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ORIGINAL ARTICLE

Clinical features, outcome, and associated factors for posterior reversible encephalopathy in Thai patients with systemic lupus erythematosus: a case-control study

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Abstract Posterior reversible encephalopathy syndrome (PRES) in patients with systemic lupus erythematosus (SLE) has been recognized increasingly. This study aimed to determine the prevalence, clinical features, brain imaging findings, outcomes, and associated factors of PRES in Thai SLE patients. SLE patients with PRES were identified from the lupus cohort of Chiang Mai University. Controls were SLE patients with a hospital number close to and actually had SLE diagnosis within 5 years of the case (case:control ratio = 1:4). Of 1,332 SLE patients, 30 episodes of PRES were identified in 24 female SLE patients (prevalence 1.80%). The mean ± SD age at SLE diagnosis and at onset of PRES was 25.02 ± 13.78 and 28.31 ± 12.61 years, respectively. Seizure was the most common presenting symptom, as seen in 28 episodes, followed by acute severe headache in 17, alteration of consciousness in 17, nausea and vomiting in 10, blurred vision in 11, and hemiparesis in 3. Abrupt increase in blood pressure and active nephritis were seen in 29 and 26 of the episodes, respectively. Urine protein/creatinine ratio > 1.00 (OR 15.72, 95% CI 3.12–79.12, $p = 0.001$) and hemoglobin < 10 gm/dL (OR 5.12, 95% CI 1.37–19.15, $p = 0.015$) were associated factors for developing PRES. During the observation period, 7 patients in the PRES group and 8 in the control group died ($p = 0.015$). PRES was uncommon in SLE patients, but associated with a high mortality rate. Active nephritis and anemia were associated factors of PRES in Thai SLE patients.

Keywords Associated factors · Lupus · Posterior reversible encephalopathy syndrome · PRES · SLE

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multiple organ involvement and the presence of autoantibodies. Delayed diagnosis and management can not only lead to organ damage but also increased mortality. Neuropsychiatric SLE (NPSLE) is not an uncommon manifestation with a prevalence rate of 14–95%, depending on the definition used. NPSLE can affect the central, peripheral, or autonomic nervous system, and can be either a focal or diffuse process, with severity ranging from mild to severe disabling conditions, resulting in significant morbidity and mortality. In general, a majority of NPSLE cases occur at the early stage of the disease, and NPSLE can be an initial manifestation of SLE occasionally [1].

Posterior reversible encephalopathy syndrome, or "PRES", is an uncommon neurological disorder, characterized by hypertension, seizures, visual disturbance, and cognitive changes, with a unique brain imaging finding that is consistent with a reversible vasogenic edema at the posterior parietal or occipital lobes on computed tomography (CT) or magnetic resonance imaging (MRI) [2–4]. The disease was first described in 1996 by Hinchey et al., in patients who had eclampsia and acute hypertensive encephalopathy and received immunosuppressive agents [5]. During the past decade, PRES in patients with SLE has been reported increasingly as a case, or case series, and also reviewed in the literature from both western [6–11] and Asian countries [12–17]. Although many reports

found that a majority of patients had active disease, particularly renal involvement, only a small number of studies were performed on a case-control study basis [9, 14]. Of interest, despite PRES being recognized increasingly, it is not included in the nomenclature of nervous system involvement in SLE [18].

This study aimed to determine the prevalence, clinical features, and outcomes of PRES in Thai patients with SLE, and also ascertain associated factors for the development of PRES by using a case-control study.

Materials and methods

The medical records from January 1986 to December 2016 of SLE patients in the Lupus Cohort of the Division of Rheumatology, Department of Internal Medicine, Chiang Mai University were reviewed. Those who had central nervous system (CNS) symptoms, and were diagnosed PRES according to an imaging study, were identified and included this study analysis. The diagnosis of SLE followed the 1997 American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus [19]. Controls were selected from SLE patients in the same cohort, who had a hospital number that was close to and actually had SLE diagnosis within 5 years of the case. The ratio of case to control was 1:4. The clinical manifestations and laboratory findings in the controls, which corresponded to the PRES group in the same SLE disease period, were used for analysis. SLE disease activity was determined by the modified SLE disease activity index-2K (mSLEDAI-2K) [20].

All of the neuro-imaging studies were reviewed by two experienced neuro-radiologists: KO and SW. The neuro-imaging findings followed the description of Bartynski et al. [3], which was classified into (a) dominant parieto-occipital pattern, (b) holohemispheric watershed pattern, (c) superior frontal sulcus pattern, and (d) partial or asymmetric expression of the three patterns. The results were classified as complete resolution, partial resolution, no response, and progression of lesions in patients with a repeated neuro-imaging study. This study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University.

Statistical analysis

The STATA 13.0 computer software (Stata Corporation, Texas USA) was used for data processing and statistical analysis. Continuous data were expressed as mean ± standard deviation (SD) and categorical data as percent. The Student's *t* test or Mann-Whitney *U* test was used to compare continuous data, and the Chi-square or Fisher's exact test for comparing categorical data, where appropriate. Logistic regression analysis was used to determine associated factors for the development of PRES and reported as odds ratio (OR) and 95% confidence interval (95% CI). A $p < 0.05$ was considered statistically significant.

Results

Twenty-four of 1332 (1.80%) subjects in the cohort of SLE patients were found to have PRES. All of them were female. Four of these patients (16.67%) had recurrent episodes of PRES (2 repeat episodes in 2, and 3 in the other 2), giving a total of 30 PRES episodes. The mean ± SD age, age at SLE diagnosis, and age at the onset of PRES in all episodes were 29.78 ± 12.25, 25.02 ± 13.78, and 28.31 ± 12.61 years, respectively, which gave a mean duration of PRES development after SLE diagnosis of 3.29 ± 3.76 years. Ten (33.33%) episodes occurred within the first year of the disease. The PRES episodes led to SLE diagnosis in 2 cases, and PRES development within 1 month after SLE diagnosis in 3. Of those who had recurrent PRES, the mean duration of recurrent episodes was 0.69 ± 0.62 years after the previous episode.

