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Analysis of Patients With Lupus Nephritis: A Single Center's Experience

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Abstract

Aim: Lupus nephritis is the major cause of morbidity and mortality of systemic lupus erythematosus. The treatment of lupus nephritis is still a significant problem. In this study, we aimed to investigation our remission rates, factors related to remission and the treatment results of lupus nephritis patients in our center.

Materials and methods: We retrospectively investigated the laboratory and the treatment results of 20 patients with lupus nephritis. The patients were grouped in terms of urine protein levels; patients with urine protein <0,3 g/day were regarded as in remission group and patients with urine protein > 0,3 g/day were regarded as in non-remission group. The relationships among clinical, laboratory, demographic parameters and remissions were investigated.

Results: Complete remission was achieved in 11 (55%) with lupus nephritis patients while 9 (45%) lupus nephritis patients had no-remission. Significant relationship was found between basal creatinine and patient remission ($p<0.05$). No relationship was found between other clinical and laboratory parameters and patient remission ($p>0.05$).

Conclusion: According to our study, significant relationship was found between basal creatinine and patient remission. The results of our treatments were similar to in the literature. Despite new studies and new drugs, the treatment of lupus nephritis is still a significant problem.

Key words: Lupus nephritis, remission, treatment results

Introduction

Systemic lupus erythematosus (SLE) is a chronic, multisystemic disease that is caused by autoantibodies to a variety of autoantigens. It is characterised by a wide variety of clinical and serological manifestations and relapsing and remitting course (1). It has a wide clinical spectrum, ranging from very mild forms to severe systemic involvement those progresses to involve major organs and may cause significant morbidity and mortality (2).

Lupus nephritis (LN) is the major cause of morbidity and mortality in SLE. Approximately 60% of patients with SLE experience clinically evident kidney involvement (1,3). Despite new studies and new drugs, the treatment of LN is still a significant problem. The adequate therapy of LN varies with the classification of the morphological findings present on renal biopsy. Immunosuppressive therapy is indicated in the great majority of patients with diffuse and focal proliferative LN and in some selected patients with membranous LN (2). In this study, we aimed to ascertain our remission rates, factors related to remission and the treatment results of LN patients in our center.

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Table I: Patients Features and comparison between remission and no-remission group

	Remission (n=11)	No remission (n=9)	p
Age(Years)	31,1±9,2	27,2 ±10,7	0,4
Gender(Male/Famale)	3/8	4/5	0,45
Antids-DNA (+)	3	4	0,6
Complement 3(g/dL)	0,72±0,58	0,90±0,66	0,5
Complement 4 (gr/dL)	0,3±0,2	0,6±0,4	0,3
Before treatment PU (gr/day)	5,2±4,7	4,4±3,5	0,6
Before Treatment SCr (mg/dl)	0,5±0,1	0,8±0,2	0,001

SCr: Serum Creatinine PU: Proteinuria

Materials and methods

Patients Features:

We retrospectively evaluated the demographic, laboratory, clinical features and treatment results of 20 patients with lupus nephritis from a renal biopsy at Yuzuncu Yil University Faculty of Medicine, Nephrology Department between June 2004 and July 2010.

Demographic, laboratory, clinical and therapy data were collected from patient files. In our study, the relationships among the clinical, laboratory and demographic features of LN patients and remission were studied. The patients with urine protein under 0,3 g/day were grouped as remission and those with urine protein over 0,3 g/day were grouped as no-remission (4).

Laboratory parameters:

A urine proteine level at 24-hour urine collection was measured by the enzymatic colorimetric method. Serum creatinine levels were examined with spectrophotometry.

Complement 3 (C3) and complement 4 (C4) rates of the patients were studied with nephelometry. Antinuclear antibody (ANA) and anti-double stranded DNA antibody (anti-dsDNA) levels were examined with indirect fluorescence.

Histopathological Classification:

Histopathological classification of LN patients was performed according to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 classification of lupus nephritis (5).

Treatment protocols:

Methylprednisolone (MP), cyclophosphamide (CyP), azathioprine (AZA) and mycophenolate mofetil (MMF) were given for the treatment of LN according to the following protocol that takes histopathological categories, clinical status and laboratory findings into consideration (2,6).

