

Chronic Schizophrenia Comorbid with Neuropsychiatric Systemic Lupus Erythematosus

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Background: The neuropsychiatric events are frequently encountered in patients with systemic lupus erythematosus (SLE). The psychotic symptoms and cognitive dysfunctions are relatively common in SLE with central nervous system (CNS) involvement. **Case Report:** We present a patient with SLE with CNS involvement, who has also carried a diagnosis of schizophrenia for nine years. The presentation of progressive cognitive impairment suggested the diagnosis of SLE with CNS involvement. The result of the neuropsychological assessment showed great improvement after a six-month immunosuppressant therapy, especially in the dimensions of verbal and visual memory. The brain perfusion scan also showed the finding of remarkable improvement after treatment. **Conclusion:** This case shows the differences and complex presentations in psychopathology, neuropsychological tests, and brain imaging in those two diseases. Clinicians should be alert for considering other organic causes for progressive cognitive impairments in the course of chronic schizophrenia.

Key words: neuropsychiatric systemic lupus erythematosus, schizophrenia, central nervous system involvement, cognitive impairment
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Introduction

Neuropsychiatric events are frequently encountered in patients with systemic lupus erythematosus (SLE). These SLE psychiatric abnormalities are common with a broad prevalence range of

17% to 75% [1]. According to the new American College of Rheumatology (ACR) criteria, the neuropsychiatric SLE (NPSLE) includes cognitive dysfunction, acute confusional state (delirium), anxiety disorder, mood disorder, and psychosis [2]. The prevalence of cognitive dysfunction in NPSLE is around 80% using standardized neuro-

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psychological tests, the prevalence of psychosis is estimated 5% [2].

We present a patient who showed symptoms of schizophrenia and several autoimmune-related symptoms for more than 10 years and a new onset of cognitive impairment, leading to a diagnosis of SLE with CNS involvement. Then, we compare and discuss the psychopathology, neuropsychological tests and brain images between those two diseases.

Case Report

A 55-year-old female patient was admitted to our psychiatric ward with the chief complaints of a restless feeling and insomnia in June 2008. After admission, we found that she had prominent cognitive impairment, especially in recent memory. Although she also had systematized delusion of persecution, we found that she did not have emotional or behavioral response to those delusions, which was similar to the condition in the long-term clinic follow up, i.e., the psychotic symptoms had not been aggravated.

Tracing back her past history, we noted that the patient claimed to have ideas of reference at the age of 26 years. Since then, she went to psychiatric clinic sometimes for feeling that her father would persecute her. About at the same time, she also had chronic glomerulonephritis and received irregular medical treatment for this problem. She had been diagnosed to have paranoid schizophrenia formally during the first hospitalization on our psychiatric ward when she was 46 years old. She presented herself with having a systematized persecutory delusion of the feeling of being monitored and followed as well as having auditory hallucinations. During that first hospitalization, she was also found to have ankylosing spondylitis, iron deficiency anemia, hypertension,

and leukopenia. She had been admitted to our psychiatric ward six times for worsened psychotic symptoms due to poor compliance in taking antipsychotic drugs, and presence of residual psychotic symptoms of persisting systematized delusions between episodes. During her fourth admission in 2005, She was suspected to have SLE for the first time because of restless legs at night, leukopenia, lymphopenia and abnormal autoimmune profiles. She received hydroxychloroquine 400 mg/day in the rheumatology outpatient clinic from 2005 to 2007. But she did not have any further signs or symptoms to be confirmed for the diagnosis of SLE, and she had not shown any prominent cognitive impairments until the index admission (the seventh admission). At that time, she performed adequately in the rehabilitation program in our day hospital and studied at the post-graduate school.

The patient had the new onset of prominent cognitive impairment and past history of autoimmune disorder. In doing thorough physical and laboratory check-ups, we found that she had photosensitivity, leucopenia, lymphopenia, impaired renal function, proteinuria and abnormal autoimmune profiles of abnormal antinuclear antibody (ANA) (1:40 +, Speckle) and IgG anticardiolipin (+, 30.3 U/ml). She received a complete battery of neuropsychological tests covering eight cognitive domains. In the publication elsewhere, we compared her z scores on neurocognitive performances in the eight cognitive domains with those of the norms in our population [3].

Figure 1 shows the patient's neurocognitive performances over the treatment course. Figure 2 is the nuclear perfusion study over the treatment course. And Figure 3 revealed brain MRI changes before and after the immunosuppressant pulse therapy.

