Systemic Lupus Erythematosus in Thai Children: Clinicopathologic Findings and Outcome in 82 Patients

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Objectives: *To define the patterns of clinicopathologic findings and to identify the risk factors for renal failure and mortality of childhood-onset systemic lupus erythematosus (SLE) in Thailand.*

Material and Method: *The study is a retrospective analysis of clinical manifestations, laboratory data, and pathologic findings, treatment modalities, and outcome of 82 patients with biopsy-proven lupus nephritis (LN) with disease onset between 1 January 1987 and 31 December 1997. All children developed these first manifestations at the age 13 years or under.*

Results: *Sixty-four (78%) patients were females and eighteen (22%) were males (ratio female/male = 3.5:1). The patients were followed for a mean period of 53.6 months (range 1 -141). The mean age at disease onset was 9.2 years (range 2-12.6). Class-IV LN, observed in 40 (48.8%) patients, was the most frequent histopathology on initial renal biopsy. Less frequent findings were class-II (30.5%), V (14.6%), I (3.7%) and III (2.4%) LN. Based on the renal histopathology and clinical presentations, patients were treated with corticosteroids alone or in combination with azathioprine or with intravenous cyclophosphamide (CYC). Methylprednisolone pulses were given in patients with clinically more severe disease. Follow-up biopsies, performed in 12 patients, showed no change in 4 patients, and were progressive in 8 patients. On final clinical evaluation, 20 patients died, 65% died from serious infections, 15% from cardiopulmonary complications, and 10% from end stage renal disease. As the whole group, survival rates were 89% and 74% at 12 and 60 months, respectively. The 5-year patient survival in class-II, class-IV and class-V LN patients were 83%, 67% and 64%, respectively. Within the group of class-IV LN, the 5-year survival in the patients treated with intravenous CYC was significantly better than those receiving prednisolone with or without azathioprine. Five-year kidney survival rates from the time of diagnosis to the endpoints of terminal renal failure were 94% for the whole group, and 100%, 96%, 91% in the class-V, class-II, and class-IV group, respectively. Initial presence of hypertension, hematuria, renal insufficiency were independent factors significantly associated with lower patient survival probabilities. There was no association of either patient and kidney survival with gender, age, cytopenia, and autoantibody level.*

Conclusions: *Infectious complications were the most common cause of morbidity and mortality in our pediatric patients with SLE. The immunosuppressive agents used to treat SLE seemed to be a major contribution to the patient survival. With judicious use of corticosteroid, intravenous CYC in severe SLE showed superior efficacy over oral prednisolone with or without azathioprine.*

Keywords: *Lupus nephritis, Hypertension, Infection, Survival, Cyclophosphamide, Methylprednisolone, Azathioprine*

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Over the last three decades, the addition of cytotoxic agents to corticosteroid has improved both the short- and long-term prognosis in children with

systemic lupus erythematosus (SLE)[1]. It has been realized that diffuse proliferative (WHO class-IV) nephritis and persistent central nervous system disease in SLE have poorest prognosis. However, the improvement of survival is attributed to both early diagnosis of patients with mild disease and improved management of severe disease. With the increasing life expectancy 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[2]. These complications, particularly infections, vascular complications, osteonecrosis, or thrombosis, are often linked with flares of the disease. Death from lupus crisis is rare today. Sepsis has replaced renal failure as the most common cause of death[3].

In our current study, we retrospectively evaluated the clinical and histopathological features, clinical course, and outcome of SLE in 82 children followed at our hospital, one of the major tertiary children's referral centers in our country over four and a half years. Our aim was mainly to identify the risk factors predicting end stage renal disease (ESRD) and mortality in our pediatric patients.