Clinical features and serologic findings of SLE patients during PRES episodes are summarized in Table 1. All but one patient had high blood pressure at PRES onset, and the mean ± SD systolic blood pressure (BPs) and diastolic blood pressure (BPd) were 186.46 ± 29.21 and 116.42 ± 16.27 mmHg, respectively. Renal involvement, particularly active lupus nephritis, was a common finding seen in 26 episodes (86.67%). Renal biopsy was performed in 12 patients who had renal involvement, with lupus nephritis class III + IV, IV, and IV + V in 1 case, 10 cases, and 1 case, respectively. One patient had end-stage renal disease prior to developing PRES. Other clinical manifestations seen during 30 PRES episodes were fever in 11 (36.67%) episodes, thrombocytopenia in 10 (33.33%) [3 also had thrombotic microangiopathy: TMA], autoimmune hemolytic anemia (AIHA) in 7 (23.33%), skin rashes in 7 (23.33%), serositis in 3 (10.00%), leukopenia in 3 (10.00%), oral ulcer in 2 (6.67%), arthritis in 1 (3.33%), and pulmonary hemorrhage in 1 (3.33%) episode. Anti-dsDNA positive and low serum complement were seen in 14 of 20 (70.00%) and 8 of 23 (34.78%) episodes tested, respectively. Within 1 month prior to the onset of PRES, intravenous cyclophosphamide (IVCY) was given in 6 episodes [4 of them also received intravenous pulse methylprednisolone (IVMP)], and plasmapheresis was performed in one.

Clinical features and outcome of PRES

Clinical, brain imaging study, treatment, and outcome of the 30 episodes of PRES are shown in Table 2. Seizure was the most common presenting symptom and seen in 28 of 30 episodes (93.33%), in which 3 (10.71%) had status epilepticus.

Table 1 Demographic data of 30 PRES episodes in 24 SLE patients

Case	Episode	Age at PRES onset/sex	Duration of SLE diagnosis to PRES (in years)	Renal involvement (renal pathology class)	BPs/BPd at PRES onset (mmHg)	Extra-renal disorders	Prior intense immunosuppressive therapy within 1 month	Anti-dsDNA	Complement
1	1	16.30/F	0	Yes	150/117	Oral ulcer, fever		Positive	Normal
2.1	2	33.81/F	1.34	Yes (IV + V)	179/104	Fever		Positive	Low
2.2	3	34.78/F	2.31	Yes	191/135	Oral ulcer		Positive	Normal
2.3	4	36.43/F	3.97	Yes	190/130	–		ND	ND
3.1	5	28.36/F	11.40	Yes (IV)	220/120	–	IVCY	Positive	Low
3.2	6	28.53/F	11.57	Yes	220/140	AIHA, thrombocytopenia		ND	Normal
4	7	23.88/F	2.95	No	190/130	Vasculitis, arthritis, rash, fever		ND	ND
5	8	30.40/F	2.08	Yes	220/120	AIHA, thrombocytopenia, TMA, fever		Negative	ND
6	9	17.97/F	5.47	Yes (IV)	165/110	Thrombocytopenia		Positive	Low
7	10	25.04/F	10.36	Yes	230/130	AIHA, serositis, thrombocytopenia, fever		ND	Normal
8	11	18.01/F	0.17	Yes (IV)	160/110	Leukopenia		ND	Normal
9	12	17.56/F	1.53	Yes (IV)	170/110	Fever		ND	Normal
10	13	17.44/F	0.04	Yes (IV)	200/100	–	IVCY	Positive	Normal
11.1	14	56.15/F	0.08	Yes	160/100	AIHA, fever	Plasmapheresis	ND	Low
11.2	15	56.58/F	0.51	Yes	150/80	Pulmonary hemorrhage, rash	IVMP + IVCY	Negative	Normal
12	16	19.27/F	0.12	Yes (IV)	220/120	Vasculitis, rash		Negative	Low
13	17	26.23/F	6.33	Yes (IV)	165/115	Thrombocytopenia, TMA, rash, serositis		Positive	Low
14	18	24.53/F	9.44	Yes (IV)	198/126	Serositis, thrombocytopenia,		Negative	Normal
15	19	28.67/F	1.64	Yes (IV)	200/130	Thrombocytopenia, rash, leukopenia		Negative	Normal
16	20	47.07/F	0.79	No	230/100	AIHA, fever, leukopenia		Positive	Normal
17.1	21	19.18/F	2.49	Yes (ESRD) (III + IV)	196/120	AIHA, thrombocytopenia, TMA, fever		Positive	Normal
17.2	22	19.43/F	2.74	Yes (ESRD)	190/145	–		ND	ND
17.3	23	19.66/F	2.97	Yes (ESRD)	212/135	–		ND	ND
18	24	36.36/F	2.03	No	142/115	Arthritis, rash, fever		ND	ND
19	25	17.22/F	2.09	Yes (IV)	180/100	AIHA, rash,		Positive	Normal
20	26	62.33/F	0	No	120/85	Thrombocytopenia, fever		Positive	ND
21	27	24.09/F	10.83	Yes	173/108	Thrombocytopenia	IVMP + IVCY	Negative	Normal
22	28	20.16/F	3.26	Yes	150/120	–	IVMP + IVCY	Positive	Low
23	29	27.56/F	0.06	Yes	180/130	–		Positive	Normal
24	30	16.45/F	0.19	Yes	194/130	–	IVMP + IVCY	Positive	Low

SLE systemic lupus erythematosus, *PRES* posterior reversible encephalopathy syndrome, *AIHA* autoimmune hemolytic anemia, *TMA* thrombotic microangiopathy, *F* female, *BPs* systolic blood pressure, *BPd* diastolic blood pressure, *ND* not done, *ESRD* end-stage renal disease, *IVMP* intravenous pulse methylprednisolone, *IVCY* intravenous pulse cyclophosphamide

Table 2 Clinical, radiologic features, treatment, and outcome of 30 PRES episodes in 24 SLE patients

