

## Histopathological Indexes of Activity and Chronicity: Predictors of Renal Outcome in Lupus Nephritis

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### Background

As it is well known that only 25 to 50% of unselected patients with lupus have abnormalities of urine or renal function early in their course, although up to 60% of adults and 80% of children may develop overt renal abnormalities later (1,2). Renal biopsy is worthwhile in all patients with lupus who have abnormal urine and/or reduced renal function because it provides prognostic information and influences initial treatment (3,4). The aim of our study was to present 1) incidence of lupus nephritis in our biopsies, 2) incidence of histopathological forms of lupus nephritis, 3) clinicopathological correlations and 4) outcome of the disease.

### Methods

Adult patients who underwent renal biopsies for SLE (Systemic Lupus Erythematosus) between April 1976 and April 2002 (26 years) at Department of Nephrology, University of Skopje, were selected. All patients fulfilled the criteria of the American Rheumatism Association for SLE diagnosis. Paraffin sections for light microscopy were stained with hematoxylin-eosin, periodic acid Schiff and Jones' silver methenamine. Frozen sections were stained with the following antisera: anti IgA, IgM, IgG, C3, C4, C1q, Fib. Semi-thin sections were analyzed during the past 9 years, and ultra-thin sections when the electron microscopy was available. All biopsies were classified according to WHO criteria. At the time of biopsy, the renal clinical evaluation was based on these criteria: proteinuria, plasma protein level, serum creatinine level and diastolic blood pressure. The data concerning all the patients with a follow-up from the time of biopsy to the time of study was obtained from the hospital files. All patients were treated with immunosuppressive treatment according to the histological class, but the treatment was not a matter of this study, it would complicate it too much. Correlations were established by Chi-squared test of Yates, renal survival was estimated by Kaplan-Meier method and correlations were made using Spearman's coefficient.

### Results

*Clinical data.* 42 patients, 4 male and 38 female, aged 15-51, were analyzed. Difference among serum levels of creatinine in different histological classes was significant ( $p=0,000$ ). Significant difference in proteinuria was not noted ( $p=0,236$ ), as well as in diastolic blood pressure ( $p=0,698$ ).

### Histological data.

Class I – one patient

Class II A – one patient, Class II b – 6 patients

Class III B – 7, Class III C – one

Class IV A – one, Class B – 7, class C – 7

Class V – 2, class B 6

Class VI – 2, interstitial form – one patient

Immunofluorescence findings were present as follows: IgA was present in glomeruli of 38/42 (90,5%) patients, IgM in 31/42 (73,9%), IgG in 39/42 (92,9%), C3 in 40/42 (95,2%), C4 16/42 (35,7%), C1q 31/42 (73,9%) and fibrinogen in 32/42 (76,2%).

*Follow-up.* Survival of patients presented significant correlation with histological activity index, Correlation Coefficient -438,  $p=0,004$ . Correlation between survival of the patients and histological chronicity index was also significant, Correlation Coefficient -621,  $p=0,000$ . 17/42 patients started chronic dialysis treatment during follow-up (renal death). Two patients died because of central nervous system lupus before development of chronic renal failure and two patients because of pancarditis and chronic heart failure.

### Discussion

According to the outcome in relation to clinical and histology findings, there has been more controversy than agreement concerning which features might be associated with a poorer outcome in lupus nephritis, and data useful to the clinician are scant. On renal biopsy, today many studies suggest that there is little or no difference in outcome between different WHO classes of nephritis in treated patients, although extensive subendothelial deposits and tubulointerstitial changes point to a poorer prognosis, as do the number of macrophages and T cells in the infiltrate. Crescents have also been related to a poorer, as in other forms of glomerulonephritis, but very extensive crescentic disease is relatively uncommon in lupus. Vascular lesions within the biopsy and intraglomerular capillary thrombi have been associated with unfavorable outcomes also, although the later observation has been contested. But, there are also studies which present that the different histologic categories, such as diffuse proliferative, focal proliferative, membranous and mesangial glomerulonephritis, are associated with different outcomes (1-4). They present that the group of patients with diffuse proliferative lupus nephritis frequently develops chronic renal failure, while those with the other forms have a better prognosis. Cumulative survival analysis presented

that the probability of renal failure 10 years after the diagnosis of lupus nephritis was significantly higher in patients with an activity index  $>11$  and a chronicity index  $>3$ , as well as that probability of no renal failure was 90% in the patients with a chronicity index of 0, in contrast to a 50% chance of those with an index  $>1$ . Thus, the activity and chronicity indexes are useful to distinguish between patients with high versus low risk to develop end-stage renal failure. Some of parameters included in the histology indexes are also characteristics of the histology class, so we can accept histopathology indexes of activity and chronicity as histological parameters of the prognosis.

#### References

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