Cavum Vergae, Liability, and Steroid Treatment: Manic Episode, Brain Imaging Findings, and Clinical Follow-up of a Systemic Lupus Erythematosus Case

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ABSTRACT

Systemic lupus erythematosus (SLE) or Lupus is a chronic and idiopathic autoimmune connective tissue disease that involves several organs and organ systems. SLE may lead to a group of psychiatric manifestations, including delirium, anxiety disorders, cognitive dysfunction, mood disorders, and psychosis, which are caused by organic or non-organic factors. In addition, it is thought that the most common cause of neuropsychiatric lupus is corticosteroid use; central nervous system involvement and inflammatory processes also have an important role in the development of psychiatric manifestations. In other respects, structural brain abnormalities induce proneness

to psychotic and manic symptoms. Along with this proneness, cavum vergae, an anomaly closely related to the anatomic areas associated with mood regulation, may precipitate manic symptoms.

In this case report, we present a manic episode case emerging after delirium, with a 1-year history of SLE, which has recently been diagnosed with cavum vergae and discuss the process of infection and corticosteroid treatment, which contributed to the proneness effect of a structural brain anomaly.

Keywords: Systemic lupus erythematosus, cavum vergae, manic episode

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INTRODUCTION

Manic symptoms (i.e. elevated mood, energy increase, decreased need for sleep) can be seen in bipolar disorders and also can emerge due to substance use, various treatments or medical illness (1). Among other medical conditions and treatments linked with manic symptoms and periods, neuropsychiatric lupus and high-dose systemic glucocorticoid treatment also play an important role (1).

Systemic lupus erythematosus (SLE) is a chronic disease with an unknown etiology, characterized with exacerbation and remission periods, involving many systems through autoantibodies, complement system and immunocomplexes (2). Clinical manifestations can include fever, arthritis, skin rashes, pericarditis, pleuritis, nephritis, anemia, leucopenia, thrombocytopenia, and central nervous system involvement in exacerbation periods (2). In addition, a variety of neurological and psychiatric symptoms are frequently seen in SLE (3,4). According to the neuropsychiatric SLE criteria defined by Association of American Rheumatology (ACR), rate of neuropsychiatric symptoms varies between 37% and 95% in SLE patients (5,6). These neuropsychiatric manifestations include delirium, anxiety disorders, cognitive disorders, mood disorders, and psychotic disorders (3,6).

Both inflammatory and non-inflammatory processes play a big role in psychiatric symptoms of SLE (2,3,4). These processes induce proneness to psychiatric manifestations. Manic mood periods are seen in nearly 3% of Lupus patients (7,8). Manic periods are thought to be related to steroid treatment which is used to control the increasing disease involvements during exacerbation periods of SLE (9). On the basis of additional predisposition (i.e. increase of inflammatory cytokines, tissue damage due to autoantibodies, non-inflammatory vasculopathy and recent stressful life events), the likelihood for psychiatric disorders, involving manic periods, increases (3).

Septum pellucidum is a membrane with two folia located in interior wall of the lateral ventricles. Cavum septum pellucidum, which is a midline unity anomaly, is developed due to these two folia's inability to unite (10). This anomaly can be partial, or can have a separate cystic form in the lateral ventricles where the two leaflets do not unite completely. This severe anomaly is called as cavum vergae (10). The incidence of cavum vergae, which is the neighbor of amygdala, hippocampus, and corpus callosum, is higher among patients with bipolar and psychotic disorders compared to the normal population (11,12,13). Cavum vergae is likely a general predisposition for manic and psychotic symptoms (14).

In this case report, the structural brain anomaly of a newly diagnosed SLE patient with manic symptoms and its possible causes (such as structural brain anomaly, steroid treatment the disease itself) are discussed and the 1-year observation of the patient is presented.

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CASE

A 25-year-old male patient, married with two children, working at irregular occupations, primary school graduate, and followed-up with SLE diagnosis for the last year and 'macrophage activation syndrome (MAS)' for the last month was consulted during his hospitalization at the rheumatology department. The patient was evaluated by the rheumatology department at the emergency service and was hospitalized with an early diagnosis of 'pneumonia caused by MAS'. *Streptococcus pneumoniae* was found in the culture of sputum and intravenous levofloxacin treatment was initiated. The patient has also been taking acetylsalicylic acid (ASA) for the last 10 months.