After receiving treatment with hydroxychloroquine, methylprednisolone, and cyclophospha-

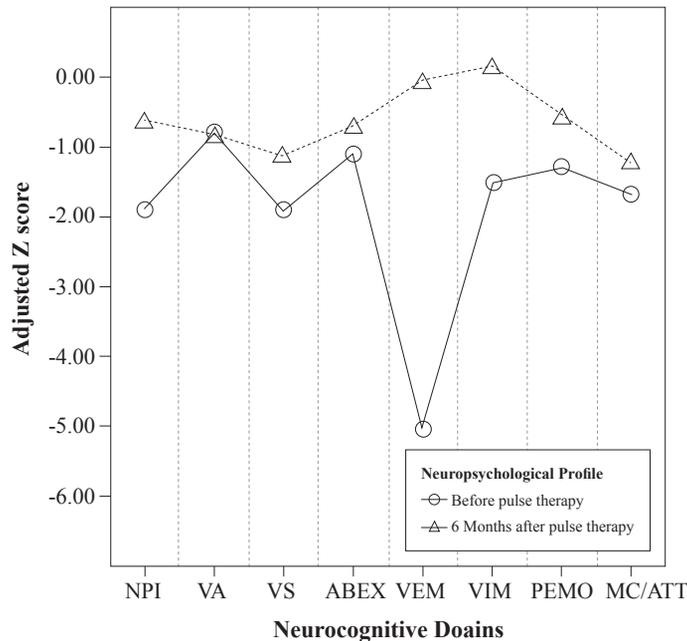


Figure 1. Patient’s neuropsychological performance over the treatment course. The scores of neuropsychological tests were calculated as the adjusted z scores in the eight neurocognitive domains using the norms of our population [3]. The line with circle: before the immunosuppressant pulse therapy. The dotted line with triangle: six months after the pulse therapy. Abbreviations: NPI = neuropsychologic performance index, VA = visual ability, VS = visual/spatial ability, ABEX = abstraction/execution, VEM = verbal memory, VIM = visual memory, PEMO = perceptual/motor, and MC/ATT = mental control/Attention.

mid pulse therapy monthly for six months, the patient improved in SLE parameters ANA (1:40, -) and decreased IgG anticardiolipin (30.3 U/ml reducing to < 15 U/ml). Her renal function was improved with decreased protein loss. She continued to receive olanzapine 20 mg per day. Her psychotic symptoms remained in a residual state with manifestations of systematic delusions but without emotional or behavioral disturbances. The results of follow-up neuropsychological tests after six months showed remarkable improvement in the domains of verbal memory (VEM) and visual memory (VIM) as well as mild improvement in the overall neuropsychological performance index

(NPI) and the domains of visual spatial ability (VS) and perceptual motor ability (PEMO) (Figure 1). Her SPECT finding showed significant improvement on the follow-up study, especially at the bilateral occipital regions (Figure 2B). But the finding of follow-up brain MRI was unchanged (Figure 3B).

Discussion

Our patients, in our opinion, had two probable diagnoses. The first diagnosis was SLE with schizophrenic symptoms, and the other one was the dual diagnosis of schizophrenia and SLE dur-

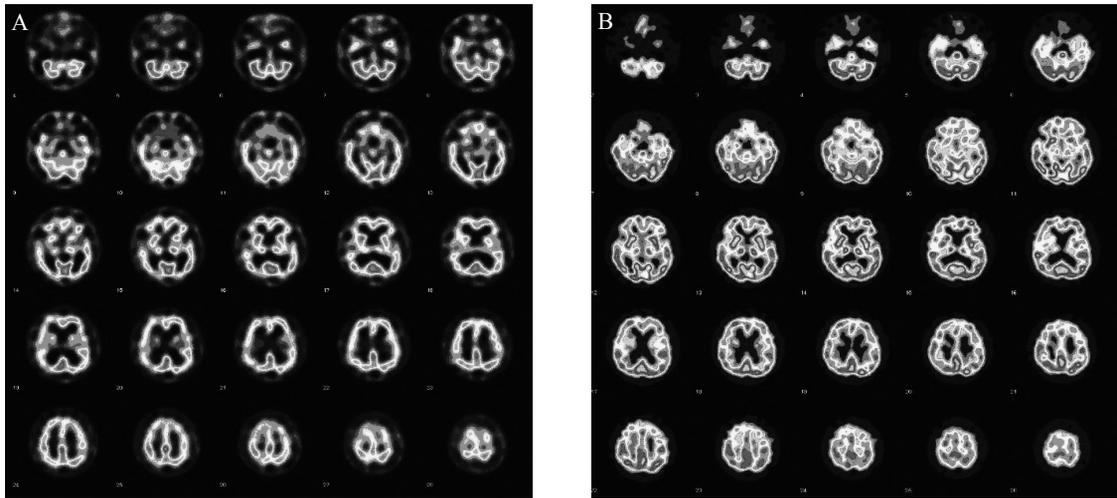


Figure 2. Nuclear brain perfusion scintigraphy over the treatment course. (A) Before the immunosuppressant pulse therapy, diffusely decreased Tc-99m ethyl cysteinate dimer (ECD) activity was revealed at bilateral cerebral hemispheres with relative preserved perfusion to bilateral occipital cortices, cerebellum, thalami, and basal ganglia. (B) Follow-up nuclear brain perfusion scan (six months after pulse therapy) showed improved perfusion to the cerebral cortices comparing to the pre-treatment images.

