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CASE REPORT

**Miki Murata · Akira Hashiramoto · Toru Yamaguchi
Chihiro Takabayashi · Takashi Yamane · Yasushi Miura
Hisamitsu Baba · Kazuo Chihara · Shunichi Shiozawa**

A case of central nervous system lupus in succession to lupus peritonitis: a difficulty in the differential diagnosis between lupus psychosis and steroid-induced psychosis

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Abstract A 55-year-old woman with well-controlled systemic lupus erythematosus (SLE) suffered from the abrupt onset of massive intractable ascites, which did not respond to conventional diuretic therapy. While treatment with methylprednisolone pulse therapy ameliorated this lupus peritonitis, neuropsychiatric symptoms then appeared. After a diagnosis of the central nervous system (CNS) lupus, pulse therapy was continued and the patient recovered from the lupus psychosis. We discuss the differential diagnosis between CNS lupus and steroid-induced psychosis with particular references to recent diagnostic methods for CNS lupus.

Key words Central nervous system (CNS) lupus · Lupus peritonitis · Lupus psychosis · Steroid-induced spsychosis

Introduction

Among various rheumatic diseases that show neurological signs and symptoms, central nervous system involvement in systemic lupus erythematosus (SLE), CNS lupus, is the most frequent and intractable manifestation with a poor prognosis. Recent progress in the methods of diagnosis made it possible to diagnose CNS lupus earlier, but the differential diagnosis between lupus psychosis and steroid-induced psychosis is still difficult clinically. Here we report the case of a patient with the manifestations of lupus psychosis which occurred after steroid pulse therapy for lupus peritonitis. In this case, a cerebrospinal fluid examination and diagnostic imaging of the brain were useful for a prompt diagnosis of CNS lupus.

M. Murata · A. Hashiramoto · Y. Miura · S. Shiozawa (✉)
Department of Rheumatology, Kobe University FHS School of Medicine, and Division of Bioregulation, Kobe University Graduate School of Medicine, 7-10-2 Tomogaoka, Suma-ku, Kobe 654-0142, Japan
Tel. +81-78-796-4543; Fax +81-78-796-4543
e-mail: shioz@ams.kobe-u.ac.jp

M. Murata · A. Hashiramoto · C. Takabayashi · T. Yamane · Y. Miura · H. Baba · S. Shiozawa
Rheumatic Disease Division, Kobe University Hospital, Kobe, Japan

H. Baba
Medical Center for Student Health and Department of Biosignal Pathology, Kobe, Japan

T. Yamaguchi · K. Chihara
Division of Endocrinology/Metabolism, Neurology and Hematology/Oncology, Department of Clinical Molecular Medicine, Kobe University Graduate School of Medicine, Kobe, Japan

Case report

In 1992, a 46-year-old woman sought medical care for a high fever, butterfly rash, polyarthritis, photosensitivity, oral ulcers, and Raynaud's phenomenon. Laboratory tests showed positive antinuclear antibody (Ab) (speckled), anti-Sm Ab, and anti-RNP Ab, as well as thrombocytopenia (platelet counts 8.4×10^4/ml). She did not take any drugs that can induce features of SLE. The diagnosis of SLE was made according to the diagnostic criteria of SLE.[1] After receiving 30 mg prednisolone (PSL) daily, her signs and symptoms improved rapidly. Since then, the disease has been well controlled with 5 mg PSL daily.

On August 28, 2001, the woman was admitted to Kobe University Hospital with abdominal distention and 10 weight gain. She was 148 cm tall and weighed 53.6 kg. Her blood pressure was 120/90 mmHg and her body temperature was 35.6°C. She was awake and alert, with no neurological abnormalities or psychiatric symptoms. While she had the abdominal distention, her cardiac and renal functions were normal. The laboratory findings were as follows: white blood cell count (WBC) 6900/mm^3; hemoglobin (Hb) 14.8 g/dl; platelet count 14.7×10^4/ml; activated partial thromboplastin time (APTT) 27.0 s; prothrombin time 100%; fibrinogen 479 mg/dl; total protein 6.4 g/dl; albumin 3.1 g/dl; AST 31 IU/l; ALT 31 IU/l; lactic dehydrogenase (LDH) 188 IU/l; creatinine 0.4 mg/dl; C reactive protein 0.11 mg/dl. Immunological tests were as follows: IgG