On the fourth day of his hospitalization, the patient was consulted to the Neurology department because of sleeplessness and agitation, with the early diagnosis of delirium and cerebral vasculitis secondary to SLE. Neurology department recommended magnetic resonance imaging (MRI) of the brain and Psychiatry consultation. The patient and his relatives were interviewed. Approximately 10 days before admission and hospitalization, he started experiencing symptoms such as breakdown, deterioration, inability to sleep at night, attention deficit, use of foul language, and visual and auditory hallucination with fluctuation through the day. Cavum vergae was detected in the MRI of the brain, and no sign of contrast matter uptake or arterial wall thickening. Thus, cerebral vasculitis was ruled out. He was regarded to have delirium and a manic episode as clinical early diagnosis depending on his medical condition and parenteral haloperidol (5 mg ampoule for three times a day) was initiated. After his oral intake increased, his haloperidol dose was doubled to 10 mg. After a 1-week follow-up with this dosage, as the patient's infection and the delirium decreased, symptoms such as obscene language use, decrease in sleep need, increase in energy, increase in self-confidence, thought acceleration and tendency to spending money which can be verbally inhibited started to emerge. As the patient was considered to have a mood disorder (manic episode) due to his medical condition, haloperidol was stopped and olanzapine 10 mg/day was administered. The patient was discharged at the same day olanzapine was administered, he did not pose any danger to himself or to his surroundings, he had adequate social support and he was disposed to work cooperatively for his medical treatment. Thus, we planned to follow him up weekly in our outpatient clinic to regulate his medication, and to hospitalize him if needed.

Two weeks later, one week after discharge, it was learned that the methylprednisolone tablet 16 mg/day was administered in the rheumatology outpatient clinic, and the patient has dropped methylprednisolone dose to 4 mg/day within one day in the follow-up. On the other hand, we learned that the patient did not regularly use the recommended treatment and manic symptoms, including decreased need for sleep, increased energy, increased in goal-directed activity, abusive speech, increased speech rate and amount, have been present for a week with an increased severity. At the same time, there was an increase in religious practices and persecution ideas and it was found that the viewing behavior, which was judged to be a visual hallucination, improved. Yet, auditory hallucinations appeared again. Since the patient had no regular medication use and increased symptoms, he was admitted to the psychiatry clinic for further examination and treatment, with.

As a result of clinical evaluation conducted by Structured Clinical Interview for DSM-IV (First et al. 2002), his diagnosis was considered as mood disorder depending on the medical condition. The Young Mania Rating Scale (YMRS) score was calculated as 33. The brain MRI was evaluated again, and cavum septum pellucidum (cavum vergae) was identified (Figure 1). According to the sections obtained from the MRI, the size of cavum ver-

Figure 1. Cavum vergae detected in the case with magnetic resonance brain imaging at T2 sequence (marked with an arrow in axial section)

gae was defined as 12.4 mm and other brain structures appeared to be normal. No pathological finding was identified in other laboratory tests.

His treatment was arranged as valproic acid 1000 mg/day and olanzapine 20 mg/day. Due to psychomotor agitation and hallucinations, intramuscular injection of zuclopenthixol acetate 50 mg/mL was applied on the second and fifth day of his admission. His levofloxacin treatment for pneumonia was discontinued. Methylprednisolone treatment for SLE was recommended to be continued for the patient might be showing macrophage activation syndrome (MAS) symptoms.

On the seventh day of admission, the patient showed partial improvement in manic and psychotic symptoms. Thus, a weekly follow-up in outpatient clinic was planned. The YMRS score at discharge was 21, 18 in the first week after discharge and 5 in the third week of follow-up. The patient's manic and psychotic symptoms were improved completely one month after discharge.