Case	Episode	Clinical features	Imaging	Radiologic pattern	Treatment	Clinical improvement*	Radiologic response	Outcome (death)
1	1	Headache, n/v, AOC, seizure	CT	Parietal-occipital	anti-HT, AED, corticosteroids	1 day	–	No
2.1	2	Headache, seizure, left temporal hemianopia	CT	Parietal-occipital	anti-HT, AED, corticosteroids	2 days	Completely resolved	No
2.2	3	Headache, blurred vision	CT	Partial expression	anti-HT, IVMP + IVCY	1 day	Partially resolved	No
2.3	4	Headache, blurred vision	CT	Parietal-occipital	anti-HT, corticosteroids	3 days	Completely resolved	No
3.1	5	AOC, seizure (status epilepticus)	MRI	Superior frontal	anti-HT, AED, corticosteroids	1 day	Partially resolved	Yes
3.2	6	AOC, seizure	MRI	Parietal-occipital	anti-HT, AED, rituximab	1 day	Partially resolved	No
4	7	Headache, n/v, AOC, seizure blurred vision	MRI	Watershed	anti-HT, AED, IVMP, IVCY	5 days	No improvement	No
5	8	n/v, AOC, seizure (status epilepticus)	MRI	Partial expression	anti-HT, AED, corticosteroids, plasma exchange	3 days	Completely resolved	Yes
6	9	Headache, n/v, AOC, seizure	MRI	Watershed, ICH	AED, corticosteroids, rituximab	1 day	Partially resolved	No
7	10	Headache, AOC, seizure, blurred vision, right hemiparesis	CT	Watershed	anti-HT, IVMP, IVCY	4 days	–	No
8	11	Headache, seizure	MRI	Parietal-occipital	AED, corticosteroids	1 day	–	No
9	12	Headache, n/v, seizure	CT	Parietal-occipital	anti-HT, AED, corticosteroids	1 day	Completely resolved	No
10	13	AOC, seizure	MRI	Partial expression	anti-HT, AED, corticosteroids	1 day	Completely resolved	No
11.1	14	AOC, seizure	MRI	Watershed	anti-HT, AED, corticosteroids	1 day	Completely resolved	No
11.2	15	AOC, seizure, right hemiparesis	CT	Partial expression	AED, corticosteroids	7 days	–	Yes, PH
12	16	Seizure	CT	Partial expression, ICH	anti-HT, AED, corticosteroids	1 day	Partially resolved	No
13	17	Headache, seizure, blurred vision	CT	Parietal-occipital	anti-HT, AED, IVMP, IVCY	1 day	–	No
14	18	AOC, seizure	MRI	Parietal-occipital	anti-HT, AED, IVMP, IVCY	1 day	Progression	No
15	19	Seizure	CT	Partial expression	anti-HT, AED, IVMP, IVCY	1 day	Completely resolved	Yes
16	20	Seizure	CT	Parietal-occipital	anti-HT, IVMP, IVCY	1 day	–	No
17.1	21	Headache, n/v, seizure, blurred vision	CT	Watershed	anti-HT, AED, corticosteroids, plasma exchange	1 day	–	No
17.2	22	Headache, n/v, seizure	CT	Parietal-occipital	anti-HT, AED, corticosteroids	1 day	–	No
17.3	23	Headache, n/v, seizure, blurred vision,	CT	Parietal-occipital	anti-HT, AED, corticosteroids	1 day	–	No
18	24	Headache, AOC, seizure	CT	Watershed	anti-HT, AED	1 day	Partially resolved	Yes
19	25	Seizure	MRI	Watershed	anti-HT, AED, IVMP, IVCY	1 day	–	Yes
20	26	n/v, AOC, seizure, blurred vision	CT	Parietal-occipital	corticosteroids	1 day	–	No
21	27	AOC, seizure (status epilepticus), blurred vision,	CT	Partial expression	anti-HT, AED, corticosteroids, IVCY, plasma exchange	3 days	Completely resolved	No
22	28	Headache, AOC, seizure	CT	Partial expression	anti-HT, AED, corticosteroids, IVCY	2 days	Progression	No

Table 2 (continued)

Case	Episode	Clinical features	Imaging	Radiologic pattern	Treatment	Clinical improvement*	Radiologic response	Outcome (death)
23	29	Headache, AOC, seizure, blurred vision,	CT	Partial expression	anti-HT, corticosteroids, IVCY	1 day	Completely resolved	No
24	30	Headache, n/v, AOC, seizure blurred vision, left hemiparesis	CT	Partial expression	anti-HT, corticosteroids, IVCY	2 days	Partially resolved	Yes

n/v nausea and vomiting, *AOC* alteration of consciousness, *CT* computed tomography, *MRI* magnetic resonance imaging, *ICH* intra-cranial hemorrhage, *anti-HT* anti-hypertensive drugs, *AED* anti-epileptic drugs, *IVMP* intravenous pulse methyl prednisolone, *IVCY* intravenous cyclophosphamide, *PH* pulmonary hemorrhage

*Improvement in alteration of consciousness and visual symptoms

Other symptoms included acute severe headache in 17 (56.67%) episodes, alteration of consciousness in 17 (56.67%), nausea and vomiting in 10 (33.33%), and blurred vision in 11 (36.67%), of which one had bilateral hemianopia and hemiparesis in 3 (10.00%). SLE disease activity determined by the mSLEDAI score at PRES onset was high (22.90 ± 7.17), even when the neurological component was excluded (mSLEDAI-N) (11.17 ± 4.62), indicating very active disease.

Brain imaging study was performed in all of the episodes (computed tomography [CT] in 20 and magnetic resonance imaging [MRI] in 10) and the mean ± SD duration of brain imaging after the onset of symptoms was 2.15 ± 1.95 days. Parietal-occipital pattern, the most common brain lesion, was seen in 13 (43.33%) episodes, partial or asymmetric expression of the three patterns in 9 (30.00%) and holohemispheric watershed pattern in 7 (23.33%), and superior frontal sulcus pattern in 1 (3.33%) episode. Intra-cranial hemorrhage (ICH) was observed in 2 episodes. The pathological lesions involved the occipital lobes in 26 (86.67%) episodes, parietal lobes in 24 (80.00%), frontal lobes in 23 (76.67%), temporal lobes in 14 (46.67%), cerebellum in 13 (43.33%), basal ganglia in 7 (23.33%), brain stem in 6 (20.00%) and thalamus in 4 (13.33%), and bilaterally in 24 (80.00%), 20 (66.67%), 19 (63.33%), 11 (36.67%), 10 (33.33%), 7 (23.33%), 4 (13.33%), and 3 (10.00%) episodes, respectively.

Anti-hypertensive and anti-epileptic drugs were prescribed in 24 and 23 episodes, respectively. The mean ± SD duration of anti-epileptic drug treatment was 32.56 ± 27.55 days. High-dose corticosteroids (8 of which were IVMP) were given in all but one episode (96.67%). IVCY was given in 8 (26.67%) episodes to control lupus activity, mainly for lupus nephritis. Rituximab was given in 2 episodes and plasma exchange in 2 to patients with TMA. All of the patients had clinical improvement, e.g., return to normal consciousness, disappearance of headache, and blurred vision with mean ± SD duration of 1.65 ± 1.50 days.