Material and Method

Retrospectively, 82 children with SLE under the age of 13 years at the time of diagnosis of SLE and with disease onset between 1 January 1987 and 31 December 1997 were included in the study. The medical records in Siriraj Hospital, including the various presentations, laboratory data at the time of biopsy and the clinical course of the patients, were reviewed. Information was obtained from patient reports and our separately-stored database. All patients fulfilled the 1982 revised criteria for the classification of SLE of the American College of Rheumatology (ACR)[4]. Patients with drug-induced lupus or with mixed connective tissue disease were excluded. Disease onset was defined as the time of diagnosis of SLE according to ACR criteria and/or renal biopsy result consistent with lupus nephritis (LN). Clinical definitions used in our study were: hematuria, > 5 red blood cells/high power field, significant proteinuria (1+ on dipstick if urine specific gravity (sp.gr) <1.015 or 2+ if sp.gr $\geq$1.015), elevated serum creatinine (Cr) level >1 mg/dL in adolescent or >0.7 mg/dL in child, hypertension with diastolic and/or systolic blood pressure >95th centile by percentile of height. Timed-urine collection for Cr clearance and urinary protein excretion was undertaken in selected cases. Urinary protein excretion greater than 40 mg/m^2/hr indicated nephrotic-ranged proteinuria. A renal biopsy was performed in all patients regardless of an active urinary sediment, proteinuria or raised serum Cr levels. Percutaneous renal biopsies under ultrasound guidance were obtained under supervision of attending nephrologists. The specimens were processed for light, immunofluorescent and electron microscopy. The renal lesions were classified according to World Health Organization (WHO) classification of LN[5]. Repeated renal biopsies, if available, were also evaluated and recorded.

Treatment was determined by disease activity and renal pathology. In patients with class-I LN, treatment was given for extrarenal manifestations of SLE. Patients with class-II and class-III LN, who had normal renal function without nephrotic-ranged proteinuria, were treated with protocol A, i.e., oral prednisolone at an initial dose of 1-2 mg/kg/day (maximum 60 mg/day) that was gradually tapered to low doses. Those with nephrotic-ranged proteinuria or with elevated serum Cr level received protocol B, i.e., azathioprine at a dose of 2-3 mg/kg/day added to prednisolone 2 mg/kg/day. Patients with class IV LN were mostly treated with protocol C, i.e., cyclophosphamide (CYC) plus oral prednisone (2 mg/kg/day, maximum 60 mg/day) over 1-2 months, which was then gradually tapered to low doses. CYC was given monthly for 6 months as a single intravenous bolus at a maximum dose of 1 g/m^2 then every 3 months for a total period of 36 months. Patients with clinically severe disease were treated with high-dose intravenous (i.v.) methylprednisolone (MP) pulses (30 mg/kg, maximum 1 g, on alternate days, 3 doses). Oral prednisone was maintained at low doses. Patients with class-V LN received prednisone and azathioprine. The treatment strategy for individual patients varied over the course of treatment. Drug doses were adjusted according to clinical response or to maintain the C3 complement and anti-DNA antibody titer levels to near normal range as much as possible. Other therapy such as hydroxychloroquine and/or antihypertensive drugs were used depending on extrarenal manifestations of SLE or complications.

Duration of follow-ups were calculated from the date of diagnosis of SLE to the last date seen, or was known to have developed ESRD. The renal outcome was classified as remission and non-remission. Remission of LN was defined as the return of urinalysis and serum Cr level to normal limits. Non-remission was classified and defined as follow: 1) persistent proteinuria, significant proteinuria longer than 3 months; 2) chronic renal insufficiency (CRI), persistent eleva-

tion of serum Cr level longer than 3 months; 3) ESRD, the degree of renal failure that required dialysis or renal transplantation. The patient survival time was defined as the time interval between diagnosis of SLE and death. The cause of death was ascertained by a review of hospital files and/or postmortem findings. The primary cause of death was categorized as renal, infection, cardiopulmonary, and other miscellaneous causes. The primary cause of death was defined as the main clinical or pathological process directly responsible for death. Renal survival was defined as the probability of maintaining adequate renal function and not requiring dialysis or renal transplantation.

Student s t-test or paired t-test was used to compare the differences of mean levels between the independent or dependent variables, respectively. The differences between the two groups were compared using the χ^2 test. The renal survival rate was estimated using the Kaplan-Meier method. The renal survival differences were compared by the log-rank test. The prognostic factors or risk factors were analyzed by multivariate logistic regression. A p value less than 0.05 was considered significant.