Because olanzapine caused sedation, its dosage was gradually reduced with the request of the patient and quetiapine was started. The patient was followed up for two months with quetiapine 200 mg/day and valproic acid 1000 mg/day. At the end of this period, the patient stopped using the medication because of the improvement in symptoms. On the other hand, he showed up to his regular outpatient clinic controls for a year. Azathioprine was stopped and methotrexate was initiated for his rheumatologic treatment, because of the orchitis side effect.

There was no sign of a new mood symptom in the one-year follow-up since the first manic period of the patient. However, during the clinical follow-up, SLE exacerbations and associated manifestations continued (non-neuropsychiatric findings such as aseptic necrosis and myositis).

Informed consent was obtained from the patient in terms of this case presentation.

DISCUSSION

In this case report, the first manic period with psychotic symptoms was overcome in a patient diagnosed with SLE in the recent year and with no

past psychiatric complaint. Manic and psychotic symptoms in this case can be associated with SLE, cavum vergae that is a structural brain anomaly, intrusive infection, and steroid use. Recovery of nearly all of the symptoms with treatment and no recurrence being seen in the follow-up indicate that, the clinical condition is stimulated with medical factors (SLE, infection, and steroid use) based on the structural predisposition represented by cavum vergae.

Cavum vergae, a structural midline brain anomaly determined in MRI, is known to be seen more frequently in psychotic disorders compared to the normal population (11,12,13). The exposure of Papez loop (hippocampus-mammillary bodies-anterior thalamus-cingulate cortex-hippocampus), which is associated with emotion regulation, is thought to play a role in this (12). In contrast, the risk increase is considered significant for anomalies larger than 6 mm, which is notable in the present case (12,4 mm) (13). This predisposition can be important in the emergence of the clinical condition, including corticosteroid use, intrusive infection, and neuropsychiatric response, depending on SLE. Thus, SLE contains the highest risk of psychiatric disorder triggered by corticosteroid (9). The distinction of psychiatric conditions stimulated by steroid from neuropsychiatric SLE (NPSLE) is usually difficult (9). Manic term development in SLE is generally thought to be associated with corticosteroid use (7,9). However, data related to dose and expiration date are limited. Usually, manic or psychotic symptoms are reported to be seen more at doses of 40 mg/day or more (9). In this case report, steroid equivalent to 20 mg/day prednisone was used for a short term.

However, there are also manic periods which are relieved with steroid use in SLE patients (15,16). Moreover, in one SLE case report, the patient had no corticosteroid use, and the first admission to hospital was in the manic period (17). Therefore, there is a multidimensional relationship between SLE, steroid use, and manic periods, and it probably emerges with an underlying predisposition. The severity of manic symptoms in our case increased after the prednisolone dose was decreased. However, this period corresponds to the first week of initiation of corticosteroid treatment. This situation is a mixing factor in the establishment of a causative relationship between starting to steroid treatment or dose reduction and manic symptoms development.

On the other hand, although there is no exacerbation which shows widespread involvement in our patient, neuropsychiatric symptoms in SLE can be an extra indication of exacerbation (3). In neuropsychiatric SLE, intracranial microangiopathy, autoantibodies, and proinflammatory cytokines and mediators are thought to play role (3,18). Conditions, such as non-inflammatory vasculopathy, bleeding due to microangiopathy, antiribosomal-P antibody, anti NR-2 glutamate receptor antibody, and inflammatory cytokines are considered to play role in the pathophysiology (18,19,20). The infection in this case as a mixing factor may have stimulated the initiation of delirium and manic episode with inflammatory cytokine increase. Likewise, the inflammatory cytokine levels are found high in patients in manic episode, and the proinflammatory period is thought to be present beneath manic periods (21). Intrusive infection and SLE exacerbation may have caused structural predisposition to turn into a psychiatric condition (the first manic episode) in our case.

Systemic lupus erythematosus an autoimmune connective tissue leading to common systemic involvement, can cause many psychiatric conditions. Organic and inorganic factors play a role in these conditions. In the regulation of mood, cavum vergae -which is a structural brain anomaly and having a close proximity to key anatomic regions- is thought to form a predisposition for emergence of manic symptoms. In the presence of such

a predisposing factor, corticosteroid use, general activation of the immune system, and inflammatory periods could result in the manifestations of manic and psychotic symptoms.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

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