A repeat brain imaging study was performed after the first one in 18 patients with mean ± SD duration of 13.46 ± 7.35 days. The brain imaging studies showed complete resolution of the lesions in 9 (50.00%) episodes, partial resolution of the lesions in 6 (33.33%), no improvement in 1 (5.56%) episode, and progressive lesions in 2 (11.11%) episodes.

Associated factors of PRES

Demographic data and co-morbidities at the first episode of PRES in 24 SLE patients were compared with 96 SLE controls, as shown in Table 3. Both groups had comparable age, age of SLE at onset, duration of SLE, and number of SLE classification criteria. Co-morbidities including diabetes mellitus, dyslipidemia, history of neurological symptoms (e.g. stroke and seizures), chronic kidney disease (creatinine

Table 3 Demographic data of SLE patients among cases with PRES and controls

	SLE with PRES (n = 24)	SLE without PRES (n = 96)	p value
Sex, female, n (%)	24 (100.00)	88 (91.67)	0.143
Current age, in years	28.89 ± 12.00	34.10 ± 11.76	0.056
Age at SLE onset, in years	24.14 ± 13.47	29.36 ± 12.16	0.068
Age at PRES, in years	27.25 ± 12.35	32.14 ± 11.83	0.076
Duration of SLE to PRES, in years	3.11 ± 3.77	2.77 ± 3.09	0.641
Median (min.–max.)	1.84 (0–11.40)	1.60 (0.02–13.51)	
Total number of criteria	5.46 ± 1.02	5.22 ± 1.90	0.403
Co-morbidities			
Hypertension, n (%)	10 (41.67)	19 (19.79)	0.025
Diabetes mellitus, n (%)	2 (8.33)	4 (4.16)	0.345
Dyslipidemia, n (%)	4 (16.67)	24 (25.00)	0.388
History of neurological disease (e.g. stroke, epilepsy), n (%)	3 (12.50)	6 (6.25)	0.298
Chronic kidney disease (creatinine > 1.5 mg/dL)*, n (%)	2 (8.33)	4/95 (4.21)	0.599
Current alcohol consumption, n (%)	0 (0.00)	6 (6.25)	0.598
Current smoking, n (%)	0 (0.00)	5 (5.20)	0.582
Thalassemia, n (%)	2 (8.33)	15 (15.62)	0.360
Anti-phospholipid syndrome, n (%)	2 (8.33)	3 (3.13)	0.261
Vasculitis, n (%)	4 (16.67)	6 (6.25)	0.099
Others, n (%)			
HBsAg+	–	1 (1.04)	
Hypothyroid	–	2 (2.08)	

Data are expressed in mean ± SD unless specified

HBsAg hepatitis B virus surface antigen

*Number of positive/number of patients tested

> 1.5 mg/dL), past or current alcohol consumption and smoking, thalassemia, history of anti-phospholipid antibody syndrome, or past history of vasculitis were comparable in both groups, except for hypertension, which was more common in the PRES group (41.67 vs. 19.79%, p = 0.025). One patient was a hepatitis B virus carrier and 2 had hypothyroidism; with both being in the control group.

In order to identify the associated factors of PRES, clinical manifestations, and laboratory findings of SLE, patients with PRES (SLE-PRES), at their last visit prior to developing PRES were used for analysis, and compared with their controls, in order to identify its associated factors. As two patients developed PRES at the time of SLE diagnosis, and 3 with known SLE were referred from other hospitals after the onset of seizures, information on their last visit prior to PRES onset was not available. Therefore, only 19 patients with clinical and laboratory data prior to the onset of PRES remained for analysis. Clinical features and serological abnormalities, according to the 1997 ACR classification criteria, SLE disease activity and blood pressure among the SLE patients with PRES and their controls are shown in Table 4. Overall, cumulative clinical manifestations and serological findings were comparable in both groups, except that patients with PRES had more significant hematological (84.21 vs. 56.57%, p = 0.026) and renal involvement (89.47 vs. 43.42%, p < 0.001) than their controls. Among those with hematological involvement, SLE patients with PRES also had more significant autoimmune hemolytic anemia [AIHA] (68.42 vs. 25.00%, p < 0.00) and thrombocytopenia (26.31 vs. 9.21%, p = 0.045).

When comparing the last visit prior to PRES onset with their controls, SLE patients with PRES had significantly higher SLE disease activity, as determined by the mSLEDAI score (10.74 ± 3.48 vs. 3.99 ± 4.18, p < 0.001), and a proportion of those had high disease activity [mSLEDAI > 10] (52.63 vs. 7.89%). The mSLEDAI score was much higher among the PRES group at the time of PRES onset than at their last visit prior to the onset of PRES (24.63 ± 6.74 vs. 10.74 ± 3.48, p = < 0.001). However, when the neurological component of the mSLEDAI score (mSLEDAI-N) was excluded, the mSLEDAI score in SLE patients with PRES did not increase significantly (12.42 ± 4.04 vs. 10.74 ± 3.48, p = 0.072), indicating that the increased mSLEDAI score at PRES onset mainly came from the neurological component.

The mean ± SD BPs and BPd, as well as the proportion of patients with uncontrolled blood pressure prior to the onset of PRES, were comparable in both groups. When comparing the prior to onset of PRES with the time of PRES onset, the latter

Table 4 Cumulative clinical features and serological findings according to the 1997 ACR classification criteria for SLE, SLE disease activity and blood pressure, and laboratory findings at last visit prior to onset of PRES among 19 SLE with PRES patients and 76 controls