Results

Eighty-two patients, 64 females and 18 males (female to male ratio 3.5:1), were registered over the study period. Table 1 presents the details of epidemiologic data. Class-IV LN was observed in 49% of our patients. Less frequent findings were class-II (30.5%), class-V (14.6%), class-I (3.7%) and class-III (2.4%). The mean age ($\pm$ SD) at the time of diagnosis of SLE was 9.3 ± 2.2 years (median 10 years, range 2.0-12.6 years). There was no significant correlation between histopathological changes and gender or age. The time from diagnosis of SLE to diagnosis of LN averaged 5.1 months (range … month to 3 years). In 86% of patients it was less than 1 year, and in the remaining 14%, more than 1 year. The mean follow-up was 4.2 ± 2.9 years, ranging from 1.3 month to 11.7 years (median 3.7 years) with 34% of patients followed for more than 5 years.

Table 2 shows clinical and laboratory data obtained at the time of initial biopsy and the histopathological findings. Proteinuria was observed in 60 patients (73%). In 46 of the selected 59 patients with class-II, class-IV and class-V LN, it was in the nephrotic range. Fifty-one patients (62%) had hematuria. About a half of the patients had impaired renal function and 44% had high blood pressure. When compared with class-I, class-II, and class-III altogether, both hematuria and proteinuria were significantly associated with class-IV and class-V LN. Hypertension was the only significant factor associated with patients with class-IV LN, compared with patients with class-I, class-II, and class-III LN (p=0.001).

Based on the results of renal histology, and on disease activity, patients were treated with different regimens (Table 3). Patients with class-I LN received prednisolone. Class-II LN patients were treated with prednisolone and azathioprine added for nephrotic-range proteinuria or for impaired renal function. Five of class-II and 4 of class-V patients were started i.v. CYC because of nephrotic nephritis features and biopsy results demonstrated some electron dense deposits at

Table 1. Epidemiologic data in children with lupus nephritis

	Class I	Class II	Class III	Class IV	Class V	Total
Number	3	25	2	40	12	82
Age at onset*(yr) (range in yr)	9.7 ± 2.6 (6.8-12.6)	9.2 ± 2.5 (2.0-12.6)	11.0 (11.0)	9.2 ± 2.1 (4.5-12.0)	9.7 ± 2.1 (4.7-12.0)	9.3 ± 2.2 (2.0-12.6)
Female: Male	3 : 0	4 : 1	0 : 2	3.4 : 1	5 : 1	3.5 : 1
Duration prior to renal biopsy*(mo)	0.6 ± 1.1	5.0 ± 9.3	2.5 ± 3.5	6.3 ± 9.5	3.3 ± 7.0	5.1 ± 8.8
Follow-up*(mo) (range in mo)	49.3 ± 9.8 (38-56)	62.6 ± 30.3 (18-134)	27.5 ± 2.1 (26-29)	49.2 ± 36.9 (1-141)	34.9 ± 35.2 (3-116)	50.7 ± 34.6 (1-141)

* Values expressed as mean $\pm$ standard deviation

Table 2. The clinical and laboratory data obtained at the time of initial renal biopsy

	Class I(n)	**Class II**(n)	**Class III**(n)	**Class IV**(n)	**Class V**(n)
Hypertension	- (n = 3)	8% (n = 25)	- (n = 2)	45%* (n = 40)	41.7% (n = 12)
Hematuria	- (n = 3)	28% (n = 25)	100% (n = 2)	92.5%* (n = 40)	75% (n = 12)
Proteinuria	- (n=3)	32% (n=25)	50% (n=2)	97.5%* (n=40)	100% (n=12)
24hr Urine Protein	NA		NA		
<4 mg/m2/hr		16%		-	-
4-40 mg/m2/hr		42%		16%	-
≥40 mg/m2/hr		42% (n = 12)		84% (n = 36)	100% (n = 11)
Elevated serum Cr	- (n = 2)	42.9% (n = 21)	- (n = 1)	62.5% (n = 40)	30% (n = 10)
Cr clearance	NA		NA		
≥90 ml/min 1.73m²		18.2%		20.7%	11.1%
15-89ml/min 1.73m²		72.7%		65.5%	88.9%
< 15 ml/min 1.73m²		9.1% (n = 11)		13.8% (n = 29)	- (n = 9)

