USEFULNESS OF RENAL BIOPSY ON THE ASSESSMENT OF TREATMENT RESPONSE TO INTRAVENOUS CYCLOPHOSPHAMIDE IN LUPUS NEPHRITIS

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INTRODUCTION

The incidence of nephritis is 16% at the beginning of the systemic lupus erythematosus (SLE) and 39% throughout evolution, with a negative impact on survival. Renal biopsy (RB) is essential for diagnosis, treatment and prognosis. The assessment of response to treatment with intravenous cyclophosphamide (IC) is based on clinical and laboratory features.

The objective of the study is to describe the therapeutic decisions after a second renal biopsy (SRB), taking into account the histopathological changes after treatment with IC. This analysis also aimed to assess the possible prognostic role of this SRB.

METHODS

We reviewed our experience in 35 patients treated with IC, who had a SRB done. In adition IC, azathioprine and/or mycophenolate was used in 14 patients. Clinical, laboratory and histological features at the time of RB and SRB were analyzed. The mean time from IC to the SRB was 30 months (SD± 9.3) and the mean follow up after the SRB was 9.2 years (SD ± 6.4).

RESULTS

Among clinical data in the RB and in the SRB we note: mean creatinine was 1.23 mg/dl (SD ± 1.08) and 0.96 mg/dl (SD ±0.45 (p<0,05)). GFR calculated by MDRD less than 60 ml/min was present in 12% and 5% of patients; and proteinuria 4.1 g/d (SD±2.8) versus 0.6 g/d (SD±1.1 (p<0,05)) respectively. Significant difference were detected in hematuria, nep hrotic syndrome and serological immune features.

A complete renal remission was reached in 60% (n=21) of patients at the time of the SRB, a partial remission in 31.4% (n=11), and no response IC in 8.6% (n=3).

The cumulative dose of IC was not different between patients with (7,5 range 6-10 g/d) and without response (10,48 g/d range 9-11,7).

A total of 9 patients showed proliferative forms in the SRB, 6 of them had proteinuria ≥ 1g/day and 3 patients proteinuria < 1 g/day.

Histological features at first and SRB

	First RB	Second RB	p
Number of glomeruli *	13 ± (6.35)	9.7 ± (4.65)	0.027
ISN Class: III and IV. A or A/C ***	35 (100%)	9 (25.7%)	< 0.005
Activity Index *	9.94 ± (3.39)	1.32 ± (1.96)	< 0.005
Chronicity index *	1.57 ± (1.61)	2.47 ± (1.79)	0.001

At the time of SRB 34.3% (n=12) of patients who only received corticoids remained only with it. Just after the SRB, 34,3% (n=12) increased or started a new immunosuppressive therapy (IST), 17.1% (n=6) remained with the same complementary IST, and 14.3% (n=5) decreased or stopped it. In 3 (8.6%) of the patients who increased/started a new IST, the indication was because of extra renal SLE activity.

Regarding IST in patients with < 1 g/day proteinuria, 12 (41%) remained with no treatment , 5 (17.24%) decreased IST, 6 (20.7%) increase and 6 (20.7%) maintain IST.

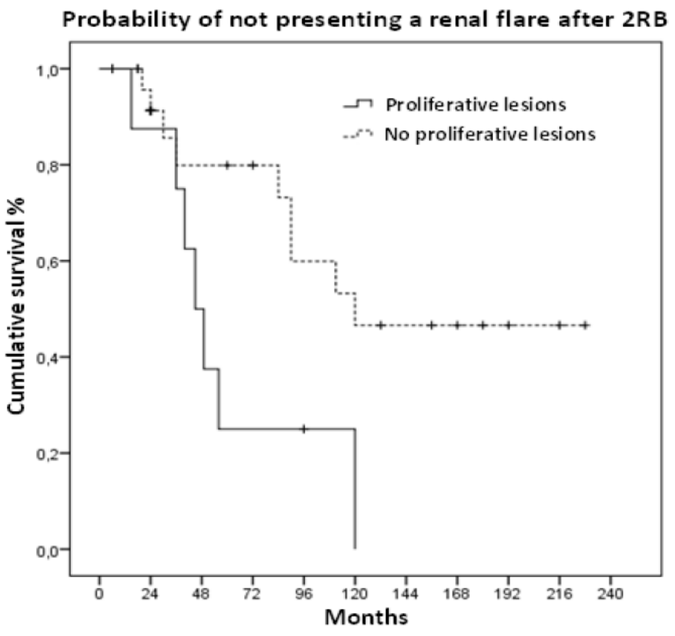
In the follow up post SRB, 34.5% (9 of 26) of patients without active lesions showed a renal flare versus 77.8% (7 of 9) patients with active lesions(p 0,04). The mean time was 120 months and 45 months respectively. One patient presented a severe adverse event (bleeding) related to the biopsy.

Clinical and laboratory features at first and SRB

Female	91.4 %		
Age (years) *	31.66 ± 12.29		
Time from 1st pulse CF until 2RB (months) *	30.46 ± 9.33		
Follow from 2BR (years)	9.2 ± DS 6.4		
	First RB	Second RB	p
Serum creatinine (mg/dl) *	1.23 ± (1.08)	0.96 ± (0.45)	0.034
MDRD < 60 ml/min **	12 (34.3%)	5 (14.3%)	0.092
Proteinuria (mg/24h) *	4114.74 ± (2896.84)	623.8 ± (1136.85)	<0.005
Haematuria **	28 (80%)	7 (20%)	<0.005
Anti-dsDNA antibodies titer *	165.05 ± (60.71)	57.74 (56.52)	<0.005
Hipocomplementemia C3 **	34 (97.1%)	11 (31.2%)	<0.005
Hipocomplementemia C4 **	29 (82.9%)	8 (22.9%)	<0.005

Response and treatment before and after SRB

Complete response	60% (n 21)
Partial response	31.4% (n 11)
No response	-8.6% (n 3)
CF cumulative dose (mg)	7934.26 ± 3339.139
Oral Prednisone before 1BR (mg/ day)	77%/ n:27
Oral Prednisone before 2BR (mg/ day)	91.4%/n:32
Another immunosuppression between 1st and 2nd RB: *Mycophenolic acid (MF)* *Azathioprine* *Azathioprine / MF*	40% (n 14) 42.86% (n 6) 42.86% (n 6) 14.28% (n 2)
Treatment post-2nd BR: *MAINTENANCE* *DECREASE* *INCREASE*	65.7% (n 23) 17.1% (n 6) 14.25% (n 5) 34.3% (n 12)
Establishment another immunosuppression post-2nd RB: Mycophenolic acid derivatives Azathioprine	14.7% (n 5) 8.6% (n 3) 5.7% (n 2)



CONCLUSIONS

While the biopsy after diagnosis is a well established practice in non-response or suspected relapse, it is a matter of debate the use of this practice in god response situations. Although the greatest diagnostic yield is in patients with proteinuria close to 1g/day, a new biopsy can be a valuable tool to distinguish patients in true remission from those in apparent remission and adjust unnecessary aggressive treatments when we find irreversible renal damage. The value of the biopsy in monitoring the treatment of patients with lupus nephritis deserves further investigation.

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