	SLE with PRES (n = 19)	SLE without PRES (n = 76)	p value
Clinical features and serological findings			
Malar rashes, n (%)	11 (57.89)	51 (67.10)	0.451
Oral ulcers, n (%)	5 (26.31)	25 (32.89)	0.581
Photosensitivity, n (%)	2 (10.52)	20 (26.31)	0.144
Discoid rashes, n (%)	7 (36.84)	34 (44.74)	0.534
Arthritis, n (%)	7 (36.84)	32 (42.10)	0.677
Serositis, n (%)	5 (26.31)	13 (17.10)	0.359
Neurological, n (%)	3 (15.78)	8 (10.53)	0.521
Hematological, n (%)	16 (84.21)	43 (56.57)	0.026
AIHA, n (%)	13 (68.42)	19 (25.00)	< 0.001
Leukopenia/lymphopenia, n (%)	10 (52.63)	32 (42.10)	0.409
Thrombocytopenia, n (%)	5 (26.31)	7 (9.21)	0.045
Renal involvement, n (%)	17 (89.47)	33 (43.42)	< 0.001
ANA, n (%)	18 (94.73)	71 (93.42)	1.000
ANA titer: median (min.–max.)	1280 (160–2560)	1280 (0–5120)	0.916
Anti-dsDNA*, n (%)	15/17 (88.23)	49/70 (70.00)	0.126
Anti-Sm*, n (%)	2/2 (100.00)	7/11 (63.63)	1.000
Anti-cardiolipin*, n (%)	2/19 (10.5)	4/38 (10.52)	1.000
Lupus anti-coagulant*, n (%)	6/13 (46.15)	9/20 (45.00)	0.948
SLE disease activity (mSLEDAI)			
mSLEDAI score prior to PRES, mean ± SD	10.74 ± 3.48	3.99 ± 4.18	< 0.001
mSLEDAI score prior to PRES > 10, n (%)	10 (52.63)	6 (7.89)	< 0.001
mSLEDAI score at PRES onset, mean ± SD	24.63 ± 6.74		< 0.001[a]
mSLEDAI-N score at PRES onset, mean ± SD	12.42 ± 4.04		< 0.072[b]
Blood pressure			
BPs prior to PRES, mmHg, mean ± SD	127.05 ± 12.77	121.16 ± 12.84	0.076
BPd prior to PRES, mmHg, mean ± SD	78.32 ± 11.40	73.32 ± 9.77	0.057
Number of uncontrolled BP, n (%)	2 (10.52)	8 (10.52)	1.000
BPs at PRES, mmHg, mean ± SD	185.79 ± 22.41		< 0.001[c]
BPd at PRES, mmHg, mean ± SD	114.89 ± 11.22		< 0.001[d]
Laboratory tests			
Hemoglobin, (gm/dL), mean ± SD	9.10 ± 1.87	11.33 ± 1.90	< 0.001
Hemoglobin < 10.0 (gm/dL), n (%)	13 (68.42)	17 (22.36)	< 0.001
White blood cell counts, ($\times 10^9$/L), mean ± SD	7.53 ± 4.88	9.48 ± 19.21	0.503
White blood cell count < 3.00 ($\times 10^9$/L), n (%)	1 (5.26)	2 (2.63)	0.492
Platelets count ($\times 10^9$/L), mean ± SD	224.33 ± 116.60	301.58 ± 292.56	0.155
Platelet < 100 ($\times 10^9$/L), n (%)	3 (15.78)	3 (3.94)	0.092
UPCR (gm protein/gm creatinine), mean ± SD	2.98 ± 2.15	1.13 ± 1.84	< 0.001
UPCR > 1.0, n (%)	17 (89.47)	23 (30.26)	< 0.001
Creatinine, (mg/dL), mean ± SD	1.61 ± 0.89	0.87 ± 0.53	< 0.001
Creatinine > 1.5 (mg/dL), n (%)	8 (42.10)	4 (5.26)	< 0.001
Albumin, (gm/dL), mean ± SD	2.87 ± 0.69	3.44 ± 0.78	0.001
Albumin < 3.0 (gm/dL), n (%)	11 (57.89)	15 (19.74)	0.002
Coomb's test +ve*, n (%)	3/9 (33.33)	5/12 (41.67)	1.000
C3* (mg/dL), mean ± SD	389.75 ± 130.12 (n = 12)	673.54 ± 338.90 (n = 13)	0.026
C4* (mg/dL), mean ± SD	111.59 ± 55.89 (n = 13)	162.77 ± 97.87 (n = 13)	0.166

Table 4 (continued)

	SLE with PRES (n = 19)	SLE without PRES (n = 76)	p value
Low complement*, n (%)	11/13 (84.61)	6/13 (46.15)	0.039
Anti-dsDNA*, n (%)	15/17 (88.23)	49/70 (70.00)	0.126

mSLEDAI modified systemic lupus erythematosus disease activity index, *mSLEDAI-N* mSLEDAI excluding neurological score, *AIHA* autoimmune hemolytic anemia, *BPs* systolic blood pressure, *BPd* diastolic blood pressure, *ANA* anti-nuclear antibodies, *anti-dsDNA* anti-double stranded DNA, *UPCR* urine protein/creatinine ratio

[a] p value between mSLEDAI score prior to PRES onset vs. mSLEDAI score at PRES onset

[b] p value between mSLEDAI score prior to PRES onset vs. mSLEDAI-N score at PRES onset

[c] p value between BPs at PRES onset vs. BPs prior to PRES onset

[d] p value between BPd at PRES onset vs. BPd prior to PRES onset

*Number of positive tests/number of patients tested

had a significant increase in BPs (185.79 ± 22.41 vs. 127.05 ± 12.77 mmHg, $p < 0.001$) and BPd (114.89 ± 11.22 vs. 78.32 ± 11.40 mmHg, $p < 0.001$).

Laboratory findings at the last visit before the onset of PRES among SLE patients with PRES and their controls are shown in Table 4**.** SLE patients with PRES had a significantly lower mean hemoglobin level (9.10 ± 1.87 vs. 11.33 ± 1.90 gm/dL, $p < 0.001$), higher proportion of those with hemoglobin < 10 mg/dL (68.42 vs. 22.36%, $p < 0.001$), higher degree of proteinuria determined by urine protein/creatinine ratio (UPCR) [in gm protein/gm creatinine] (2.98 ± 2.15 vs. 1.13 ± 1.84, $p < 0.001$), higher proportion of those with UPCR > 1.0 (89.47 vs. 30.26%, $p < 0.001$), higher serum creatinine (1.61 ± 0.89 vs. 0.87 ± 0.53 mg/dL, $p < 0.001$), higher proportion of those with serum creatinine > 1.5 mg/dL (42.10 vs. 5.26%, $p < 0.001$), lower mean serum albumin (2.87 ± 0.69 gm/dL vs. 3.44 ± 0.78 gm/dL, $p = 0.001$), higher proportion of those with serum albumin < 3.0 gm/dL (57.89 vs. 19.74, $p = 0.002$), lower mean complement C3 level (389.75 ± 130.12 vs. 673.54 ± 338.90 mg/dL, $p = 0.026$), and higher proportion of those with a low complement C3 level (84.61 vs. 46.15%, $p = 0.039$) when compared to the controls. There was no significant difference in proportion of the number of patients with a positive test for serum anti-dsDNA antibodies in either group.

