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Clinical outcomes in lupus nephritis. Report of a series of cases of the Central Military Hospital of Bogotá

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Abstract

The following retrospective series of cases aims to describe the characteristics and clinical outcomes of patients at the Central Military Hospital of Bogotá with proliferative lupus nephritis. It is frequently found at the time of diagnosis proteinuria, 37% of them in nephrotic range, and alterations in uroanalysis. We describe the results of the main hematological and immunological variables. We did not find differences between the types of induction nor in the outcomes as: percentage of remission, decrease of creatinine and proteinuria reduction.

Key words: lupus nephritis, immunosuppression.

Desenlaces clínicos en nefritis lúpica.Reporte de una serie de casos del Hospital Militar Central de Bogotá.

Resumen

La presente serie retrospectiva de casos, pretende describir las características y desenlaces clínicos de los pacientes del Hospital Militar Central de Bogotá, con nefritis lúpica proliferativa. Es frecuente encontrar al momento del diagnóstico proteinuria, 37% de ellas en rango nefrótico y alteraciones en el uroanálisis.

Describimos los resultados de las principales variables hematológicas e inmunológicas. No encontramos diferencias entre los tipos de inducción ni en los desenlaces como: porcentaje de remisión, disminución de creatinina y reducción de proteinuria.

Palabras clave: nefritis lúpica, inmunosupresión.

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Introduction

Lupus nephritis (LN) is one of the most severe manifestations of systemic lupus erythematosus (SLE) and occurs in 30% to 50% of patients[1]. Its clinical manifestations depend on the degree of renal involvement, proteinuria being described in 90%, hematuria in 80% and deterioration of renal function between 40% and 80% of the cases. There is a clinical correlation with the histopathological class, considering classes III, IV and V of high serological activity. Class IV was recognized as the most active and worst prognosis of LN, which presents between 35% and 60% of renal biopsies. Different induction schemes with different outcomes are described in the literature.

In cases of treatment with cyclophosphamide, the NIH treatment reports remission of 85% and Euro-lupus remission of 71% [2,3]. Mycophenolate mofetil induction reports remission of 56.2%[4]. There is no consensus on the superiority of one induction scheme over another when evaluating the population in Latin America[5]. We considered it convenient to identify the severity of LN and the outcomes with the different induction therapies in the patients treated at our institution.

Objectives and hypotheses

To describe the clinical characteristics and outcomes of patients at the Central Military Hospital of Bogotá with diagnosis of lupus nephritis.

Design

Observational and descriptive study as in series of cases.

Materials and methods

A descriptive, retrospective study in which the patients of the Central Military Hospital of Bogotá, who consulted the nephrology and rheumatology services, were included in the period between January 1st of 2009 and January 1st of 2014, and who met the clinical pathological definition and criteria of LN in accordance with the criteria of the Clinical Practice Guidance for Glomerulonephritis KDIGOISN / RPS[1].

The suspicion diagnosis was confirmed by renal pathology. Patients with an unconfirmed diagnosis of the disease were excluded. Demographic, clinical and laboratory data were collected by reviewing medical records. No written informed consent was required for this study because it was a risk-free investigation according to Resolution 8430 of 1993. The study met the basic research principles proclaimed in the Helsinki Declaration of the World Medical Association. The data were stored and analyzed with the software SPSS version 18. Quantitative variables are described by measures of central tendency and qualitative as relative frequencies.

Results

During the period described, the diagnosis of LN was confirmed in 21 patients, of whom 2 did not meet the inclusion criteria when they did not complete the follow-up suggested. One presented LN Class I, and 2 had no renal disease report available. The study population consists of 16 patients: 11 women (57.1%), with a mean age of 34.87 years (18-67 years) and 100% of the patients were mestizos. The mean of the follow-up time was 95.14 months (3 - 152 months) (Table 1).

The proportion of non-renal symptoms found, according to the BILAG6 scale, at the time of diagnosis was: general 25%; cardiorespiratory 31%; gastrointestinal 0%; hematological 13%; mucocutaneous 44%; musculoskeletal 38% and neurological 0%. Only non-renal SLE symptoms were present in 2 patients. Class I: 1 patient, class II: 3 patients, class III: 5 patients, class IV: 8 patients, not available (NA): 2 patients.

Regarding basal laboratory variables, mean creatinine was 1.15 mg / dL (0.51-4.99 mg / dL), the average estimated glomerular filtration rate (GFR) (CKD-EPI) was 93.39 ml / min / 1.73 M2 (10.97-148.09 ml / min / 1.73 m2) and mean BUN was 18.71 mg / dL (7.5-45.5 mg / dL) (Table 2).

Table 1.