* WHO class (I+II+III) vs. WHO class IV, p<0.01; WHO class (I+II+III) vs. WHO class V, p<0.01; n, total number of the patients; NA, not available

Table 3. Therapeutic regimens used in relation to initial histopathology

	Class I **(n=3)**	**Class II** **(n=25)**	**Class III** **(n=2)**	**Class IV** **(n=40)**	**Class V** **(n=12)**
Protocol A*	3	9	-	2	2
(plus MP§)	(-)	(1)		(2)	(-)
Protocol B	-	11	2	7	6
(plus MP§)		(1)	(-)	(-)	(-)
Protocol C	-	5	-	31	4
(plus MP§)		(-)		(4)	(1)

*Oral prednisolone 1-2 mg/kg/day initially;
oral prednisolone 2 mg/kg/day initially plus azathioprine 2-3 mg/kg/day;
oral prednisone initially 2 mg/kg/day plus iv cyclophosphamide;
§ high-dose iv methylprednisolone pulses

subendothelium, besides mesangium on electron microscopy. Nine patients with class-IV LN were given prednisolone with or without azathioprine because CYC was not available until mid 1990. Six of the patients died of serious infections. One had persistent proteinuria and there was remission in the other two patients with one developed LN flare at 2 years after the diagnosis. Of 31 class-IV LN patients receiving i.v. CYC, 2 patients (6.5%) developed ESRD at 3.3 and 3.5 years after the diagnosis. Nine of 82 patients received MP pulses for severe SLE-related complications such as cerebral vasculitis, severe cutaneous vasculitis, myocarditis, or rapidly progressive renal dysfunction.

During the therapy with corticosteroid, cataract was detected in 30 (37%) patients, glaucoma in 23 (19%), osteoporosis in 2 (2.5%), subcutaneous fat necrosis in 2 (2.5%) and glucose intolerance in 3 (3.7%). Twenty-nine patients had short stature at the last date of follow-ups. Cataract and glaucoma were mostly reversible after treatment and the dose reduction of prednisolone. Common side effects of i.v. CYC therapy were nausea and vomiting mostly within the first 24 h of administration. Common sites of infection were urinary tract, skin and respiratory tract with less frequent sites being bone and central nervous system.

During the study, 12 children had repeated biopsy because of flare-ups of nephritis or progressive deterioration in renal function. The final clinical-pathological evaluation is summarized in Table 4. A worsening of histopathology was found in 8 patients with no changes in classification in 4. Five of 8 patients with worsened biopsy grades received i.v. CYC. Two patients were in remission and 3 still had proteinuria after the change of treatment regimens. One received oral prednisolone combined with azathioprine. The other two died of severe vasculitis and pulmonary hemorrhage in one and from cerebral vasculitis in the other. In the 3 class-IV LN patients with unchanged biopsy grades, i.v. CYC was restarted in 2 patients who lately entered remission. The other developed ESRD even during the first course of i.v. CYC.

The final clinical evaluation in relation to the histopathology of the initial biopsy is shown in Table 5. Renal disease was in remission in 41 patients (50%).

Table 4. The results of repeat biopsies relating to initial histopathology

Class of LN in initial biopsy (n*)	Repeat biopsy		Final classification	
	Patient Number	Time from initial biopsy (year)	II	IV
I (n=3)	1	3.5		1
II (n=25)	5	2.3;3;3;3;6.2	1	4
IV (n=40)	3	3.3;4,6		3
V (n=12)	3	2.5;2.5;6.5		3

Table 5. Outcome relating to histopathology on initial biopsy

	Class I (n=3)	Class II (n=25)	Class II (n=2)	Class IV (n=40)	Class V (n=12)	Total (n=82)
Remission (%)	2 (67)	18 (72)	2 (100)	17 (43)	2 (17)	41 (50)
Non-remission (%)	1 (33)	7 (28)	-	23 (57)	10 (83)	41 (50)
- Proteinuria	1	7	-	17	9	34
- CRI	-	2	-	1	1	4
- ESRD	-	2	-	2	-	4
Death (%)	-	4 (16)	-	11 (27)	5 (42)	20 (24)

