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The relationship of systemic lupus erythematosus activity and histopathology of renal biopsy

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Abstract

Purpose: Detection of the relationship between the activity of SLE and the histopathology of renal biopsy.

Patients and methods: This is a cross-sectional study. It included one hundred Egyptian patients with SLE according to the 2015 ACR/SLICC Revised criteria. SLE Disease Activity Index (SLEDAI) and renal biopsy were done on all patients in addition to the routine investigations.

Results: Of the one hundred patients; Nine are males and 91 are females with a mean age ± standard deviation of 32.28 ± 9.59 years. The mean value of SLEDAI was 11.92 ± 3.92. Lupus nephritis (LN) was found in 85 patients (85%) included 5 patients (5%) having class 1, 73 patients (73%) having class 2, and 7 patients (7%) having class3 LN. SLEDAI mean value is directly proportional to the class of LN increasing from 10.6 ± 3.91 in normal cases to 16 ± 3.92 in class III LN.

Conclusion: The relationship between the SLEDAI score and the histopathological study of renal biopsy in patients with SLE is strong and significant with a mean value of SLEDAI directly proportional to the class of LN.

Keywords: lupus nephritis, renal biopsy, SLEDAI score

Introduction

Systemic lupus erythematosus (SLE) is the prototype of autoimmune diseases characterized by multi-system involvement. Renal involvement is common with nearly 50% of SLE patients having lupus nephritis (LN) during the course of their disease and about10% of patients with LN developing the end-stage renal disease [(1).] LN is a significant cause of morbidity and mortality in patients with SLE. Renal dysfunction at the time of diagnosis and delayed response to treatment was associated with a bad prognosis.[(2)] For the-se reasons, we should identify factors that can predict early renal affection.[(3)]

LN was classified into six stages according to the extent of glomerular damage in renal biopsy samples by the International Society of Nephrology/Renal Pathology Society (ISN/RPS) in the 2003 classification.[(4)] The most important classes were class III and IV because they have more disease activity and worse renal prognosis . After publishing, different studies have proofed

the clinical value and utility of the 2003 classification in diagnosing LN [5]. On the other hand, other studies reported the need to improve the classification because non-glomerular lesionnns, such as vascular and tubule-interstitial lesions, have great significance in predicting the prognosis of LN [6and7]. So, the classification was revised in 2016 by ISN/ RPS and published in 2018 [8]. The activity index (AI) and chronicity index (CI), which were published in 1983 were included in the 2016 revision [9].

Evaluating disease activity in SLE is very important to take decisions of treatment by the physician. Disease activity assessment should be discrete from actual injury as this is important for both prognosis and the proper treatment. Many activity indices are used in the assessment of SLE patients with SLEDAI (Systemic Lupus Erythematosus Disease Activity Index) being the most important one of these indices [10].

The purpose of this study is to investigate the relationship of SLEDAI and the histopathology study of renal biopsy.

Patients and methods

This study which is cross-sectional included one hundred patients with SLE without clinical evidence of renal affection recruited to the department of rheumatology and rehabilitation in Sohag university hospital in the period from March 2017 to March 2020. The study followed the tenets of the declaration of Helsinki and was approved by the ethics committee of the Sohag faculty of medicine. Written informed consent was obtained from all patients after explaining the rationale of the study in addition to the benefits and risks of the procedures.

Inclusion criteria:

- Patients aged 17 -60 years.
- SLE Patients fulfilling the 2015 ACR/SLICC Revised criteria.

Exclusion criteria:

- Patients with diabetes mellitus, hypertension, or hyperlipidemia.
- Patients with underlying chronic active hepatitis or vasculitis.
- Patients with another connective tissue disease, mixed or overlapping syndrome.
- Patients with any type of nephropathy other than lupus nephritis

Methods:

All patients underwent complete clinical evaluation including detailed history taking and complete general and rheumatological examination in addition to the following investigations:

1. Routine investigations including complete blood count with the differential leucocytic count, kidney function tests, protein/creatinine (P/C) ratio (), 24-hour urinary protein, serum uric acid, lipid profile, coagulation profile, liver function tests, and abdominal ultrasonography.
2. Renal biopsy: is done by the radiologist under ultrasound guidance at the radiology department of Sohag university hospital. A disposable 16 -gauge biopsy needle is used under local anesthesia to reach the lower pole of the kidney with the patient in the prone position.
3. Histopathological examination of the biopsy specimen is done at the pathology department of the Sohag faculty of medicine
4. Assessment of disease activity by calculation SLEDAI score as follows:

- SLEDAI=0 no disease activity
- SLEDAI= 1-5 mild disease activeity
- SLEDAI= 6 -10 moderate activity
- SLEDAI =11-19 high disease activety
- SLEDAI equal or more than 20 very high disease activity

Results

This study included 100 patients with SLE according to the 2015 ACR/S-LICC Revised criteria.