Table 5 shows the treatment received prior to the onset of PRES among SLE patients with PRES and those without. SLE patients with PRES received a significantly higher dose of daily prednisolone (33.16 ± 18.80 vs. 16.25 ± 14.20 mg/day, $p < 0.001$), and had a higher proportion of those receiving prednisolone of more than 15 mg/day (73.68 vs. 34.21%, $p = 0.002$), but a significantly lower proportion of those receiving hydroxychloroquine (15.78 vs. 47.36%, $p = 0.012$). There was no significant difference in the number of patients receiving immunosuppressive drugs or their type and dosage.

Differences in demographic data, cumulative clinical features, and laboratory findings were preceded by multiple logistic regression analysis, in order to determine factors that might predict the development of PRES (Table 6). Only recent proteinuria UPCR > 1.00 (OR 15.72, 95% CI 3.12–79.21, $p = 0.001$) and recent hemoglobin < 10 gm/dL (OR 5.12, 95% CI 1.37–19.15, $p = 0.015$) were found to be the associated factors in the development of PRES.

Mortality rate

With a mean ± SD duration of 1.64 ± 1.74 years follow-up, 7 patients (29.17%) in the PRES group died. Four deaths (57.14%), or 16.67% of PRES cases, occurred within 3 months after PRES onset. Causes of death were pneumonia in 5 cases, urinary tract infection in 1 case, and pulmonary hemorrhage in 1. The mean ± SD mSLEDAI and mSLEDAI-N score at the time of PRES onset prior to death was 17.25 ± 2.87 and 7.25 ± 5.06, respectively. Only 8 patients (8.33%) in the control group died, with a mean duration of 2.03 ± 2.00 years follow-up ($p = 0.015$).

Discussion

A 1.80% prevalence of PRES in SLE patients was identified in this study, indicating that PRES is an uncommon manifestation in SLE. The prevalence of PRES in this study was in the range of 0.69% reported from Taiwan [16] and 2.02% from Korea [14]. The prevalence in study and other reports from Asia [14, 16] might have been much higher than that reported from western countries. Although PRES in SLE have been reported from western countries, its prevalence was not able to be determined [6–8, 10, 11]. Three hospitals in Toronto, of which one also was a large lupus clinic, reported only 7 cases of PRES in SLE identified over 2.5 years [7]. Interestingly, 6 of these patients were Asian ethnics. The high prevalence of PRES in SLE among the Asian population might be related to more severity in SLE patients, as well as the high prevalence of lupus nephritis among Asian populations [21, 22]. It should be noted that one-third of the PRES episodes in this study

Table 5 Treatment received prior to onset of PRES among 19 SLE patients with PRES and 76 controls

	SLE with PRES (n = 19)	SLE without PRES (n = 76)	p value
Prednisolone, n (%)	19 (100.00)	76 (100.00)	1.000
Prednisolone, (mg/day)	33.16 ± 18.80	16.25 ± 14.29	< 0.001
Prednisolone > 15 mg/day, n (%)	14 (73.68)	26 (34.21)	0.002
Intravenous pulse methylprednisolone, n (%)	5 (26.31)	0	< 0.001
Hydroxychloroquine, n (%)	3 (15.78)	36 (47.36)	0.012
Hydroxychloroquine (mg/day)	266.67 ± 115.47	236.11 ± 93.05	0.558
Immunosuppressive drugs, n (%)	15 (78.94)	43 (56.57)	0.074
Mycophenolate mofetil, n (%)	6 (31.57)	12 (15.78)	0.116
Mycophenolate (mg/day)	1666.67 ± 605.53	1541.67 ± 541.81	0.691
Methotrexate, n (%)	1 (5.26)	2 (2.63)	0.492
MTX (mg/week)	15.00	12.50 ± 3.54	0.480
Azathioprine, n (%)	0	8 (10.52)	0.351
Azathioprine (mg/day)	0	50.00 ± 23.14	
Cyclophosphamide, n (%)	8 (42.10)	21 (27.63)	0.220
Cyclophosphamide (mg/month)	925.00 ± 103.51	966.67 ± 220.42	0.916
Cyclosporine, n (%)	0	1 (1.31)	1.000
Cyclosporine (mg/day)	0	200.00	

Data are expressed as mean ± SD unless specified

occurred within the first year of their SLE diagnosis, and PRES led to the diagnosis of SLE in two patients, thus indicating that PRES tended to occur at the early stage of SLE. The onset of PRES in the early stage of SLE also has been recognized [7]. Furthermore, a majority of the patients also had active nephritis at the time of PRES onset.

The clinical features of PRES, including acute onset of hypertension, headache, nausea/vomiting, blurred vision, and seizures were common in this study, and similar to those previously reported [6–14, 16, 17]. However, only 42.85% of patients had a seizure in Barber's series [7], which was lower than in others. Acute severe headache and seizures were the result of a sudden increase in intra-cranial pressure by abruptly increased blood pressure. Blurred vision was related to the involvement of lesions that involved posterior circulation of the brain, as confirmed by CT or MRI scan in almost 90% of the episodes [23]. The outcome of treatment in terms of neurological deficit in the present study was rather good, as the visual symptoms and seizures as well as neurological deficit recovered within a few days after blood pressure were controlled. This was confirmed by the improvement or disappearance of lesions in repeated brain imaging studies of

Table 6 Risk factors of PRES among SLE patients

	Univariate analysis			Logistic regression analysis		
	OR	95% CI	p value	AOR	95% CI	p value
Age at SLE onset, in years	0.94	0.89–0.99	0.042			
Age at PRES, in years	0.94	0.89–0.99	0.045			
Hypertension	2.52	0.74–8.16	0.081			
Hemoglobin < 10.0 gm/dL	6.58	1.80–26.62	0.001	5.12	1.37–19.15	0.015
Platelet < 100 ($\times 10^6$/L)	5.80	0.59–73.08	0.043			
Creatinine > 1.5 mg/dL	13.09	2.81–67.10	< 0.001			
Albumin < 3.0 gm/dL	5.13	1.53–17.33	0.002			
UPCR > 1.0	19.59	4.00–182.44	< 0.001	15.72	3.12–79.21	0.001
Prior to PRES mSLEDAI score > 10	12.96	3.23–53.19	< 0.001			
Prednisolone > 15 mg/day	5.38	1.58–20.88	0.002			
Use of hydroxychloroquine	0.21	0.04–0.83	0.012			
Use of immunosuppressive drugs	2.88	0.80–12.90	0.074			

OR odds ratio, *AOR* adjusted odds ratio, *95% CI* 95% confidence interval, *mSLEDAI* modified systemic lupus erythematosus disease activity index, *UPCR* urine protein/creatinine ratio

approximately 83.33% of the episodes in the present study; however, 3 (16.67%) episodes showed no improvement or progressive lesions. This prevalence was similar to that recently reviewed by Ferreira et al. [23]. The rapid resolution of the imaging studies supported the capillary leakage from systemic hypertension and the effects of vascular endothelium as the cause of PRES [5].