Seven patients with class-II nephritis, 17 with class-IV, and 9 with class-V had persistent proteinuria. Of 4 class-II LN patients with impaired renal function, 2 patients developed ESRD following the transformation to class-IV LN in one and severe renovascular complications in the other. Severe infections were the most common cause of death, accounting for thirteen of twenty deaths (65%). Eight patients died of sepsis and five had adult respiratory distress syndrome secondary to severe pneumonia. The organisms causing sepsis in the patients were *staphylococcus aureus*, *Streptococcus pneumoniae*, *streptococcal* group D, *Escherichia coli*, *Serratia marcescens* and *Candida albican*. *Aspergillosis* and *Pseudomonas aeruginosa* were found in one patient expired from pneumonia. Seven patients died within the first year of management. Three patients were on azathioprine and prednisolone, and four received i.v. CYC. The other six died after the first year. One of the patients developed Steven-Johnson syndrome complicated with staphylococcal septicemia. Four developed SLE flares while receiving immunosuppressive drugs; two were taking azathioprine and prednisolone, and the others received CYC every three months and daily prednisolone. All received pulse MP for SLE flares prior to death because of infection. Three (15%) of 20 patients died of cardiopulmonary complications. One patient with LN class-IV and one with class-V died of a pulmonary hemorrhage. The other with LN class-II died of cardiac failure secondary to myocarditis. Two (10%) patients died owing to SLE related ESRD. Socioeconomic status of their families was attributed to the patients and their parents' decision to stop the renal replacement therapy.

Five-year kidney survival rates from the time of diagnosis to ESRD were 94% (95% confidence interval (CI) 128.2%-141.5%) for the whole group, 91% for the subgroup of class-IV patients, 96% for class-II, and 100% for class-V. The patient survival rates as a whole were 89% and 74% at 1 and 5 years (95% CI 91.9%-118.6%), respectively. The 5-year patient survival rates in 40 class-IV LN patients were 67%. The patients with class-V LN had poor patient survival, compared to class-II LN (64% vs 83% at 5 years, p=0.006). The initial presence of hypertension (log rank=4.33, P=0.037), hematuria (log rank=4.10, P=0.043), impaired renal function (log rank=4.21, P=0.040) were also the parameters significantly associated with poor patient survival. Gender, the presence of any clinical manifestations, cytopenia, autoantibody levels including of antinuclear antibody, anti dsDNA, and C_3 at the time of biopsy were not significantly associated with adverse outcomes. As the whole group, there were no significant differences in outcomes between the treatment groups. Within the group of WHO class-IV LN,

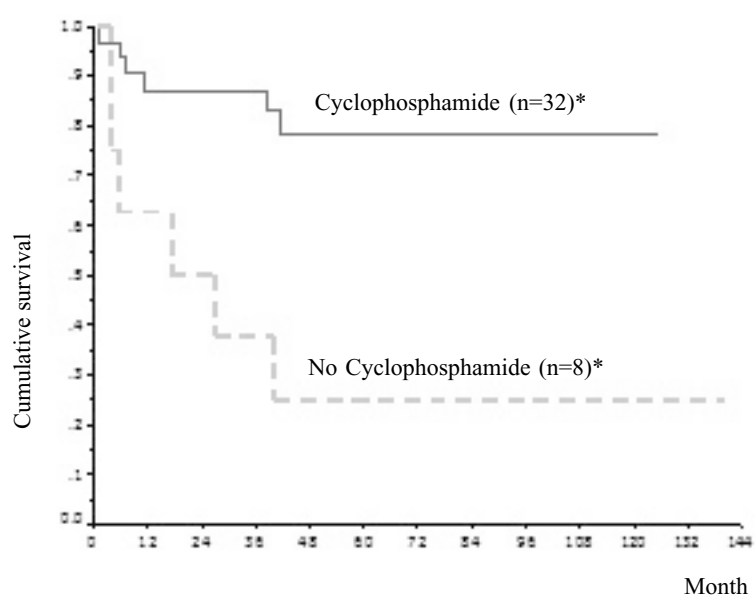

Fig. 1 Probability of survival in patients with class IV Lupus nephritis according to initial treatment regimen with vs without i.v. cyclophosphamide. *p=0.009.

the 5-year survival in the group treated with i.v. CYC (79%) was significantly better than that of patients receiving prednisolone with or without azathioprine (25%) despite comparable clinical and biochemical findings (Figure 1, log rank=11.01, P=0.009).

