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Characteristics, treatments and outcome of psychosis in Thai SLE patients

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ABSTRACT

Objectives: To study the clinical characteristics and outcomes of psychosis and its clinical correlation with disease activity in Thai systemic lupus erythematosus (SLE) patients.
Methods: From 750 SLE patients, 36 episodes of psychosis or psychotic depression in SLE patients were retrospectively identified between June 1999 and June 2009 at Srinagarind Hospital, Khon Kaen University. The clinical characteristics, laboratory analyses, disease activity, treatments and outcomes were studied.
Results: A total of 35 SLE patients had 36 psychotic episodes that consisted of 29 psychotic episodes and 7 psychotic depressive episodes. Eleven episodes (30.6%) occurred during the first manifestation of lupus. Psychotic symptoms included persecutory delusion (50%), bizarre delusion (44.4%), third person auditory hallucinations (44.4%) and visual hallucinations (36.1%). Twenty four episodes (67%) were associated with active lupus in CNS and other organs. All patients received immunotherapy and psychotropic treatments. Psychosis and depressive psychosis were treated with antipsychotics and antidepressants for a mean duration of 71 and 410 days. One death resulted from suicide, and one of thirty four cases (2.9%) had a reoccurrence within a mean follow-up period of 44 months.
Conclusion: About one-third of the psychotic episodes occurred during the first manifestation of lupus. Persecutory delusion, bizarre delusion, third person auditory hallucination, and visual hallucination were common. During psychotic episodes, lupus activity was active in other parts of CNS and organs in 67% of patients. Depressive psychosis required psychotropic treatment longer than psychosis alone. The psychiatric outcome was very favorable. Most of psychotic episodes (97.1%) were fully remitted and rarely showing recurrences.

Systemic lupus erythematous (SLE) is an autoimmune disorder which manifests with systemic inflammation. It can cause abnormalities to either the central or the peripheral autonomic system and can result in a wide range of neuropsychiatric (NP) disorders. In 1999, American College of Rheumatology (ACR) presented neuropsychiatric systemic lupus erythematosus (NPSLE) as a standardized group of SLE-induced NP disorders [1]. NPSLE which required psychiatric attention included acute confusional state (delirium), affective disorders, cognitive impairment, and psychosis. Since clinical presentations and laboratory findings varied widely among each of the NPSLE patients, further study was warranted for each individual disorder.

Psychosis and seizure were the only 2 NP manifestations in which ACR included in diagnostic criteria for SLE [2]. Psychosis is a mental state which is characterized by hallucination, thought disturbance and disorganized behavior. The clinical condition is probably mediated by autoantibodies, microvasculopathies and the intracranial production of inflammatory mediators [3]. Many studies have found that the prevalence of psychosis ranged from 1 to 22.3% [4–14] in the SLE population. Psychosis may be influenced by disease-related psychological stressors [15] and it usually has occurred during an aggravation of lupus activity, especially skin rashes and vasculitis [12,13]. Treatment options for psychosis in lupus patients included the use of immunosuppressive agents to control disease activity and supportive management with psychotropic medications [16]. However, characteristic, treatment and outcomes of this rare syndrome are not well established. Furthermore, none of the previous publications have mentioned psychotic depression which appears to be an overlap syndrome between depression and psychosis. By using the definition of NPSLE from ACR, this group of SLE patients who had been diagnosed with either psychosis or psychotic depression were studied in order to report the following: 1) their clinical characteristics and laboratory data, 2) treatment options for patients, and 3) and long term outcomes of patients.

Patients and methods

This study was approved for all research procedures by the Ethics Committee in Human Research of the Khon Kaen University (EC code: HE521089).