After being given as 1 mg/kg daily for four weeks, MP dosage was continued at 0,2 mg/kg/day as maintenance dosage by reducing the present dosage to 4 mg in a week. Cyclophosphamide at 10 mg/kg was given intravenously every month for 6 months. After that, it was given once every two months using the same dosage. AZA was started at 1 mg/kg daily and was gradually increased to a 2-3 mg/kg/day dosage. MMF was given as a 1-2 g/day dosage.

Statistical analysis:

The data was given as numerical percentages, averages and standard deviations. To determine the relationship between the factors affecting complete remission, chi-square testing of categorical variables was used. The level of significance was accepted as $p<0.05$. Statistical analysis was performed using SPSS 11,5.

Results

Demographic and laboratory data of the patients is given in table I. Thirteen (65%) LN diagnosed patients were women and seven (35%) were men. Average age of the patients was determined to be 29±10 years (17-46 years). No relationship was found between gender or age and remission ($p>0.05$) (Table I).

Before treatment, except for one patient (5%), patients had plasma creatinine levels that were lower than 1,0 mg/dl. Before treatment, creatinine levels of remission group were lower than no-remission group ($p<0,001$) (Table I). Relationship was found between basal serum creatinine levels of the patients and remission ($r=p<0.001$).

While ANA was determined to be positive in 20 (100%) patients, anti-dsDNA was found to be positive in seven (35%) patients and negative in 13 (65%) patients. No relationship was found

between anti-dsDNA positivity and remission (p>0.05) (Table I).

Serum C3 and C4 were found at low levels in twelve (60,4%) patients. In those who were remission, C3 and C4 levels were lower, but this difference was not statistically significant (p>0.05) (Table I).

Eleven patients (55%) had proteinuria levels in the nephrotic range before treatment. No relationship was found between basal proteinuria levels of the patients and remission (p>0.05) (Table I).

According to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 classification of lupus nephritis, class 4 LN was most frequently (nine patients (45%) and class 3 LN second frequently (five patients) determined (Table II).

Table II. Classifications of LN patiens and remission rates

Class	Remission (n=11)	No-Remission (n=9)	Total (n=20)
1	1	0	1
2	3	0	3
3	1	4	5
4	4	5	9
5	2	0	2

Immunosuppressive therapy was given to patients for treatment. Immunosuppressive treatments given to patients and remission rates were shown in table III.

Conclusion

Clinical remission of renal dysfunction is predictive of improved long-term prognosis in patient and renal survival, even for patients with the most severe forms of lupus nephritis (7).

Serum creatinine levels of LN patients were determined 1.3 g/dl and over it was reported between 8% and 28.5% (8, 9). Arfaj et al. (10) reported that 65.9% of patients had creatinine clearance under 75 ml/min. Korbet et al. (7) found that serum creatinine levels in remission patients were significant lower than in no-remission patients. In our study, except for one patient (5%), creatinine levels of patients were lower than 1,0 mg/dl. Relationship was found between basal serum creatinine levels of the patients and remission (p<0,001) (Table 1). Before treatment, creatinine levels of remission group were lower than no-remission group (p<0.001). But this data might be not important because of creatinine levels of groups was normally.

It is known that LN is mostly seen in teenagers and women (2). Kobert et al. (7), Austin et al. (11) and Gunes et al. (12) found that age and sex did not affect disease remission. In our study, no relationship was found between gender or age and remission.

Kobert et al. (7) found that out of 86 LN patients 100% were ANA positive, while 96,5% were anti-dsDNA Ab positive. Gunes et al.(12) while ANA was determined to be positive in 41 (100%) patients, anti-dsDNA was found to be positive in 25 (60,9%) patients and negative in 16 (39,1%) patients. In our study while ANA was determined to be positive in 20 (100%) patients, anti-dsDNA was found to be positive in seven (35%) patients and negative in 13 (65%) patients. Similar to our study, Kobert et al. (7), Austin et al. (11) and Gunes et al. (12). Not found that relationship between anti-dsDNA and remission in LN patients.