Discussion

In children, SLE usually occurs in adolescence. It is uncommon before the age of 10 years and very rare before 5 years[6]. However, a recent French multicenter study of 155 patients who had the onset of SLE before 16 years of age indicated that SLE developed in 15% before the age of 8 years[7]. Compared with our patients, 24% had the onset before the age of 8 years and 6% before the age of 5 years. All of our patients in the youngest group presented with the symptoms of nephrotic syndrome and/or acute nephritis but without cutaneous or musculoskeletal manifestations commonly found in SLE. As previously described, clinically overt nephropathy is more often a presenting clinical manifestation of SLE in children than in adults[1, 8]. In childhood SLE, girls are affected about five times more frequently than boys. Children usually have a more severe disease at onset. They also have higher rates of organ involvement, and a more aggressive clinical course than in adults. Younger patients have been found to be twice as likely to require high-dose prednisone[9] and more frequently to have renal involvement (range 28-100%) comparing to adults[6, 10].

The clinical picture of LN is mostly related to the severity of histological abnormalities on renal biopsy. The more severe histological forms of nephritis tended to have more severe renal manifestations[1,11]. Overall 60-80% of children with SLE had abnormal urine sediments or renal function early in the course of the disease[12]. Most patients with acute rapidly progressive renal insufficiency, heavy proteinuria, and red and white cell casts had class-IV LN. As in our study, the patients with class-IV LN were frequently found to have hematuria, proteinuria and hypertension compared to the other groups. However, patients with hematuria, proteinuria with or without nephrotic syndrome with a normal or subnormal glomerular filtration rate may have any classes of glomerular lesions. It has been well recognized that patients with severe histologic lesions could be clinically asymptomatic[11]. More than half of our 40 patients with class-IV LN had normal serum Cr levels and approximately 20% of class-II LN had nephrotic-ranged proteinuria. A review of 167 Taiwanese children with SLE demonstrated that 10-15% of class-II LN had nephrotic status and only 62% of class-IV nephritis had significant hematuria[13]. Because treatment differs for each forms of SLE nephritis, a renal biopsy is suggested at the time of initial presentation in patients with an active urine sediment or abnormal renal function[14].

Lupus patients face a range of complications from the disease itself or the long-term complications of therapeutic agents used for SLE. Infection has been one of the leading causes of morbidity and mortality, accounting for 11-23% of all hospitalizations in adult SLE[3]. It has been realized that therapeutic, disease-related and genetic factors all contribute to an increased susceptibility to infections in lupus patients[2]. The most common sites of infections are skin, bladder, joints, brain, lungs and blood. In our patients, urinary tract, skin and respiratory tract were the common sites of infection similar to other two studies in Thai adults[15, 16]. About 50% of deaths among Thai adults with SLE resulted from infections[15,17] compared to 65% in our study. Thus, pediatric patients could be more susceptible to infectious complications possibly due to more severe disease and aggressive clinical course as well as the prolonged use of immunosuppressants. Wongchinsri et al[16] studied infectious complications in 191 Thai adults with SLE during 1994-1999. *Salmonella* species were the most common pathogens, followed by *Escherichia coli* and *Mycobacterium* tuberculosis in that study. In Europe, lupus patients (studied in 1999) died of infections in 28.9%, primarily from bacterial sepsis originated from either a pulmonary, abdominal or urinary source[18]. Wang et al reported that 72% of deaths in Taiwanese children with SLE were caused by infections most commonly from possible hospital-acquired pseudomonas infections. On the contrary, the common organisms causing infections in our patients were community-acquired. This suggested that poor self-hygienic care could contribute to the relatively high incidence of infection.