Recurrent episodes of PRES occurred in 20% of the patients in this study, which was slightly higher than the 15.53% in that of Lai et al. [16]. Patients who had recurrent episodes in this study had very active lupus nephritis and poorly controlled hypertension. In addition, ICH was observed in 2 (6.67%) episodes in this study, which was lower than the 15.38% in that of Lai et al. [16], and the 26.92% in a recent review by Ferreira et al. [23]. Despite ICH being identified, neurological symptoms in these 2 patients improved shortly after their blood pressure was under control. Hypoalbuminemia (< 20 gm/L) and thrombocytopenia ($< 30 \times 10^9$/L) were found to be risk factors associated with ICH [16]. However, the patients who had 2 episodes of ICH in this study did not have hypoalbuminemia or thrombocytopenia.

Treatment of PRES in SLE includes the use of antiepileptic and anti-hypertensive drugs. High-dose corticosteroids and immunosuppressive drugs are used according to the activity and severity of organ involvement in SLE. It should be noted that patients in the PRES group had a tendency to receive more cyclophosphamide and mycophenolate mofetil, which might reflect more in this group on active disease and nephritis, and a higher proportion of patients in the control group received more hydroxychloroquine, which might reflect less severity of the disease, as determined by the mSLEDAI score prior to the onset of PRES.

The development of PRES shortly after IVMP and IVCP has been previously mentioned [24–26], and 6 patients in the present study had been given intravenous IVCY (4 of them also received IVMP) within 1 month prior to developing PRES. High-dose glucocorticoids might enhance abnormal vascular tone and the cytotoxic effect of cyclophosphamide on the vascular endothelium has been proposed as the mechanism [25, 26]. However, it is difficult to assume that PRES was attributed to these 2 drugs, as SLE patients who developed PRES tended to have active disease and received many medications. In addition, the number of reported PRES cases in SLE patients seems to be very small when compared with the number of SLE patients that have been given IVMP and IVCY. Therefore, the role of these 2 medications in the development of PRES needs further studies.

The mortality rate of 29.17% in PRES patients in this study was significantly higher than that of the controls. The 16.67% of deaths that occurred within 3 months after PRES onset also was also high. It should be noted that the major causes of death were not related directly to PRES. The mortality rate was reportedly 30.00% from South Africa [27], 26.92% from Taiwan [16], 13.33% from Korea [14], 7.69% from India [13], and 4.76–6.25% from Mexico [9, 28]. However, there was no mortality reported from Canada [7], USA [6], or Malaysia [12]. Whether the high mortality rate was related to ethnicity or the healthcare system was not clear. In this study, the high mortality rate might have been related to a very active disease and the presence of extra-renal manifestations, as determined by the very high mean ± SD mSLEDAI score of 22.90 ± 7.17 during PRES episodes and even 11.17 ± 4.62 when the neurological component was excluded (mSLEDAI-N). A high SLEDAI score ≥ 18 without the neurological component (SLEDAI-N) has been associated with increased mortality [16]. The mSLEDAI-N in patients in this study was lower than that reported by Lai et al. [16], as 4 points from the complement and the dsDNA components were not included in the scores.

This study found that anemia (hemoglobin < 10 gm/dL) and proteinuria (UPCR > 1.0) were associated factors of PRES. The presence of active nephritis during PRES episodes has been well recognized. However, in a multicenter case-controlled study involving 48 cases of PRES and 96 controls, Merayo-Chalico et al. [9] found that hypertension, renal dysfunction, lymphopenia, SLEDAI score of ≥ 6, and younger age at onset were independent associated factors of PRES. In another case-controlled study involving 15 cases of PRES and 48 controls, Jung et al. [14] found that only renal insufficiency (creatinine ≥ 1.5 mg/dL) was an independent risk factor of PRES. To the authors' knowledge, the presence of anemia found in this study has never been described as an independent associated factor of PRES in SLE. Further studies need to confirm this finding.

The strength of this study was due to it being a controlled study. The control subjects were recruited from the same SLE cohort, had a hospital number that was close to the case, and SLE diagnosis within 5 years to the case, which ensured that the cases and controls had similar lupus healthcare. Despite many studies having reported that active lupus nephritis is a risk factor for PRES in SLE, only a few of them were performed on a case-control basis [9, 14]. However, there are still some limitations in this study. The medical records were reviewed retrospectively, therefore, some clinical and laboratory data might be missing. In addition, the treatment of SLE and PRES depended on discretion of the consultant rheumatologists. Not all patients had received an MRI brain imaging study either initially or for follow-up, mainly due to the reimbursement in healthcare policy for the patients, which made the precise location of the lesions and follow-up of the disease difficult. However, all brain imaging in this study was reviewed by neuro-radiologists, who were well experienced in reading neuro-imaging. Therefore, errors in interpretation or misclassification of the lesions would likely be minimal. The small number of cases might be an issue and have some impact on the statistical analysis. However, the 30 PRES

episodes among 24 patients from a single center in this study should not be considered as small when compared with the 48 PRES episodes among 43 patients from the multicenter study of Merayo-Chalico et al. [9]. Lastly, the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC-DI) was not determined in this study. It might be of interest to see if the SLICC-DI was associated with the mortality rate in this study. The presence of high SLICC damage score has been shown to associate with high mortality [29].

Conclusion

This study described the clinical characteristics and associated factors of PRES in Thai patients with SLE. PRES usually occurred in those who had active disease, particularly active renal involvement. The clinical features, brain imaging study, and outcomes of PRES in Thai patients with SLE were similar to those described previously. The presence of high-degree proteinuria (UPCR > 1.0), which reflected underlying active nephritis and anemia (recent hemoglobin < 10 gm/dL), was found to be an independent associated factor of PRES. The presence of anemia as an associated factor of PRES needs to be confirmed.