Characteristics of the group with lupus nephritis and induction schemes

Número	Género	Edad	Clase	Síntomas no renales	Fecha de ingreso	Inducción	Mantenimiento
1	F	36	ND	MC,ME	22/04/10	MF-P: Remisión parcial con recaída NIH (03-13, 04-13, 05-13, 07-13, 08-13, 11-13): No respuesta	MF,P
2	M	26	III	ME	10/01/13 23/02/10	P - H: Remisión completa	P,H
3	M	33	IV	MC,G		MF-P: Remisión parcial con recaída NIH (07-12, 08-12, 09-12, 10-12, 11-12, 12-12): Remisión parcial con recaída R (12-13): Remisión parcial	MF,P,H
4	M	40	III	MC,ME	03/02/09	MF-P-H: Remisión parcial con recaída Euro-lupus 2012 (09-07, 24-07, 14-08, 29-08, 12-09, 27-09): Remisión completa	AZ,D,H
5	F	25	IV	CR, H	01/03/11	MF-P: Remisión completa	-
6	F	55	IV	-	22/09/09	AZ-D-H: Remisión completa	AZ,D,H
7	F	67	II	-	24/03/09	AZ-P-H: Remisión completa	H
8	F	27	I	CR	04/08/12	AZ-D-H: Remisión completa	D,H
9	F	29	III	MC	10/11/13	NIH (11-13, 12-13, 01-14, 02-14): Pendiente 2 dosis	
10	M	34	II	MC,ME	18/12/13	IECA y ARA II	
11	F	28	IV	CR,MC	29/10/12	NIH (11-12, 12-12, 01-13, 02-13, 03-13, 04-13): Remisión completa AZ,D,H	
12	F	31	ND	MC,CR,H	05/07/11	MF-P-H: Remisión completa	MF,P,H
13	M	24	III	ME	25/02/09	Euro-lupus (9 dosis en 2009): Remisión parcial con recaída R (01-11): Remisión parcial con recaída NIH (02-13, 03-13, 04-13, 05-13, 06-13, 07-13): Remisión parcial con recaída	MF,P,H
14	F	44	IV	ME	28/01/09	MF-D-H: Remisión completa	MF,D
15	M	30	II	G	06/05/12	MF-P: Remisión parcial con recaída NIH (09-13, 10-13, 11-13, 12-13, 01-14, 02-14): Remisión parcial	MF,P,H
16	F	43	III	ME	16/03/09	AZ - H: Remisión completa	AZ,H
17	M	18	IV	G, CR	18/12/12	NIH (02-13, 03-13, 04-13, 05-13, 06-13, 06-13): Remisión completa	MF,D,H
18	F	35	IV	MC,CR	30/05/12	Euro-lupus 2012 (18-08, 03-09, 13-09, 28-09, 12-10, 29-10): Remisión parcial con recaída MF-D-H: Remisión parcial	MF,D,H
19	M	23	IV	G,MC	25/11/10	MF-D-H: Remisión parcial	MF,D,H

G: General, MC: Mucocutaneous, ME: Musculoskeletal, CR: Cardiorespiratory, H: Hematologic. Mycophenolate Mofetil, P: Prednisone, H: Hydroxychloroquine, AZ: Azathioprine, D: Deflazacort, ACEI: Angiotensin converting enzyme inhibitors, ARA II: Angiotensin receptor antagonists.

In the baseline urine sample, the mean urinary density was 1.018 (1.009-1.031), mean pH was 5.8 (5-6.5), proteinuria was 79%, hematuria was 84%, and leukocyturia was 37% of the samples. Mean baseline proteinuria was 2480 mg / 24 hours (91-6640 mg / 24 hours). Patients with proteinuria in the nephrotic range correspond to 37% of the population (Table 2).

The proportion of anti-DNA positive antibodies was 64% and C3 hypocomplementemia 71% and C4 57%.

The mean value of leukocytes was 8500 / mm3, hemoglobin was 13.1 g / dL and platelet 263362 / mm3.

At the end of the follow-up period, the average creatinine level was 1.00 mg / dL (0.5-2.59 mg / dL) and the mean FGe (CKD-EPI) rate was 91.86 ml / min / 1.73 m2 (20.05-116.03 ml / min /1.73 m2). In 13% (σ = 3.33) of the population there was deterioration in the EGF rate. Mean proteinuria was 1470 mg / 24 hours (51.5-1955 mg / 24 hours) with a decrease in proteinuria in 75% (σ = 3843) of the population analyzed.

14 patients (87.5%) achieved some type of remission at 6 months, of which 8 patients (50%) achieved complete remission and 6 (37.5%) partial remission. Among patients with complete remission, no relapse was found during follow-up period (median 70 months). In 5 patients with partial remission, evidence of relapse was found during follow-up (median 120 months). No differences were found between patients treated with cyclophosphamide and mycophenolate mofetil. Among patients with proliferative LN, 41.6% had induction with NIH regimen, 25% with Euro-lupus regimen and in 5.5% of patients induction was performed with mycophenolate mofetil and prednisolone (Table 1). There was no association between use of the NIH regimen and total or partial clinical response (p = 0.09). No association was found between the NIH regimen and the decrease in proteinuria (p = 0.2). There was no association between the use of mycophenolate mofetil and total or partial clinical response (p = 0.14).