Several studies of childhood LN have identified prognostic parameters such as male sex, black race, age at onset before puberty, persistent hypertension, impaired renal function, nephrotic syndrome, anemia, class-IV nephritis, and increased histological index scores[12]. When considering causes of death due to disease activity of SLE, renal disease, as measured by either serum Cr or qualitative urine protein excretion, is an important predictor of mortality[2]. In children, the Activity (AI) and Chronicity (CI) indices which provide information regarding to severity of acute or chronic injury to the kidneys in LN have been exam-

ined in some studies to predict renal outcome[19-21]. However, there was no agreement on such conclusion. The clinical feature most consistently associated with a poor prognosis is class-IV nephritis, especially when this type of nephritis is associated with hypertension[9,22,23]. In our study, hypertension at the initial presentation as well as hematuria and impaired renal function in pediatric patients also indicated poor prognosis for patient survival. A similar pattern in Thai adults was also previously reported by Shayakul et al[17]. In view of the limitations of the present study, we could not detect any correlation between persistent hypertension and patient survival. Over the last three decades, 5-year survival improved to 90% and 10-year survival to 85%[1]. In our patients with class-II, class-IV and class-V, the 5-year kidney survival was greater than 90% in each group. The 5-year patient survival interestingly was not comparable; i.e., 83%, 67% and 64%, respectively. As the survival among the patients with SLE improves, because of early diagnosis, recognition of mild disease, and the addition of cytotoxic agents, these patients are now faced with considerable morbidity due to the sequelae of disease activity and side effects of medications. Important treatment decisions are based mainly on evidence of major organ involvement, including nephritis, neuropsychiatric disease, and severe hematologic disease[14]. Four of our 13 patients who died from infections received i.v. MP pulses due to SLE flares prior to the time of death. In adult and childhood-onset SLE, high-dose corticosteroid use has been shown to be a significant contributor to organ damage[24] and serious infection leading to a cause of death[25-29]. Intravenous CYC, which is commonly used for proliferative renal disease and CNS involvement, has dramatically improved the survival of children with SLE over the past 20 years[30]. In our study, we demonstrated a significantly better patient survival in class-IV LN patients treated with i.v. CYC compared to prednisolone with or without azathioprine. Several studies[31-35] of childhood LN demonstrated satisfactory outcome of i.v. CYC in terms of both kidney and patient survival rates. Recently, Lehman et al[32] reported significant improvement in proteinuria and renal function in childhood SLE nephritis treated with intravenous cyclophosphamide given monthly for six months and then every three months.

In summary, infectious complications were the most common cause of morbidity and mortality among our pediatric patients with SLE. In addition to the disease itself, therapies used to treat SLE seemed to be a major contribution to the patient survival. This should reinforce the importance of carefully balancing the benefits and side effects when selecting medications to control SLE as well as encouraging the children and their family to learn about their disease and self-care to help prevent morbidity.

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โรคเอสแอลอีในเด็กไทย: พยาธิสภาพของไตและการพยากรณ์โรคในผู้ป่วย 82 ราย

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การศึกษานี้เป็นการวิเคราะห์ข้อมูลย้อนหลังของกลุ่มผู้ป่วยเด็กที่เป็นโรคเอสแอลอี 82 ราย เพื่อแสดงถึงปัจจัยเสี่ยงที่เป็นไปได้สำหรับผู้ป่วยในการบ่งชี้ถึงการพยากรณ์โรคที่ไม่ดี โดยการรวบรวมข้อมูลของผู้ป่วยที่เริ่มมีอาการของโรคเอสแอลอีก่อนอายุ 14 ปี ในช่วงเวลาตั้งแต่เดือนมกราคม พ.ศ. 2530 จนถึงเดือนธันวาคม พ.ศ. 2540 อันประกอบด้วยข้อมูลต่างๆ ได้แก่ อาการและอาการแสดงของโรค ผลการตรวจทางห้องปฏิบัติการ พยาธิสภาพของไต แนวทางการรักษา และผลของการรักษา