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Compliance of ethical standard

Disclosures None.

Ethical approval This study was performed in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the Ethical Committee of the Faculty of Medicine, Chiang Mai University.

References

1. Govoni M, Bortoluzzi A, Padovan M, Silvagni E, Borrelli M, Donelli F et al (2016) The diagnosis and clinical management of the neuropsychiatric manifestations of lupus. J Autoimmun 74:41–72
2. Lamy C, Oppenheim C, Meder JF, Mas JL (2004) Neuroimaging in posterior reversible encephalopathy syndrome. J Neuroimaging 14: 89–96
3. Bartynski WS, Boardman JF (2007) Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. AJNR Am J Neuroradiol 28:1320–1327
4. Fischer M, Schmutzhard E (2017) Posterior reversible encephalopathy syndrome. J Neurol 264:1608–1616
5. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A et al (1996) A reversible posterior leukoencephalopathy syndrome. N Engl J Med 334:494–500
6. Ishimori ML, Pressman BD, Wallace DJ, Weisman MH (2007) Posterior reversible encephalopathy syndrome: another manifestation of CNS SLE? Lupus 16:436–443
7. Barber CE, Leclerc R, Gladman DD, Urowitz MB, Fortin PR (2011) Posterior reversible encephalopathy syndrome: an emerging disease manifestation in systemic lupus erythematosus. Semin Arthritis Rheum 41:353–363
8. Magnano MD, Bush TM, Herrera I, Altman RD (2006) Reversible posterior leukoencephalopathy in patients with systemic lupus erythematosus. Semin Arthritis Rheum 35:396–402
9. Merayo-Chalico J, Apodaca E, Barrera-Vargas A, Alcocer-Varela J, Colunga-Pedraza I, Gonzalez-Patino A et al (2016) Clinical outcomes and risk factors for posterior reversible encephalopathy syndrome in systemic lupus erythematosus: a multicentric case-control study. J Neurol Neurosurg Psychiatry 87:287–294
10. Kur JK, Esdaile JM (2006) Posterior reversible encephalopathy syndrome—an underrecognized manifestation of systemic lupus erythematosus. J Rheumatol 33:2178–2183
11. Gatla N, Annapureddy N, Sequeira W, Jolly M (2013) Posterior reversible encephalopathy syndrome in systemic lupus erythematosus. J Clin Rheumatol 19:334–340
12. Shaharir SS, Remli R, Marwan AA, Said MS, Kong NC (2013) Posterior reversible encephalopathy syndrome in systemic lupus erythematosus: pooled analysis of the literature reviews and report of six new cases. Lupus 22:492–496
13. Varaprasad IR, Agrawal S, Prabu VN, Rajasekhar L, Kanikannan MA, Narsimulu G (2011) Posterior reversible encephalopathy syndrome in systemic lupus erythematosus. J Rheumatol 38:1607–1611
14. Jung SM, Moon SJ, Kwok SK, JH J, Park KS, Park SH et al (2013) Posterior reversible encephalopathy syndrome in Korean patients with systemic lupus erythematosus: risk factors and clinical outcome. Lupus 22:885–891
15. Liu B, Zhang X, Zhang FC, Yao Y, Zhou RZ, Xin MM et al (2012) Posterior reversible encephalopathy syndrome could be an underestimated variant of "reversible neurological deficits" in systemic lupus erythematosus. BMC Neurol 12:152
16. Lai CC, Chen WS, Chang YS, Wang SH, Huang CJ, Guo WY et al (2013) Clinical features and outcomes of posterior reversible encephalopathy syndrome in patients with systemic lupus erythematosus. Arthritis Care Res (Hoboken) 65:1766–1774
17. Fujieda Y, Kataoka H, Odani T, Otomo K, Kato M, Fukaya S et al (2011) Clinical features of reversible posterior leukoencephalopathy syndrome in patients with systemic lupus erythematosus. Mod Rheumatol 21:276–281
18. The American College of Rheumatology (1999) The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. Arthritis Rheum 42:599–608
19. Hochberg MC (1997) Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 40:1725
20. Uribe AG, Vila LM, McGwin G Jr, Sanchez ML, Reveille JD, Alarcon GS (2004) The Systemic Lupus Activity Measure-revised, the Mexican Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), and a modified SLEDAI-2K are adequate instruments to measure disease activity in systemic lupus erythematosus. J Rheumatol 31:1934–1940
21. Jakes RW, Bae SC, Louthrenoo W, Mok CC, Navarra SV, Kwon N (2012) Systematic review of the epidemiology of systemic lupus erythematosus in the Asia-Pacific region: prevalence, incidence, clinical features, and mortality. Arthritis Care Res (Hoboken) 64: 159–168
22. Mok MY, Li WL (2010) Do Asian patients have worse lupus? Lupus 19:1384–1390

23. Ferreira TS, Reis F, Appenzeller S (2016) Posterior reversible encephalopathy syndrome and association with systemic lupus erythematosus. Lupus 25:1369–1376
24. Jabrane M, Ait Lahcen Z, Fadili W, Laouad I (2015) A case of PRES in an active lupus nephritis patient after treatment of corticosteroid and cyclophosphamide. Rheumatol Int 35:935–938
25. Chennareddy S, Adapa R, Kishore BK, Rajasekhar L (2013) Posterior reversible encephalopathy syndrome in systemic lupus erythematosus following methylprednisolone: report of two cases. Int J Rheum Dis 16:786–788
26. Jayaweera JL, Withana MR, Dalpatadu CK, Beligaswatta CD, Rajapakse T, Jayasinghe S et al (2014) Cyclophosphamide-induced posterior reversible encephalopathy syndrome (PRES): a case report. J Med Case Rep 8:442
27. Budhoo A, Mody GM (2015) The spectrum of posterior reversible encephalopathy in systemic lupus erythematosus. Clin Rheumatol 34:2127–2134
28. Baizabal-Carvallo JF, Barragan-Campos HM, Padilla-Aranda HJ, Alonso-Juarez M, Estanol B, Cantu-Brito C et al (2009) Posterior reversible encephalopathy syndrome as a complication of acute lupus activity. Clin Neurol Neurosurg 111:359–363
29. Sutton EJ, Davidson JE, Bruce IN (2013) The systemic lupus international collaborating clinics (SLICC) damage index: a systematic literature review. Semin Arthritis Rheum 43:352–361