Discussion

Lupus nephritis (LN) was first recognized by Sir William Osler (1895) as part of SLE. But it was only after 1940 that its pathophysiology was widely known. Since then there has been a change in the natural history of renal involvement by SLE. The long-term prognosis was favorably modified by the use of corticosteroids introduced in the 1960s and subsequently by cytostatic and cytotoxic agents that decrease the disease activity.

Table 2.

Clinical characteristics of the population with lupus nephritis.

Característica	Media	Desviación Estandar	Media	Error Estandar	Mínimo	Máximo
Edad (años)	34,9	12,7	32,0	3,2	18	67,0
SEXO	7 Hombres (43%) y 9 Mujeres (57%)					
Creatinina (mg/dl)	1,2	1,1	0,9	0,3	0,5	5,0
TFG (ml/min/1. 73m2)	93,4	39,4	101,7	9,8	11,0	148,1
BUN (mg/dl)	18,7	10,2	18,5	2,6	7,5	45,5
Leucocitos	8606,9	4418,8	7105,0	1104,7	4690,0	21790,0
Hemoglobina (g/dl)	13,2	1,8	13,4	0,5	10,0	17,1
Plaquetas	265688	68913	257000	17228	83000	363000
Densidad urinaria	1,0	0,0	1,0	0,0	1,0	1,0
pH urinario	5,8	0,6	6,0	0,2	5,0	6,5
Hematuria (N /campo)	17,6	24,5	12,0	6,1	0,0	100,0
Proteinuria 24 h (mg)	2205,9	1845,3	1745,0	461,3	91,0	6640,0
C3 (mg/dl)	64,6	33,5	51,8	9,0	15,0	133,0
C4 (mg/dl)	11,5	8,6	9,0	2,3	1,7	24,1

The prognosis and response to treatment depend on the initial histological pattern, with lesions limited to mesangium (Type I and II) and with proliferative variants (Type III and IV) having a poor prognosis. High rates of chronicity limit the therapeutic response whereas the activity criteria are markers of inflammatory progression and demand prompt initiation of therapeutic regimen. Rapidly progressive behavior, defined as the loss of more than 50% of renal function over a period of less than 3 months, or the presence of more than 50% of growth on renal biopsy, is another marker of critical disease progression And demands rapid and timely action[7,8].

The response to therapy in patients treated timely is not always immediate. In the first months of induction the partial remission rate is around 80%, indicating a decrease in proteinuria and stabilization of the azoates. This is the reason why maintenance therapies should be sustained for periods longer than 1 year after referral is achieved[9].

At the moment, complete remission is defined as patients who reduce proteinuria to <0.3 g / d or proteinuria ratio Pru / CrS creatinine: <0.2, hematuria <10xc, inactive extrarenal disease and normalization of serological tests. Partial remission is considered if proteinuria decreases below 1 g / day[10].

From the introduction of steroids by Polak in 1964 to modern immunosuppression, overall survival and free dialysis period of patients with LN has improved. At the present time, the initial therapy of LN is based on the findings of the renal biopsy, with proteinuria <1 g / 24 hours and a decrease in serum creatinine being a predictor of good prognosis in the long term. Remission in the first 6 months is associated with greater dialysis-free survival and less exposure to immunosuppressants[11,12].

In our patients, 75% had decreased proteinuria and 87.5% reached some type of remission. It is important to note that proteinuria was found in the nephrotic range in 37% of the patients, when early initiation of therapy is clearly essential.

Since the 1980s, the Pulses of cyclophosphamide associated with steroids showed improvement in renal survival and disease remission, making it the standard treatment. The good results of combined regimens and low doses of immunosuppressants have resulted in lower toxicity derived from therapy. For this reason, mycophenolate, an agent with lower side effects and supported by the Chan, Ginzler, Contreras, ALMS (Aspreva Lupus Management Study) and 2 meta-analyzes of 2007, was introduced as part of the therapeutic tools. It showed no inferiority to the regimens based on cyclophosphamide. In some of these experiments the clinical results were slightly superior[13-20]. In our study, we did not find differences in the response to the different induction regimens (cyclophosphamide or mycophenolate) with respect to histological types studied, type of remission achieved, nor other outcomes. This finding is consistent with the results of the previously mentioned studies.

CONCLUSIONS

Among patients with proliferative lupus nephritis of the Central Military Hospital of Bogotá Colombia, there are similar rates of remission and relapse as described in the general population. We found no difference in the percentage of remission, decrease of creatinine and proteinuria, when we compared cyclophosphamide-based induction regimens with mycophenolate.

Conflict of Interest

The authors declare no conflict of interest.

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