Saudi J Kidney Dis Transpl 2009;20(3):424-428

Saudi Journal of Kidney Diseases and Transplantation

Original Article

Prognosis and Predictors of Convulsion among Pediatric Lupus Nephritis Patients

Fatemeh Beiraghdar[1], Abbas Maddani[2], Saeed Taheri[1,3], Mir Mohsen Sharifi-Bonab[4], Taher Esfahani[2], Yunes Panahi[1,5], Behzad Einollahi[1]

[1]Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, [2]Nephrology Unit of Medical Pediatric Center of Tehran Medical University, Tehran, [3]Dr Taheri Medical Research Group, Tehran, [4]Neurology Department, Tabriz University of Medical Sciences, Tabriz, [5]Research Center for Chemical Injuries, Tehran, Iran

ABSTRACT. In this study, we aimed to analyze features and outcome of convulsion in pediatric lupus nephritis patients. We retrospectively reviewed data of 14 Iranian children with lupus nephritis who developed seizures and compared them with a group of the same number of well matched pediatric lupus nephritis patients. Higher serum creatinine levels and higher frequencies of anemia and lymphopenia were observed in the convulsion group. Multivariable logistic regression analysis revealed that the only risk factor for development of convulsion in pediatric lupus patients with nephritis was lymphopenia. Survival analysis showed that convulsion had no impact on patient and renal function outcomes in our pediatric lupus nephritis subjects. In conclusion, we found that lymphopenia is a predictive factor for convulsion occurrence in our patients and special attention to neurological status assessment may be needed in this situation.

Keywords: Pediatric, Childhood, SLE, Lupus nephritis, Convulsion, Neurological manifestations

Introduction

Systemic lupus erythematosus (SLE) is a multiorgan disorder of autoimmune origin with significant morbidity and mortality.[1,2] Approximately 25% of all cases of SLE occur in the first two decades of life.[3] Childhood onset SLE has variable clinical manifestations and an unpredictable natural history and frequently have more severe disease at presentation and worse outcomes.[4-6]

Even with current improved survival of lupus patients, complications from disease process or from its concomitant therapy currently contribute to the major causes of morbidity and mortality in these patients.[7] Poor prognosis is associated with diffuse proliferative (WHO class IV) nephritis and persistent central nervous system disease.[8] In this study, we retrospectively analyzed our data to find potential factors which can

Correspondence to:

Dr. Yunes Panahi
Research Center for Chemical Injuries
Baqiyatallah Hospital
Mollasadra St.
Tehran, Iran
E-mail: Yunes.panahi.phd@gmail.com

Table 1. Differences in characteristics of patients in case and control groups

Variables		Seizure in childhood lupus nephritis		
		Case	Control	*P*
Gender (male)		21 %	13 %	NS.
Disease class				NS.
	II	0 %	6.7 %	
	III	7.1 %	13.3 %	
	IV	85.7 %	73.3 %	
	V	7.1%	6.7 %	
Rash		43 %	47 %	NS.
Oral ulcer		21 %	20 %	NS.
Arthritis		71 %	67 %	NS.
Hematuria		100 %	87 %	NS.
Nephrotic Syndrome		71 %	80 %	NS.
Anemia		93 %	53 %	0.035
Lymphopenia		86 %	33 %	0.008
Hypertension		71 %	60 %	NS.
Renal failure		21 %	13 %	NS.
Death		7 %	20 %	NS.
Age		11.1 ± 2.2	11.2 ± 1.7	NS.
Creatinine at diagnosis		1.5 ± 0.9	1.1 ± 0.6	0.04
Activity index		8.0 ± 3.1	7.8 ± 4.2	NS.
Chronicity index		3.3 ± 2.8	3.0 ± 2.0	NS.
Follow up period (years)		3.3 ± 1.7	3.0 ± 2.0	NS.

predict occurrence of seizures in the management process of pediatric patients with lupus nephritis.

Materials and methods

Demographic

In this single center report, we retrospectively reviewed data of 14 Iranian children with lupus nephritis who developed seizures during their follow up at Pediatric Nephrology Department of Tehran University of Medical Sciences during the period from 1985 to 2005. The diagnosis of systemic lupus erythematosus met the criteria adopted by the American Rheumatism Association (ARA).[9] To characterize disease activity, we used the criteria of SLEDAI (Systemic Lupus Erythematosus Disease Activity Index).[10]

Unfortunately, because of the retrospective nature of the study, we were unable to retrieve data about the features and severity of seizures in these patients. In all cases, however seizures were not life threatening or associated with permanent complications.

We extracted the following data from our data registry: age, gender, creatinine at diagnosis, pathological class of nephritis, CH50 complement percentages, activity index, chronicity index, having malar rash, having oral ulcers, musculoskeletal involvement, pericarditis, hematuria, nephrotic syndrome, anemia, lymphopenia, hypertension, treatment modalities, end stage renal disease requiring renal replacement therapy and death.

