibrosis were present in all cases (100%). Extra-glomerular small blood vessels showed increased wall thickness in 3 cases (100%).

DISCUSSION

Renal involvement is quite common in systemic lupus erythematosus. It occurs in approximately 60 percent of patients and is a major source of morbidity (Beck andSalant, 2009). However there are multiple different histological subtypes of lupus nephritis (LN) and the optimal treatment varies with the subtype (BombackandAppel, 2010). It is therefore important to identify the histological type in order to guide treatment. Comparable clinical features may be observed even with very different classes and types of lupus nephritis. Therefore, early renal biopsy may be helpful in planning the treatment (Wen, 2011).

In our study, 83% patients were females; females to male ratio being 5:1, a finding which is consistent with other published data (Chakravarty et al., 2007). In our study population the average age of the patients was 22 years. In case of females, the average age was 26 years. In a study conducted in Iran to assess correlation of clinical and pathological findings in patients with lupus nephritis; among the 144 patients, 122 (84.7%) were females with a mean age at presentation of 25.6±10.3 years (range 2 to 63 years) (Nezhadand Sepaskhah, 2008); findings which are consistent with our study results.Rabbani, et al., in a study spanning over 5 year reported that the SLE is a disease of predominantly females in their third decade with an average age being 31 years (Rabbani et al., 2004).

The histological examination showed that 13 cases (43%) fell in ISN/RPS class IV, 6 cases (20%) in ISN/RPS class V, 5 cases (17%) in ISN/RPS class III and 3 cases (10%) each in ISN/RPS classes II and VI. A retrospective study reported from Iran by Nezhadand Sepaskhah; on patients with systemic lupus erythematosus; reported similar distribution patterns as was observed in our study; with 17.3% patients in ISN/RPS class II; 12.1% patients in ISN/RPS class III; 54.9% patients in ISN/RPS class IV and 16.6% patients falling in ISN/RPS class V (Nezhadand Sepaskhah, 2008). In another study of 110 patients with lupus nephritis conducted in Iran; Kuroiwa, et al reported that 59% patients had ISN/RPS class IV lupus nephritis (Kuroiwa et al., 2009).

Renal involvement is common in patients with SLE and is a major source of morbidity. SLE is much more common in women and affects a younger population. Renal biopsy is recommended even in SLE patients with normal renal function tests owing to comparable clinical features among various ISN/RPS classes as well as high prevalence of asymptomatic renal disease. Advanced disease is more common in our population, earlier renal biopsy can effectively guide clinical management and improve overall clinical outcomes significantly.

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