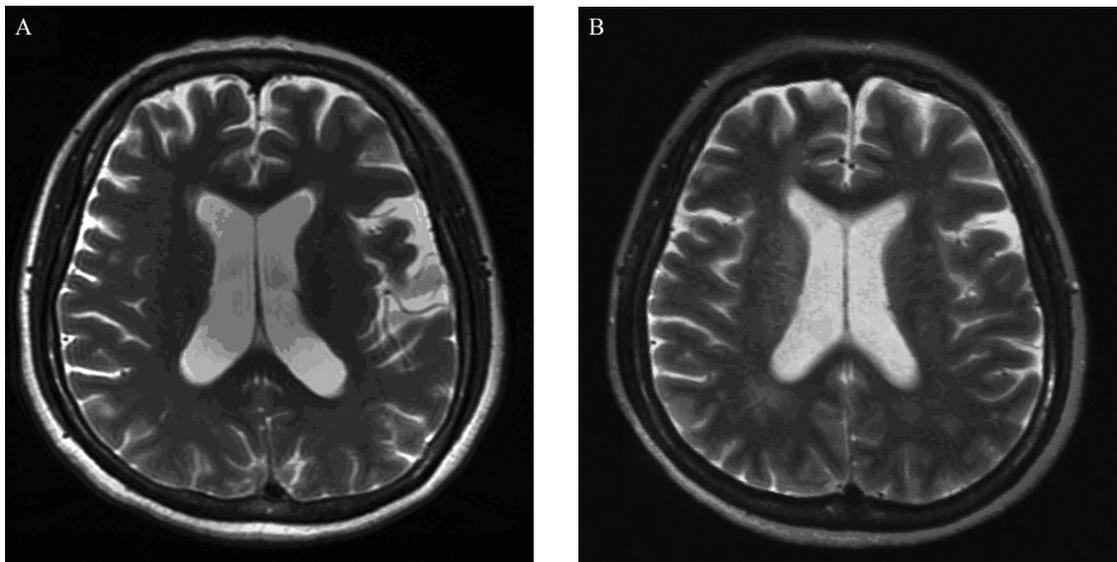


Figure 3. Brain magnetic resonance imaging (MRI) over the treatment course. (A) Before the immunosuppressant pulse therapy, it showed mild brain atrophy, ventriculomegaly and leukoaraiosis. (B) Follow-up brain MRI (six months after pulse therapy) showed no obvious change on the follow study.

ing its clinical course. Here, we are going to discuss those issues in the contexts of psychotic symptoms and neurocognitive functions as well as the findings of her brain SPECT and MRI.

In the literature, the prevalence of psychosis due to SLE has been around 3%-5% [2]. Lupus psychosis is characterized as usually occurring early in the course of the disease and associated with other SLE clinical and biological features. Most patients with SLE are diagnosed within one year after the onset. The psychotic symptoms are responded to immunosuppressant treatment, and long-term remission is frequent [4]. A nine-year delay between psychosis and SLE diagnosis shown in this patient is uncommon. The psychotic symptoms of our patient were responded well to antipsychotic drugs but not to low dose immunosuppressants in the rheumatology outpatient clinic. In the treatment course of our patient, her residual psychotic symptoms of systematized delusions were not respond to immunosuppressant pulse therapy. Because of this clinical finding, we favored the dual diagnoses of schizophrenia and NPSLE for this patient. But we do not know if the treatment response of her psychotic symptoms to immunosuppressants would have been better if she had received them earlier in the course of the disease.