Treatment strategies

In our institution, the initial therapy was orally administered corticosteroids (CS) prescribed at a dose of 2 mg/kg per day to all patients, with a daily maximum of 60 mg/day; the decision to add an immunosuppressant depended on the individual patient's clinical condition. Additional therapy with immunosuppressants including intravenous cyclophosphamide (CP), azathioprine (AZA) and mycophenolate mofetil (MMF) was also included in the induction regimen in patients with worse clinical course. Hydroxychloroquine was used regarding skin manifestations and complications.

Maintenance treatment varied for individual pa-

Table 2. Logistic regression for evaluating independent impact of risk factors

Variables		Sig.	Odds Ratio (OR)	95% C.I. for OR
Anemia		0.907	1.231	0.037- 40.494
Creatinine level at entrance		0.711	0.769	0.191- 3.093
Lymphopenia		0.045	0.030	0.001 -.930
Sex (male)		0.254	0.160	0.007- 3.730
Age		0.283	1.514	0.710- 3.229
Class	Class (II)	0.333	1	-
	Class (III)	1	5382526030	0
	Class (IV)	0.476	17.729	0.007 - 48043.746
	Class (V)	0.890	0.593	0.000- 988.469
Follow up duration		0.530	0.832	0.470 - 1.475

tients and was adjusted according to the clinical course of each patient. AZA was used for patients presenting before 2001 and MMF after 2001.

Statistical analysis

Software SPSS v. 13.0 (SPSS corp. IL, USA) was used for all data analyses. Paired t test and non parametric χ^2 and Mann-Whitney U tests were used where appropriate. Multivariate logistic regression was used for analyzing independent effects of individual variables on occurrence of convulsion. Kaplan Meier method was used for survival analysis. $P< 0.05$ was considered significant.

Results

Of overall 60 pediatric lupus nephritis patients diagnosed and followed at our clinic, 14 (23%) were found to have convulsions during their follow up period. Of these, 11 (79%) were female and 3 (21%) were male. Mean age was 11.1 ± 2.2 years. 12 (86%) patients had class IV; 1 (7%) had class III and another patient had class V lupus nephritis on renal biopsy. All patients had histories for hematuria and proteinuria. 6 (43%) had malar rash, 3 (21%) had oral ulcer, 10 (71%) arthritis, 7 (50%) pericarditis, 10 (71%) nephrotic syndrome, 13 (93%) anemia, 12 (86%) lymphopenia, and 10 (71%) hypertension. Mean time period from initiation of disease symptoms to documentation of nephritis was 2.6 (1-9) months.

Table 1 shows differences in patients with and without convulsion. Anemia, lymphopenia and higher mean initial serum creatinine level was significantly more frequently observed in patients presenting with seizures.

Independent impact of potential risk factors for development of seizures in our study subjects was evaluated by multivariable logistic regression analysis revealing lymphopenia as the only risk factor (table 2).

Most patients received a combination therapy

Figure 1. Patients survival in convulsive and non-convulsive pediatric lupus nephritis patients

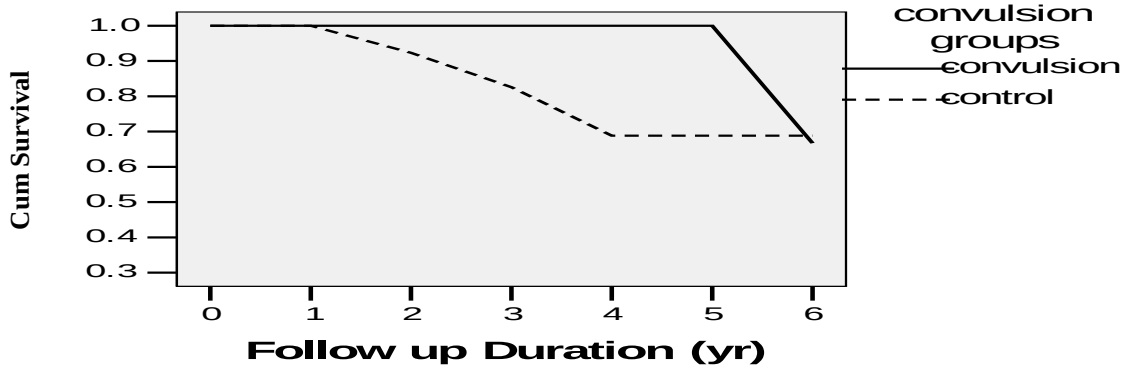
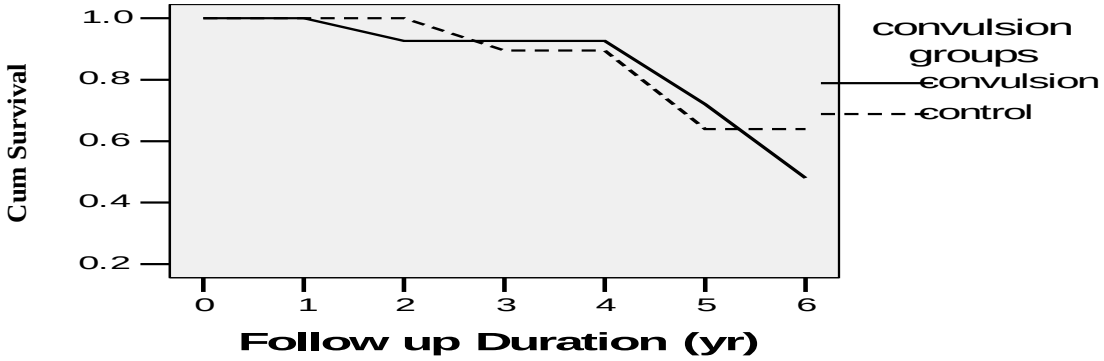


