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Research Article

SLE Nephritis Clinical Features and Renal Lesion: Tripoli Central Hospital Experience

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Abstract

Background: Lupus nephritis (LN) is a known complication of systemic lupus erythromatosis (SLE).

Aim: To study the relationship between clinical features of SLE and LN classes at presentations.

Method: Patients' files were reviewed retrospectively for the clinical symptoms, signs, laboratory results and histopathology reports of kidney biopsy of SLE patients for 8 years. All patients had CBC, bleeding and clotting time. Blood pressure measured before conducting percutaneous renal biopsy (PRB).

Statistical analysis: Data was collected and analyzed by IBM-SPSS version19.0 (SPSS, Chicago, IL, USA).Student's t-test, one-way ANOVA and analysis of variance were used for statistical analysis. $P < 0.05$ was considered statistically significant.

Results: One-hundred twenty seven SLE patients files' were reviewed, 51 patients had been diagnosed as LN after their PRB specimens examined by pathologist. Patients were 44 females (86.3%), 7 males (13.7%), with a mean age of 31 year ± 2.3 (standard error of mean). Bilateral lower limbs (BLL) edema and hypertension (HTN) reported in 16 patients (31%), BLL edema and hematuria detected in 12 patients (24%), BLL edema only reported in 7 patients (14%). Generalized edema plus hematuria described in 6 patients (12%). Oliguria with muscle weakness and generalized edema described in 4 patients (8%).Muscle weakness and generalized edema reported in 3 patients (6%), and BLL edema plus face puffiness only reported in 3 patients (6%). White blood cell count (WBC) mean was 8.46 x 10^3 ± 0.57, ranged between 4.8 -13.0 x 10^3/ µl. Hemoglobin mean was (11.4g ± 0.22), ranged (9.5 – 13g/dl). Platelets mean was 170 x 10^3/µl ± 10.3, ranged between 124 – 301x 10^3/µl. Erythrocyte sedimentation rate (ESR) ranged between 2.00 – 84.00 mm after 1st hour, with a mean of 40 ± 5.86.Mean protein excretion in urine/24 hours was 2.22g/L ± 0.19, 0.30 – 2.22 g/L. LN activity index mean was (5 ± 1.0) ranged0.00 – 14. Chronicity index mean (1.95 ± 0.52), and ranged between 0.00 – 10.00. Histopathological findings were; Class I reported in 7 patients (14%), class II in 11 patients (22%).Class III reported in 5 patients (10%), class IV in 18 patients (35%) and class V in 10 patients (20%). Advanced sclerotic LN (class VI) was not described in the studied patients. Patients' age affected protein excretion in 24hrs urine, LN activity and chronicity index significantly ($P = 0.02$, $P< 0.0001$, $P< 0.0001$) respectively. Multivariate analysis revealed significant correlation between LN classes and protein excretion in urine/day, i.e. class III, IV and V had significantly increased protein excretion in urine $P = 0.04$, 0.025 and 0.021respectively. LN class IV associated significantly with BLL edema only, and with BLL edema plus facial puffiness at presentation ($p = 0.01$, $P=0.02$).

Conclusion: Clinical feature and 24 hours protein excretion in urine were related significantly to LN classes and patients' age at presentation. Early detection of clinical SLE features, and LN classes will reduce subsequent complications and health services cost.

INTRODUCTION

SLE has a wide spectrum of clinical and immunological abnormalities.SLE etiology and pathogenesis are not clearly identified. Autoimmune reactions due to improper central or peripheral deletion of auto-reactive lymphocytes in SLE had been attributed to SLE pathogenesis and etiology, and that led to formation of characteristic auto antibodies to double strand-DNA, nuclear antigens and membrane phospholipids [1-4]. Furthermore, it had been claimed that abnormal immune regulatory mechanisms, environmental and genetic risk factors might had stimulatory autoimmune reactions in susceptible people [5,6].

LN appears to be more prevalent in certain ethnic groups. It was reported that 45% of African Americans, 42% of Chinese, and 30% of Caucasian SLE patients had evidences of renal involvement [7]. Another multi-ethnic USA cohort study of SLE patients reported that renal disease occurred in 51% of Africans and 43% of Hispanics and in 14% of Caucasians [8]. Chinese patients with new onset SLE, 31% patients had active renal disease at first presentation [9], and the overall incidence of LN was 60% after 5 years post-SLE diagnosis [10].

Kidney involvement by LN classified into six different classes [5]. Although LN has different clinical and histological features, there is usually intercrossing among the LN microscopic

histopathological findings. Mixed LN lesions and transformation of one lesion to other due to disease progression were reported in about 35% of LN patients [11].

SLE is not uncommon diseases in Libya particularly in female. Up to our knowledge, there were not any published data about the commonest LN class, and any relationship between clinical features and LN classes at presentation. Therefore, this study was conducted to study the common LN classes and to assess any relationship between the clinical presentation and LN classes.