C3 and C4 levels are one of the important indicators in diagnosing lupus nephritis. A decrease in complement levels was found in 60-84% of patients in some studies (13). Serum C3 and C4 levels were found to be low in 60% of our patients. These results show similarities with the data in the literature (8,9 and 13). Korbet et al.(7) and Austin et al. (11) found that C3 levels in unremitted patients were significant lower than in remitted patients. To the contrary, in our study, C3 levels of remission group were found to be lower than no-remission group. However, this difference was no significant (p>0,5).

Proteinuria rates in nephrotic level in LN were reported as 26-48,5% (8,9 and 13). Korbet et al. (7) and Gunes et al. (12) not found that relationship between basal proteinuria level and remission. In our study, nephrotic level urine protein was found in 55% of the patients. Additionally, no relationship was found between basal protein level and remission in our study.

There are a lot of studies comparing treatment regimens in literature. Nevertheless the treatment of LN is still a significant problem. Different centers continue to use different treatment protocols. In addition, adverse effects of the treatment may cause significant problems (e.g., infertility, neutropenia). All of these facts make treatment standardization difficult (6,14 and 15).

The immunosuppressive drugs MP, CyP and AZA were the most widely used agents. In the majority of randomized controlled trials, compared to CyP or AZA plus steroids versus steroids alone. In those studies, CyP plus steroids

Table III: Immunosuppressive treatments and remission rates

Treatment	Remission (n=11)	No Remission (n=9)	P
MP (n=3)	2	1	
MP+CyP (n=3)	0	3	
MP+AZA (n=7)	4	3	0,2
MP+CyP+AZA/MMF (n=4)	3	1	
MP+AZA+CyS (n=2)	2	0	
MP+CyS(n=1)	0	1	

MP: Methylprednisolone CyP: Cyclophosphamide CyS: Cyclosporine
AZA: Azathioprine MMF: Mycophenolate Mofetil

reduced the risk of doubling of serum creatinine compared to steroids alone but had no impact on mortality. The risk of ovarian failure was significantly increased. AZA plus steroids reduced the risk of all cause mortality compared to steroids alone, but did not alter renal outcomes. Neither therapy was associated with increased risk of major infection (6).

Other drug for treatment of LN is MMF. Hu et al. (16) gave MMF to 23 diffuse proliferative LN patients and conventional high dose CyP treatment to another 23 patients. After treating for 6 months, 50% decrease in proteinuria in MMF group was found significantly more than the CyP. Chan et al.(4) reported that for the treatment of diffuse proliferative lupus nephritis, the combination of MMF and MP is as effective as a regimen of CyP and MP followed by AZA and MP.

In our study, the most common treatment was given as a MP+AZA combination seven (35%) patients. With this combination, complete remission was achieved in four LN patients while three LN patients had no remission. Second common treatment was given as a MP+CyP+AZA/MMF combination four (16%) patients who were class 3 and 4. With this combination, complete remission was achieved in three LN patients while one LN patients had no remission. Cyclosporine (CyS) not use in lupus nephritis. But to our one patients that previously had been diagnosed with glomerulonephritis was given CyS.

As a result, complete remission was achieved in 11 (55%) LN patients while nine (%45) LN patients had no remission. Relationship was found between basal creatinine and patient remission. No relationship was found between other basal clinical and laboratory parameters and patient remission. The results of our treatments were similar to those in the literature. However, remission is still a problem in LN.

Lupus Nefritli Hastaların Analizi: Tek Merkez Deneyimi

Özet

Amaç: Lupus nefriti sistemik lupus eritematozisin major mortalite ve morbidite nedenidir. Lupus nefritinin tedavisi önemli bir problem olmaya devam etmektedir. Bu çalışmada, merkezimizde takip ettiğimiz lupus nefriti hastalarının remisyon oranlarını, remisyona etki eden faktörleri ve tedavi sonuçlarını araştırdık.

Gereç ve yöntem: Lupus nefritli 20 hastanın klinik, laboratuar ve tedavi sonuçları retrospektif olarak değerlendirildi. Hastalar, proteinürisi 0,3 g/gün altında olanlar remisyon grubu, 0,3 g/gün'ün üstünde olanlar ise remisyonda olmayan grup olarak ayrıldı. Hastaların klinik, laboratuar ve demografik özellikleri ile hastalığın remisyonu arasındaki ilişki araştırıldı.