จากผลการศึกษา พบว่า ในผู้ป่วยทั้งหมด 82 ราย เป็นเพศหญิง 64 ราย เพศชาย 18 ราย คิดเป็นสัดส่วนเพศหญิงต่อเพศชายเท่ากับ 3.5 ต่อ 1 ระยะเวลาที่ผู้ป่วยมาติดตามการรักษาโดยเฉลี่ยประมาณ 53.6 เดือน ผู้ป่วยเริ่มมีอาการแสดงของโรคในช่วงอายุ 2 ถึง 12.6 ปี คิดโดยเฉลี่ยประมาณ 9.2 ปี พยาธิสภาพของไตเป็นแบบ WHO class IV มากที่สุด (48.8%) รองลงมาคือ class II, class V, class I และ class III ตามลำดับ แนวทางในการเลือกใช้ยา อันได้แก่ การใช้ corticosteroid อย่างเดียว หรือใช้ร่วมกับการกิน azathioprine หรือการฉีด cyclophosphamide (CYC) ขึ้นอยู่กับอาการแสดงของโรค และพยาธิสภาพของไต การใช้ยาฉีด methylprednisolone พิจารณาให้ในรายที่มีอาการของโรคที่รุนแรงมาก ในช่วงระหว่างการติดตามผู้ป่วย มีการตรวจชิ้นเนื้อไตซ้ำ ในผู้ป่วยจำนวน 12 ราย ไม่พบมีการเปลี่ยนแปลงของ WHO class ใน4 ราย แต่พบ 8 รายมีลักษณะทางพยาธิสภาพของไตที่รุนแรงมากขึ้น ในช่วงท้ายของการติดตามผู้ป่วย พบว่า ผู้ป่วยเสียชีวิตจำนวนทั้งหมด 20 ราย ส่วนใหญ่ (65%) เสียชีวิตจากการติดเชื้อ อีกส่วนหนึ่งเสียชีวิตจากภาวะแทรกซ้อนทางหัวใจ ระบบทางเดินหายใจ และไตวายระยะสุดท้าย อัตราการรอดชีวิตที่ 1 ปี ของผู้ป่วยทั้งหมดเท่ากับ 89% และที่ 5 ปี เท่ากับ 74% โดยที่ผู้ป่วยในแต่ละกลุ่ม WHO class II, class IV และ class V มีอัตราการรอดชีวิตที่ 5 ปี เท่ากับ 83%, 67% และ 64% ตามลำดับ กลุ่มผู้ป่วย WHO class IV ที่ได้รับการรักษาด้วยยาฉีด CYC มีอัตราการรอดชีวิตที่ 5 ปี สูงกว่ากลุ่มที่ได้รับ prednisolone อย่างเดียวหรือได้ร่วมกับ azathioprine ในระหว่างการติดตามผู้ป่วยในช่วง 5 ปี พบมี 4% เกิดไตวายระยะสุดท้ายในกลุ่มผู้ป่วย WHO class II และ 9% ใน class IV จากการวิเคราะห์ความสัมพันธ์ในอัตราตายของผู้ป่วยกับอาการแสดงรวมถึงผลการตรวจของผู้ป่วยในระยะแรก พบว่า ความดันโลหิตสูง ปัสสาวะปนเลือด และการทำงานของไตที่ลดลงเป็นปัจจัยเสี่ยงที่มีผลต่ออัตราการรอดชีวิตของผู้ป่วย

โดยสรุป การติดเชื้อเป็นปัญหาสำคัญของความเจ็บป่วยและเป็นสาเหตุการตายที่พบบ่อยที่สุดในผู้ป่วยเด็กที่เป็นโรคเอสแอลอี ภาวะแทรกซ้อนดังกล่าวน่าจะเป็นผลพวงจากการใช้ยากดภูมิคุ้มกันในผู้ป่วยเหล่านี้ อย่างไรก็ตามการใช้ยากลุ่ม corticosteroid อย่างเหมาะสมและด้วยความระมัดระวัง ร่วมกับยาฉีด CYC ในผู้ป่วยเด็กที่เป็นโรคเอสแอลอีซึ่งมีอาการรุนแรง ให้ผลการรักษาที่ดีกว่าการกิน prednisolone อย่างเดียวหรือให้รับประทานร่วมกับ azathioprine