METHOD

Clinical data of 127SLE patients were collected. They were 104 females and 23 males. Ultrasound guided PRBs were done for 59 patients. Only 51biopsies had sufficient PRB specimens for histopathological examination [12]. PRBs were conducted at Medical Department, and examined microscopically in Pathology Department at Tripoli Central Hospital -Libya, during May 2008 - Sept 2016.

Biopsy specimens were sent to pathology department in container containing 4.5% buffered formaldehyde. Specimens were sectioned and stain by hematoxylin and eosin (H&E), periodic acid-Schiff. Pathological parameters of disease activity and chronicity were done by pathologists according to semi-quantitative scoring system of biopsy specific features [13-15]. LN lesions were reported according to the International Society of Nephrology and Renal Pathology Society of lupus nephritis classification system (Figure 1).

Statistical analysis

Statistical analysis was conducted by IBM-SPSS, version19.0 statistical software (SPSS, Chicago, IL, USA). Quantitative data were expressed as (mean ± SEM), and range (minimum, maximum). Student's t-test, one-way ANOVA analysis of variance were used to test the significant relation between clinical features and LN classes at presentation. P value of <0.05 was considered statistically significance.

RESULTS

LN patients were 44 females and 7 males. Male patients' age ranged between 28 – 49 years and female patients' age ranged between 17 – 38 years. Mean age of the studied patients was31

Class I **Minimal mesangial lupus nephritis**
Normal glomeruli by light microscopy, but mesangial immune deposits by immunofluorescence.

Class II **Mesangial proliferative lupus nephritis**
Purely mesangial hypercellularity of any degree or mesangial matrix expansion by light microscopy, with mesangial immune deposits. A few isolated subepithelial or subendothelial deposits may be visible by immunofluorescence or electron microscopy, but not by light microscopy.

Class III **Focal lupus nephritis**
Active or inactive focal, segmental or global endo-or extracapillary glomerulonephritis involving <50% of all glomeruli, typically with focal subendothelial immune deposits, with or without mesangial alterations.

Class IV **Diffuse lupus nephritis**
Active or inactive diffuse, segmental or global endo- or extracapillary glomerulonephritis involving ≥50% of all glomeruli, typically with diffuse subendothelial immune deposits, with or without mesangial alterations. This class is divided into diffuse segmental (IV-S) lupus nephritis when ≥50% of the involved glomeruli have segmental lesions, and diffuse global (IV-G) lupus nephritis when ≥50% of the involved glomeruli have global lesions. Segmental is defined as a glomerular lesion that involves less than half of the glomerular tuft. This class includes cases with diffuse wire loop deposits but with little or no glomerular proliferation.

Class V **Membranous lupus nephritis**
Global or segmental subepithelial immune deposits or their morphologic sequelae by light microscopy and by immunofluorescence or electron microscopy, with or without mesangial alterations. Class V lupus nephritis may occur in combination with class III or IV in which case both will be diagnosed.

Class VI **Advanced sclerotic lupus nephritis**
≥90% of glomeruli globally sclerosed without residual activity.

Figure 1 Revised classification of LN [5].

year ± 2.3, with standard deviation (STD) of 10.3, and variance (var) of 100 (Table 2).

Patients had BLL edema and hypertension were 16 patients (31%). BLL edema and hematuria reported in 12 patients (24%), BLL edema only was detected in 7 patients (14%). Generalized edema plus hematuria observed in 6 patients (12%), and generalized edema with HTN reported in 6 patients (12%). Generalized edema, muscle weakness and oliguria reported in 4 patients (8%), and generalized edema plus muscle weakness reported in 3 patients (6%).BLL edema with facial puffiness detected in 3 patients (6%) (Table 1).

One or two days before PRB appointment; WBC count was normal in most of patients with a mean of 8.500 ± 0.57 and range of4.8 -13.0 x 10^3/µl, STD of 2.5 and var of 6.24. Hemoglobin ranged between 9.5 – 13g/dl with a mean of 11.3 ± 0.22. Platelets count ranged between 124 – 301x 10^3/µl with a mean of 170 x 10^3/µl ± 10.3, STD 45.1 and var of 210.8. ESR ranged between 2.00 – 84.00 with a mean of 40 ± 5.86, and STD of 25.6, and var of 653.1.

Protein excretion in urine/24 hours ranged between 0.30 – 2.22gm/L with a mean of 4.00gm/L ± 0.84, and STD of 4.38, and var of 5.16. LN activity index ranged with 0.00 – 14, with a mean of 5.00 ± 1.01, STD of 4.38 and var of 5.16. Chronicity index of LN ranged between 0.00 – 10.00, with a mean of 1.95 ± 0.52, STD of 2.27 and var of 19.22. (Table 2).

PRB specimens' histopathological examination revealed; Class I- (minimal mesangial) LN was detected in 7 patients (14%). Class II- (Mesangial proliferative) LN was detected in 11 patients (22%), class III-(focal) LN was detected in 5 patients (10%). Class IV- (diffuse) LN was reported in 18 patients (35%). Class V- (membranous) LN was seen in 10 patients (20%). Class VI - LN was not reported in the studied patients (Table 2).