Bulgular: Onbir (%55) hastada tam remisyon saptanırken, 9 (%45) hastada ise remisyon saptanmadı. Bazal kreatinin ile remisyon arasında anlamlı ilişki vardı (p<0,05). Diğer klinik ve laboratuar parametreleri ile remisyon arasında anlamlı bir ilişki saptanmadı (p>0,05).

Sonuç: Çalışmamızda bazal kreatinin ile remisyon arasında anlamlı bir ilişki saptandı. Sonuçlarımız literatürdeki çalışmalarla benzerlik göstermekteydi. Yeni çalışmalar ve ilaçlara rağmen lupus nefritinin tedavisi önemli bir problem olmaya devam etmektedir.

Anahtar kelimeler: Lupus nefriti, remisyon, tedavi sonuçları

References

1. Smith PP, Gordon C. Systemic lupus erythematosus: clinical presentations. Autoimmun Rev 2010; 10:43-45.
2. Appel GB, Radhakrishnan J, D'Agati V. Secondary glomerular disease. In Brenner BM (eds). Brenner & Rector's The Kidney. Philadelphia: Saunders 2008; 1067-1146.
3. Cameron JS. Systemic lupus erythematosus. In: Neilson EG, Couser WG (eds) Immunologic renal diseases, 2nd edn. Lippincott-Raven, Philadelphia 2001; 1057-1104.
4. Chan TM, Li FK, Tang CS, Wong RW, Fang GX, Ji YL, et al. Efficacy of mycophenolate mofetil in patients with diffuse proliferative lupus nephritis. Hong Kong-Guangzhou Nephrology Study Group. N Engl J Med 2000; 343:1156-1162.
5. Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, Appel GB, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. Kidney Int 2004; 65:521-530.
6. Flanc RS, Roberts MA, Strippoli GF, Chadban SJ, Kerr PG, Atkins RC. Treatment for lupus nephritis. Cochrane Database Syst Rev 2004; (1):CD002922.
7. Korbet SM, Lewis EJ, Schwartz MM, Reichlin M, Evans J, Rohde RD. Factors predictive of outcome in severe lupus nephritis. Lupus Nephritis Collaborative Study Group. Am J Kidney Dis 2000; 35:904-914.
8. Uthman IW, Muff arij AA, Mudawar WA, Nasr FW, Masri AFM. Occasional series: Lupus around the world. Lupus nephritis in Lebenon. Lupus 2001; 10:378-381.
9. Shayakul C, Org-aj-yooth L, Chirawang P. Lupus nephritis in Thailand: Clinicopathologic findings on outcome in 569 patients. Am J Kidney Dis 1995; 26:300-307.
10. Al Arfaj AS, Khalil N, Al Saleh S. Lupus nephritis among 624 cases of systemic lupus erythematosus in Riyadh. Saudi Arabia Rheumatol Int 2009; 29:1057-1067.
11. Austın HA, Boumpas DT, Vaughan EM, Balow JE. Predicting renal outcomes in severe lupus nephritis: Contributions of clinical and histologic data. Kidney Int 1994; 45:544-550.
12. Gunes C, Keles M, Uyanik A, Cetinkaya R, Sari RA. *Treatment Results of Patients With Lupus Nephritis: A Single* Center's Experience. EAJM 2010; 42:132-136.
13. Rabbani MA, Tahir MH, Siddiqui BK, Ahmad B, Shamim A, Shah SM, et al. Renal involvement in systemic lupus erthematosus in Pakistan. J Pak Med Assoc 2005; 55:328-332.
14. Ehrenstein MR, Isenberg DA. Systemic Lupus Erythematosus in adults, clinical features and etiopathogenesis. In Isenberg DA, Woo P, Glass D (eds). Oxford Textbook of Rheumatology. Oxford:Oxford University Pres 2005; 819-842.
15. Sayarlıoğlu H, Sayarlıoğlu M, Doğan E. SLE nefriti ve gucel tedaviler. Türk Nefroloji Diyaliz ve Transplantasyon Dergisi 2007; 16:159-168.
16. Hu W, Liu Z, Chen H, Tang Z, Wang Q, Shen K, et al. Mycophenolate mofetil vs cyclophosphamide therapy for patients with diff use proliferative lupus nephritis. Chin Med J 2002; 115:705-709.