Demographic data:

the 100 patients included; 9males, and 91 females with a mean age ± standard deviation of 32.28 ± 9.59 years, a median of 31.5 years, and an IQ range of 25-37.5 years as shown in Table 1.

Table (1): Distribution of the studied patients according to age and gender (No.=100).

Characteristics	Summary statistics
Age (year)	
Mean± S.D.	**32.28 ± 9.59**
Median (IQ range)	**31.5 (25 – 37.5)**
Gender	
Male	**9 (9%)**
Female	**91 (91%)**

Clinical findings:

The 100 patients with SLE had a mean disease duration of 15.56± 7.99 months with a range of 11-24 months and a median duration of 12 months.

Sixty one patients (61%) had fever, 48 patients (48%) had malar rash, 79 patients (79%) had photosensitivity, 79 patients (79%) had oral ulcers, 31 patients (31%) had alopecia, 41 patients (41%) had Raynaud's phenomenon, 86 patients (86%) had arthralgia and arthritis, 18 patients (18%) had serositis and 15 patients (15%) had neurological signs.

Laboratory findings:

twenty-eight of the patients had leucopenia (28%), 54 had anemia (54%), 25 had thrombocytopenia (25%), 41 had low C3 (41%), 27 had low C4 (27%), 30 had hematuria (30 %) and 12 had pyuria (16%).

All the study cases were positive for ANA (100%), 61were positive for Anti-dsDNA (61%) and 65 were positive for Anti-sm (65%).

The protein creatinine ratio test had a mean of 0.11 ± 0.06mg/mg, a median of 0.1, and a range of 0.06-0.16.

SEDAI:

The mean SLEDAI score was 11.92 ± 3.92 with a median of 12 and IQ range of 9.25 – 14

Table(2). SLEDAI score

SEDAI	
Mean± S.D.	**11.92 ± 3.92**
Median (IQ range)	**12 (9.25 – 14)**

Renal biopsy:

The renal biopsy was done on all the 100 study patients and the histopathological examination revealed nephritis in 85 patients (85%) and normal kidney in 15 patients (15%). The nephritis cases were fallen into 3 classes; class LN included 5 patients (5%), class II LN in 73 patients (73%), and classIII LN in 7 patients (7%) (table-3).

Table (3): Distribution of the studied patients according to renal biopsy (No.=100).

Renal biopsy	No. (%)
Normal	15 (15%)
Class I LN	5 (5%)
Class II LN	73 (73%)
Class III LN	7 (7%)

As regards SLEDAI; the relation to LN was strong (p=0.004) with a mean value of SLEDAI directly proportional to the class of LN increasing from 10.6 ± 3.91 in normal cases to 16 ± 3.92 in class III LN (Table 4, Figure 1).

Table (4): the relation between renal biopsy and SLEDAI (No.=100)

Investigations			Renal biopsy		P-value
	Normal 15 (15%)	Class I LN 5 (5%)	Class II LN 73 (73%)	Class III LN 7 (7%)	
SLEDAI Mean± S.D. Median (IQ range)	 10.6 ± 3.91 10 (8 – 13)	 8.2 ± 3.03 9 (5 – 11)	 12.05 ± 3.66 12 (10 –14)	 16 ± 3.92 16 (13 – 19)	 0.004*

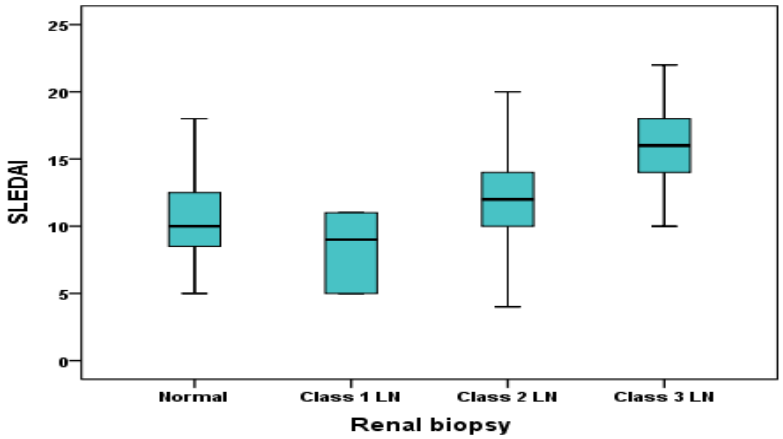

Figure (1): The relation between renal biopsy and SELDAI (No.=100)

b) The relations between SLEDAI and different findings:

1- An insignificant relation was detected between SLEDAI and the age of the patients, gender, and PCR. While a strong positive correlation was detected between SLEDAI and disease duration ($p=0.03$ and $r=0.218$).
2- As regards clinical data; a significant relation was detected only between SLEDAI and neurological disorders ($p<0.001$).
3- As regards laboratory findings; highly significant relations were found between SLEDAI and all the laboratory findings except ant-sm.

Logistic regression analysis of predictor variables of abnormal renal biopsy: the univariate analysis revealed that malar rash, serositis, anti-dsDNA, SLEDAI can significantly predict an abnormal renal biopsy with an odds ratio of 7.29, 0.29, 7, 1.19, and 5.47 respectively. While the multiple analysis revealed that SLEDAI cannot predict abnormal renal biopsy with an adjusted odds ratio of 1.05.

Discussion

This prospective observational study included one hundred patients with SLE. In addition to routine investigations, renal biopsy was done to all patients to detect the prevalence of lupus nephritis.

Eighty-five patients were found to have pathological evidence of lupus nephritis thus yielding a prevalence of 85% with class II LN forming most cases (73%).

In addition, the class of LN is strongly related to both SLEDAI scores and can predict abnormal renal biopsy especially class II and III.

Ishizaki et al [(11)] examined 182 patients with Systemic lupus erythematosus and renal biopsy. Disease activity was assessed using SLEDAI and BILAG. Forty-eight patients who had a normal urinary analysis with no renal impairment at the time of biopsy were divid-

ed into 2 groups: group 1 with lupus nephritis included 36 patients and group 2 with normal kidneys included 12 patients. In the silent LN group, 72% had class 1/ II and 17% had class III/IV.

Wakasugi et al [12] retrospectively investigated the frequency of class III and IV LN through renal biopsy in 195 patients with SLE (86 patients of them having no clinical renal manifestations). They reported a frequency of 15% especially in patients with a high titer of anti-dsDNA (with a cut-off level of 40 IU/ml) and low levels of C3 (with a cut-off level of 55mg/dL). The sensitivity was 77% while the specificity was 73%.

We prospectively investigated the prevalence of all classes of LN in patients with no clinical evidence of renal affection due to SLE. We did not report any case of class IV while 7% of cases were found to have class III.

Also, Chelliah et al [13] retrospectiveely evaluated the relation between renal histopathological examination and anti-dsDNA, C3, and C4 levels in 50 patients with SLE. They found class II (14%), class IV (70%), class V (8%), class IV, and V (8%). The prevalence of anti-dsDNA was 97.1%, low C3 was 68%, and low C4 74% with LN as a whole with a positive predictive value of anti-dsDNA of 100% and thus proliferative LN can be predicted by anti-dsDNA, low C3, and low C4.

We reported class II as the most common stage of LN within our sample (73%) but we found no cases with class IV or V. In our study, the prevalence of anti-dsDNA in all cases with LN was 57% while that of low C3 was 38% and that of low C4 was 26%.

A retrospective case-control study of Alba et al [14] compared 127 cases with biopsy-proven LN to 206 cases with SLE and no nephritis as a control group. The case group were younger in age, more associated with black ethnicity, and with high levels of anti-dsDNA, anti-RNP, Anti-SM, and lupus anticoagulant and hence concluded that the presence of such risk factors is associated with a higher risk of renal involvement. Compared to their study, our study was prospective, and all patients were Egyptian with no ethnic variations. Also, we found no relation between the result of renal biopsy and the age of the patient nor anti-SM. However, we detected a similar significant relation between the pathological state of the kidney and the presence of anti-dsDNA.

Conclusion

In this study, we found that the relation between LN and SLEDAI was strong (p=0.004) with a mean value of SLEDAI directly proportional to the class of LN increasing from 10.6 ± 3.91 in normal cases to 16 ± 3.92 in class 3 LN.

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