Figure 2. Renal function survival in pediatric lupus nephritis patients with and without convulsion



with cyclosporine and or cyclophosphamide. Because of limited sample size and variant types of treatments, meaningful analysis was not possible in our cases and controls. One patient among cases and three from the controls died, survival analysis was not different among the two groups (figures 1 and 2).

Discussion

Neurological involvement in SLE has been recognized since Olser's description of the disease.[11] Similar to the earlier reports 23% of our patients had nervous system involvement.[12] In this study, we observed that pediatric lupus nephritis patients with evidence of CNS involvement had no different renal and patient outcomes. This finding is in contrast to the previous studies which proposed neurological manifestation as a poor prognostic factor for patients with SLE.[13,14] It was also reported that neurological disease has a tendency to develop with more severe renal disease.[13] All of our patients had lupus nephritis and this association therefore cannot be evaluated in our study.

Because of the small sample size it was not possible to have any meaningful analysis of the treatment regimens, nevertheless most of the patients had received cyclophosphamide and or cyclosporine. Although in Bivariate analysis, higher creatinine levels at entrance, having anemia and lymphopenia were detected as potential risk factors for convulsion, multivariate logistic analysis after adjustment for other potential risk factors revealed lymphopenia as the only risk factor for development of convulsion in pediatric lupus nephritis patients (table 2). This finding is in agreement with previous reports demonstrating lymphopenia as a predictive factor for occurrence of convulsion in SLE patients.[13]

In conclusion, our study, similar to previous reports lymphopenia was the only predictive factor for convulsion in pediatric lupus nephritis patients. Future studies with larger sample size seem necessary for confirming our findings.

References

1. Klein-Gitelman M, Reiff A, Silverman ED. Systemic lupus erythematosus in childhood. Rheum Dis Clin North Am 2002;28(3):561-77, vi-vii. Review.
2. Ardoin SP, Schanberg LE. The management of pediatric systemic lupus erythematosus. Nat Clin Pract Rheumatol 2005;1:82-92.
3. King KK, Kornreich HK, Bernstein BH, et al. The clinical spectrum of systemic lupus erythematosus in childhood. Arthritis Rheum 1977;20 (2 Suppl):287-94.
4. Meislin AG, Rothfield N. Systemic lupus erythematosus in childhood. Analysis of 42 cases, with comparative data on 200 adult cases followed concurrently. Pediatrics 1968;42:37-49.
5. Tucker LB, Menon S, Schaller JG, et al. Adult- and childhood-onset systemic lupus erythematosus: a comparison of onset, clinical features, serology, and outcome. Br J Rheumatol 1995; 34:866-72.

6. Font J, Cervera R, Espinosa G, et al. Systemic lupus erythematosus (SLE) in childhood: analysis of clinical and immunological findings in 34 patients and comparison with SLE characteristics in adults. Ann Rheum Dis 1998; 57:456-9.
7. Bongu A, Chang E, Ramsey Goldman R. Can morbidity and mortality of SLE be improved? Best Pract Res Clin Rheumatol 2002;16:313-32.
8. Supavekin S, Chatchomchuan W, Pattaragarn A, et al. Pediatric systemic lupus erythematosus in Siriraj Hospital. J Med Assoc Thai 2005;88 Suppl 8:S115-23.
9. Tan EM, Cohen AS, Fries JF, *et al*. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25: 1271-7.
10. Liang MH, Socher SA, Larson MG, et al. Reliability and validity of six systems for the clinical assessment of disease activity in SLE. Arthritis Rheum 1989;32:1107-18.
11. Osler W. Classics: On the visceral complications of erythema exudativum multi-forme. Am J Med Sci 1976;271(1):106-17.
12. Benseler SM, Silverman ED. Neuropsychiatric involvement in pediatric systemic lupus erythematosus. Lupus 2007;16(8):564-71.
13. Gibson T, Myers AR. Nervous system involvement in systemic lupus erythematosus. Ann Rheum Dis 1975;35(5):398-406.
14. Estes D, Christian CL. The natural history of systemic lupus erythematosus by prospective analysis. Medicine (Baltimore) 1971;50(2):85-95.