From 1 June 1999 to 1 June 2009, a total of 750 SLE patients were registered in the database at Srinagarind hospital, Faculty of Medicine, Khon Kaen University, Thailand. The database was coded in the

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ICD-10 format. As ACR has previously proposed, mental disorders which have occurred from a direct consequence of SLE can be considered under two categories: "mental disorder due to general medical condition" in the Statistical Manual of Mental Disorders 4th edition (DSM-IV) [17] and "organic mental disorder" category in the International Statistical Classification of Diseases 10th Revision (ICD-10) [18] nomenclatures. The database was scrutinized using the ICD code as above and a total of 76 inpatients and outpatients records were found. All records were included in this study. The clinical information of each visit of every patient was collected, and then all of the psychiatric episodes were carefully reviewed. Since the main objective was to study real NP episodes, the criteria ensured that all of psychotic episodes did not occur as a result of other metabolic or medication-induced conditions. The majority of steroid-induced psychosis usually occurred within 5–14 days [19] after initiating and increasing corticosteroid dosage, and these episodes were likely to respond after the dose had been tapered within a week. Therefore, psychotic episodes which occurred within 5–14 days after initiating and increasing steroid therapy, and the psychotic episodes which responded to dose tapering within 7 days were excluded due to a high possibility that the episodes were actually steroid induced psychosis [20,21]. Overall, a total of 40 records were excluded for the following reasons: 1) 12 records were incomplete, 2) 10 records did not meet at least four of ACR 1997 criteria for SLE [2], and 3) 18 episodes were likely to be steroid-induced psychosis. None of patients have had a preexisting primary psychotic disorder.

From the 36 remaining records, 17 patients had not had complete follow up by the end of June 2009. In order to detect any psychotic episode during loss of follow up, one psychiatrist performed the Mini International Neuropsychiatric Interview, Thai version 5 (MINI Thai version 5), module L (psychotic disorders) [22], via phone calls with all patients and knowledgeable caregivers. Thus, it was very unlikely that any psychotic episode would have been missed.

Patient data were retrospectively reviewed from medical records. Demographic data collected were the age of onset of SLE, clinical manifestations of SLE, laboratory findings of SLE during each psychotic episode, characteristics of psychotic episode, duration, treatments and outcomes of each episode. Hematologic involvement was defined by having the autoimmune hemolytic anemia (AIHA) blood picture with a positive direct Coomb's test. Renal involvement was defined by evidence of protein in the urine of more than 0.5 g/day, or presenting of red blood cells, or confirmation via renal biopsy. Central nervous system (CNS) involvement was defined by diagnosis of other neurological disorders than psychosis. In the investigations, the most significant result of the repeated evaluations done during each psychotic episode like complete blood count and serum complement level, that could explain the temporal relationship with the NP symptoms, was used. A complete resolution of positive symptoms and a return of function reported by caregivers were considered as remission.

Results

Patients

All of the patients were Thai. Thirty five patients had a total of thirty six psychotic episodes. There were 29 psychotic episodes and 7 psychotic depressive episodes; only 1 patient in the psychosis group had a recurrence of psychosis. Average ages were 29.97 (SD ± 12.77) and 26.14 (SD ± 7.96) years for psychosis and psychotic depression group, respectively. Most of the patients were female with only three males (11%) in the psychosis group.

SLE manifestations, characteristic of psychotic episodes and psychotic depression episodes

In the psychosis group, an average delay of psychosis from SLE onset was 35.9 months (SD ± 52). In 9 patients (32.1%), psychosis appeared in first visit of SLE. Twenty-two (75.8%) patients were being treated with corticosteroids at an average dose of 27.7 mg/day (SD ± 23.4). For the psychotic depressive group, 2 episodes (29%) appeared in first visit of SLE. All patients (100%) were being treated with corticosteroids at an average dose of 45 mg/day (SD ± 21.4). The average delay from lupus onset was 40.1 months (SD ± 44.6).

From the total subjects of both groups, active organs involvement occurred in 24 episodes (67%). Active organ involvement included renal (39%), hematologic (36%), skin rashes (22%), central nervous system (19%), arthritis (8%), vasculitis (5%), and cardiac (3%). Central nervous system involvement, other than psychosis, was comprised of 4 cerebral ischemia, 2 seizures and 3 encephalopathies. Twenty nine patients (80.6%) were being treated with corticosteroids at an average dose of 31.1 mg/day (SD ± 23.8). All of demographic data and SLE manifestations that occurred during psychotic episodes are summarized in Table 1.