Protein excretion in urine/day, LN activity and chronicity were significantly affected by an increase of patients' age (P = 0.02, P < 0.0001, P <0.0001 respectively). Furthermore, statistical analysis revealed significant increase of protein excretion in urine in class III, IV and V LN (P = 0.04, P =0.025 and P =0.021 respectively). BLL edema only, and BLL edema with facial puffiness increased significantly with an increase of patients' age (p = 0.01, P=0.02 respectively), as well LN activity and chronicity were significantly affected by patients' age increase (P<0.0001) (Table 3).

DISCUSSION

Kidney injuries are either due to local renal diseases as pyelonephritis or manifestations of systemic diseases such as SLE, amyloidosis and vasculitis or both. Detection of LN pathological class, activity and chronicity are essential for management and prognosis in LN [16,17]. Clinical symptoms, signs and laboratory results at first presentation and follow up in SLE patients are important, and must be considered carefully, while they are important for prediction of LN classes in about 70-80% of LN patients [18-20].

Literatures review showed that SLE was more predominated in female with a ratio of 9:1(female: male). In this study, patients

Table 1: Symptoms and signs at presentation.

Symptoms& signs	No. of patients	%
Generalized edema, muscle weakness	**3**	6
Generalized edema, muscle weakness, oliguria	**4**	8
Generalized edema, hematuria	**6**	12
BLL edemas, Face puffiness	**3**	6
BLL edema	**7**	14
BLL, hematuria	**12**	24
BLL, hypertension	**16**	31
Total	**51**	**100%**

Table 2: Patients' age, blood tests, protein in urine, LN activity and chronicity at presentation.

Parameter	N	Minimum	Maximum	Mean	Std. Error	Std. Deviation	Variance
age	51	17.00	49.00	31.05	2.30	10.03	100.72
WBC	51	4.80	13.00	8.46	0.57	2.50	6.24
Hb	51	9.50	13.00	11.35	0.22	1.00	0.91
platelets	51	124.00	301.00	170.05	10.53	45.91	210.83
ESR	51	2.00	84.00	40.05	5.86	25.55	653.05
PT	51	11	14	12.3	1.2	0.62	0.1
INR	51	1.0	1.3	1.15	0.3	0.1	0.4
Ur-protein	51	0.30	4.00	2.22	0.19	0.84	0.70
activity	51	0.00	14.00	5.00	1.01	4.38	19.22
chronicity	51	0.00	10.00	1.95	0.52	2.27	5.16

Table 3: LN classes, and their frequency and percentage at presentation.

Pathological lesion	Patients No.	%
Class I: Minimal mesangial LN	7	14%
Class II: Mesangial proliferative LN	11	22%
Class lll: Focal LN	5	10%
Class IV: Diffuse LN	18	35%
Class V: Membranous LN	10	20%
Class VI: advanced sclerotic LN	0	0%
Total	51	100%

diagnosed as SLE patients were 127 patients. They were 82% female and 18% males (8.2:1.8 ratio female: male). This ratio was not different significantly from the previous reported ratio.

Hanly et al., reported that about 38% of SLE patients had LN, and LN was more common in women than men in certain ethnic groups [21]. Our results revealed that LN lesions were found in about 40.1% of patients participated at presentation, and showed females had LN more than males (44 females and 7 males (8.6:1.4). LN predominance in females reported in this study supported Hanly et al., and Lim & Drenkard reported data [21,22]. The higher rate of LN observed in this series in females was possibly because, the patients were mostly females and /or PRB acceptance by females was more than males. Reasons made male patients refused PRB than females were not clear.

Clinical symptoms and signs as BLL swelling, puffiness of face, increase body weight, dyspnea, and muscle weakness were reported in patients enrolled in this study with different proportions. In this study, 24 hours protein excretion in urine ranged between 300mg-4.00gm/24h/1.75 m^2, while normally in Man, protein excretion in urine is about 150-200 mg/day/1.75 m^2. Protein excretion in urine increased significantly with an increase in patients' age, and also with LN class III & IV at presentation in this study. The presenting symptoms and signs significant correlation with protein excretion and LN classes, this might be due to increased protein loss in urine. The increased protein excretion in urine could be due to late presentation in some patients and/or LN progression, and the associated heart comorbidity that was reported common with heavy proteinuria [23].

Our results showed that class I reported in 14%, class II in 22%, class III in 10%, and class V in 20% of the studied patients. Class IV was the commonest LN classes in this series (35%). The higher frequency of class IV LN in this study might be due to late presentation and/or delay in conducting PRB. Furthermore, increased percentage of class IV at presentation may explain the significant association between symptoms, signs and proteinuria with class IV-LN at presentation.

CONCLUSION

Clinical features and patients' age are significantly related to LN classes at presentation. Early diagnosis of SLE and LN by clinical features and histopathology are essential for early treatment to reduce late complications and services cost.

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