In our patients, the domains with marked improvement after a six-month treatment were verbal memory and visual memory, whereas those with mild improvement were the overall neuropsychological performance index, visual spatial ability, and perceptual motor ability. As described elsewhere [3], the relatively impaired domains for schizophrenia were abstraction/execution, verbal memory, visual memory and attention. SLE-associated cognitive dysfunction include impaired verbal memory, visuoconstructional abilities, and decreased psychomotor speed [5-7]. Our patient

was found to have predominant symptoms of delusion and hallucination characteristic of paranoid schizophrenia with relative preservation of abstraction/execution function before this index admission. Impaired in verbal memory, visual memory, visual spatial ability, and perceptual motor ability might have been related to SLE since they responded well to immunosuppressant pulse therapy. The neuropsychological findings in this patient can be interpreted as those of a case of acute or sub-acute NPSLE with prominent impairment in the domains of verbal memory, visual memory, visual spatial ability, and perceptual motor ability, superimposed on the course of paranoid schizophrenia without prominent cognitive impairment.

On brain MRIs, the images associated with schizophrenia are enlargement of the lateral and the third ventricles and decreased brain tissue in the temporal lobe and medial temporal structures [8]. The finding of brain SPECT shows that temporal lobe hypoperfusion is frequently associated with ipsilateral frontal lobe hypoperfusion, especially during a specific task [9]. On the other hand, the findings of the brain MRI of NPSLE commonly shows small punctate focal lesions in subcortical white matter (15%-60%), cortical atrophy, periventricular white matter changes, ventricular dilatation, and major infarcts. The SPECT finding reveals widespread multifocal patchy hypoperfusion in the parietal lobes (65%-80%), frontal lobes (57%-65%), temporal lobes (46%-57%), and basal ganglia (12%-30%) [10]. In our patient, the findings of brain SPECT were not typical of chronic schizophrenia, but were more likely those of NPSLE. To differentiate lesions of active and chronic NPSLE is also hard because of the rather wide-spread patchy hypoperfusion. But we suggest that the findings on brain SPECT indicate acute rather than chronic NPSLE, because brain perfusion was improved after receiving immuno-

suppressant therapy. The findings of brain MRI were non-specific and unchanged with treatment. Therefore, we cannot judge whether the findings of brain MRI come from schizophrenia or NPSLE. The relationship between the change of occipital lobe in SPECT and improvement in neurocognitive function in this patient still needs further discussion for their correlation.

In patient's past history, she was diagnosed to have chronic glomerulonephritis when she was 26 years old. To pinpoint the definite time is difficult when SLE activities are flared up. Based on the findings of our patient's clinical presentation, treatment response, brain image and psychological tests, we favored the choice of the dual diagnosis of schizophrenia and SLE during its clinical course. This case does remind us of the importance of surveying autoimmune profiles in a patient presenting with psychotic symptoms, cognitive dysfunction and related clinical signs and symptoms of autoimmune disease. We should keep alert for any acute worsen cognitive function and related autoimmune symptoms in a patient with paranoid schizophrenia with relatively preserved cognitive function.

References

1. Stojanovich N, Zandman-Goddard G, Pavlovich S, Sikanich N: Psychiatric manifestations in systemic lupus erythematosus. *Autoimmun Rev* 2007; 6: 421-6.
2. Ainiala H, Hietaharju A, Loukkola J, et al.: Validity of the new American College of Rheumatology criteria for neuropsychiatric lupus syndromes: a population-based evaluation. *Arthritis Rheum* 2001; 45: 419-23.
3. Liu SK, Hsieh MH, Huang TJ, et al.: Patterns and clinical correlates of neuropsychologic deficits in patients with schizophrenia. *J Formos Med Assoc* 2006; 105: 978-91.
4. Pego-Reigosa JM, Isenberg DA: Psychosis due to systemic lupus erythematosus: characteristics and long-term outcome of this rare manifestation of the disease. *Rheumatology* 2008; 47: 1498-502.
5. Emori A, Matsushima E, Aihara O, et al.: Cognitive dysfunction in systemic lupus erythematosus. *Psychiatry Clin Neurosci* 2005; 59: 584-9.
6. Petri M, Naqibuddin M, Carson KA, et al.: Cognitive Function in a Systemic Lupus Erythematosus Inception Cohort. *J Rheumatol* 2008; 35: 1776-81.
7. Monastero R, Bettini P, Del Zotto E, et al.: Prevalence and pattern of cognitive impairment in systemic lupus erythematosus patients with and without overt neuropsychiatric manifestations. *J Neurol Sci* 2001; 184: 33-9.
8. Harrison PJ: The neuropathology of schizophrenia: a critical review of the data and their interpretation. *Brain* 1999; 122: 593-624.
9. Camargo EE: Brain SPECT in neurology and psychiatry. *J Nucl Med* 2001; 42: 611-23.
10. Govoni M, Castellino G, Padovan M, Borrelli M, Trotta F: Recent advances and future perspective in neuroimaging in neuropsychiatric systemic lupus erythematosus. *Lupus* 2004; 13: 149-58.