Psychotic elements of both groups included persecutory delusion (50%), bizarre delusion (44.4%), third person auditory hallucinations (44.4%), complex visual hallucinations (36.1%), auditory and visual hallucinations (17%), and controlled delusions (17%). From the 7 depressive psychotic episodes, guilty delusion occurred 3 times (43%). According to DSM-IV criteria, the average severity of depression was moderate by 5.5(SD ± 1.4). The characteristics of psychosis in each group are detailed in Table 2.

Investigation

During psychotic episodes, the average blood levels of both C_3 and C_4 were normal in both groups. ANA was positive in 33 patients (92%), antiphospholipid antibody was positive in 3 patients, but we were unable to perform anti-ribosomal P antibody testing. Neuroimaging (CT or MRI) was done in 21 episodes (72%) during psychosis, and abnormal findings were described in 15 of the 21 patients (72%). Seven of the fifteen (47%) patients had mild to moderate brain atrophy while other abnormalities included 4 ischemic processes at frontal lobe and basal ganglia, 1 leptomeninges involvement and 4 white matter hyperintensities. Lumbar puncture was performed in 15 patients, and elevated protein levels (above 45 mg/dL) were found in 6 samples. EEG was performed on 3 patients and all three demonstrated encephalopathy by exhibiting a diffused slow wave, while 2 of them had co-existing epileptic activity.

Neuropsychiatric treatment and outcome

All 36 psychotic episodes required hospitalization and both immunotherapy and symptomatic treatments were also required. Patients were treated with methylprednisolone 1 g daily for 3 days (58.3%) or cyclophosphamide 500 mg every 2 weeks (8%) or with both (19.4 %). All of psychotic episodes required antipsychotic treatment; haloperidol, risperidone, and quetiapine were used in 23, 4 and 2 episodes. All episodes were fully remitted with an average haloperidol dose and duration of treatments of 5.9 (SD ± 7.7) mg/day and 71 (SD ± 61) days. Depressive psychotic patients required both antidepressant and antipsychotic treatment. A combination of fluoxetine and haloperidol was used in six (85%) patients with an average dose of 30 mg/day and 5 mg/day. The mean duration of treatment in depressive psychosis was 410 days (SD ± 379 days) due to the prolonged use of antidepressant. Another patient (15%) was successfully treated with a combination of paroxetine and risperidone.

One death occurred from suicide by a drug resistant patient in the psychosis group. One (2.9%) of thirty four remaining patients had a recurrence of psychosis after 4 years of remission while other psychotic episodes remitted completely during the mean follow up of 44 (SD ± 29.7) months.

Table 1
Demographic data and clinical manifestations of lupus during psychotic episodes.

Demographic data	Psychosis episodes	Depressive psychotic episodes
	(*N* = 29)	(*N* = 7)
Age (years)	29.97 ± 12.77	26.14 ± 7.96
Appear in first visit of SLE	9 (32.1%)	2 (28.6%)
Previous episode of lupus psychosis	1	0
Delay of psychotic presentation (months)	35.9 ± 52	40.1 ± 44.6
Organ involvement		
Any organ involvement	20 (69%)	4 (57.1%)
Renal	11 (37.9%)	3 (42.9%)
Vasculitis	1 (3.4%)	1 (14.3%)
Pulmonary	0 (0%)	0 (0%)
Cardiac	1 (3.4%)	0 (0%)
Serositis	0 (0%)	0 (0%)
Hematologic	12 (41.4%)	1 (14.3%)
CNS (other than psychosis)	6 (20.7%)	1 (14.3%)
Skin rash, vasculitis	6 (20.7%)	2 (28.6%)
Arthritis	2 (6.9%)	1 (14.3%)
Medications		
Corticosteroid	22 (75.8%)	7 (100%)
Average corticosteroid (mg/day)	27.7 ± 23.4	45 ± 21.40