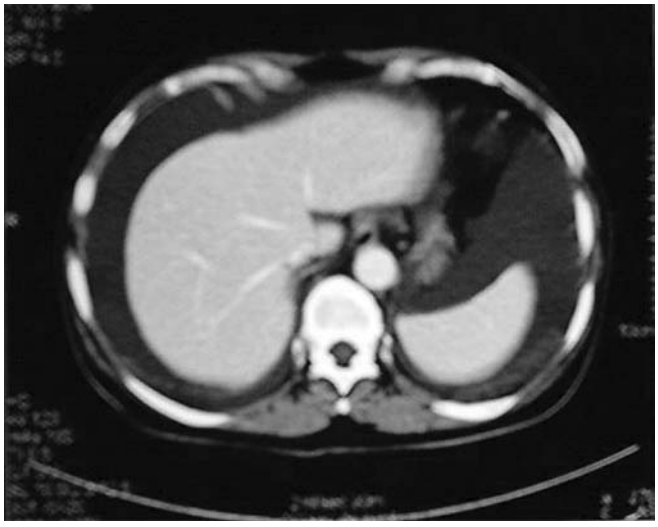

Fig. 1. Computed tomography of the abdomen on admission showing massive ascites

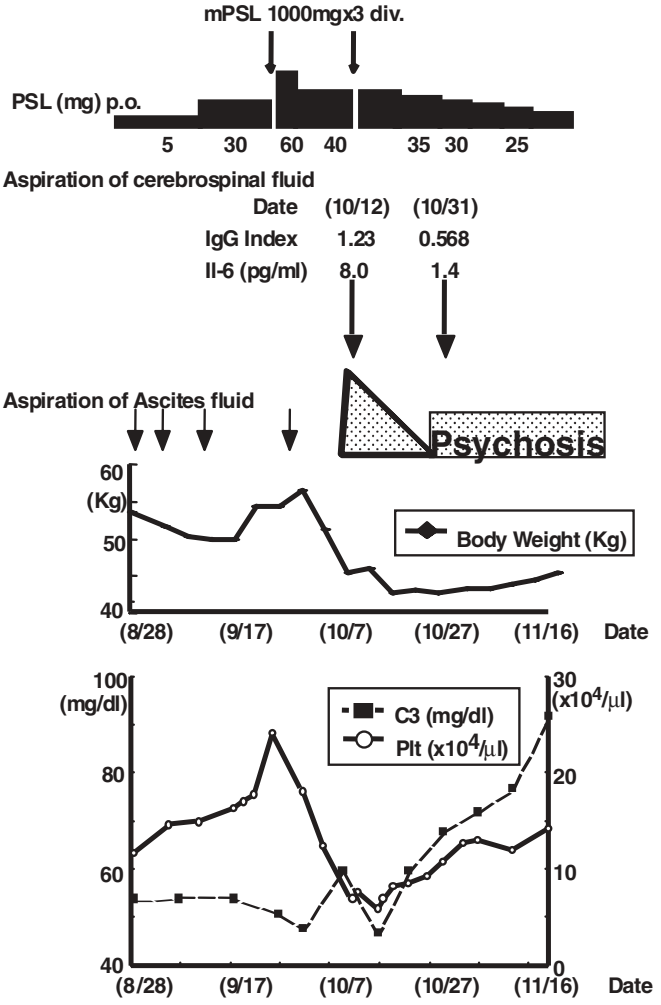

Fig. 2. The clinical course of the patient with two periods of methylprednisolone pulse therapy. *Arrows* indicated pulse therapy and the aspiration of cerebrospinal fluid and ascites fluid. Note the increment level of both C3 and platelet numbers after the second pulse therapy

1210 mg/dl; C3 54 mg/dl; C4 13 mg/dl; CH50 15.0 U/ml; antidouble strand DNA Ab 10.0 IU/ml; antisingle strand DNA Ab 34.7 IU/ml; anti-RNP Ab index 184.1; anti-Sm Ab index 32.4.

An X-ray study showed small bilateral amounts of pleural effusion, and increased gas in both ileum and colon. Ultrasonography and computed tomography (CT) of the abdomen showed massive ascites, with no signs of thrombosis or stenosis in the inferior vena cava. Liver, spleen, pancreas, and kidneys were all normal (Fig. 1). CT and magnetic resonance imaging (MRI) showed no thickening of either the bowel wall or the urinary bladder wall. The ascites were yellow in color, and examination showed total protein 3.4 g/dl, LDH 77 IU/l, glucose 128 mg/dl, adenosine deaminase (ADA) 7.1 IU/l, and carcinoembyonic antigen (CEA) less than 0.5 ng/ml. A polymerase chain reaction (PCR) and culture testing for tuberculosis as well as bacteriological examinations were all negative, and her cytology was Class II.

Since her ascites were unresponsive to diuretic treatment, including 20 mg furosemide and 25 mg spironolactone daily, a total of 6700 ml ascites were aspirated (Fig. 2). Because no evidence of infection or malignancy was shown by the laboratory findings, a diagnosis of lupus peritonitis was strongly suspected as the cause of the massive ascites.

We started 3-day methylprednisolone (1000 mg d.i.v.) pulse therapy on September 28, 2001. After this treatment, the ascites diminished rapidly, and did not reappear after her diuretics had been discontinued. On October 11, 2001, however, the patient manifested a fever exceeding 38.0°C, along with visual and auditory hallucinations, poriomania, and paranoia. A psychiatric consultation took place and the condition was diagnosed as a symptomatic psychosis. At this point, the patient's serum electrolytic concentrations of Na and K were within the normal limit at 138 meq/l and 3.8 meq/l, respectively.

In order to distinguish between steroid psychosis and CNS lupus, some of the patient's cerebrospinal fluid was drawn on October 12, 2000. The fluid was crystal clear and the pressure was 7.5 cmH_2O. The concentrations of protein and glucose were normal. The cytology was negative for malignancy, and cultures were negative for microbial pathogens. While polymorphonuclear leukocytes and interferon-alpha were undetectable, her IgG index and interleukin-6 (IL-6) were significantly increased at 1.23 and 8 pg/ml, respectively. Single-photon emission computed tomography (SPECT) showed decreased blood flow in the cerebrum (Fig. 3A). Since these results were consistent with findings of CNS lupus, a second course of steroid pulse therapy (methylprednisolone 1000 mg d.i.v., 3 days) was started on October 11, 2001. Haloperidol at 9 mg daily and chlorpromazine at 2.5 mg daily were also administered. The second pulse therapy proved effective and the patient's psychiatric symptoms gradually improved. Both haloperidol and chlorpromazine were discontinued on November 20, 2001.

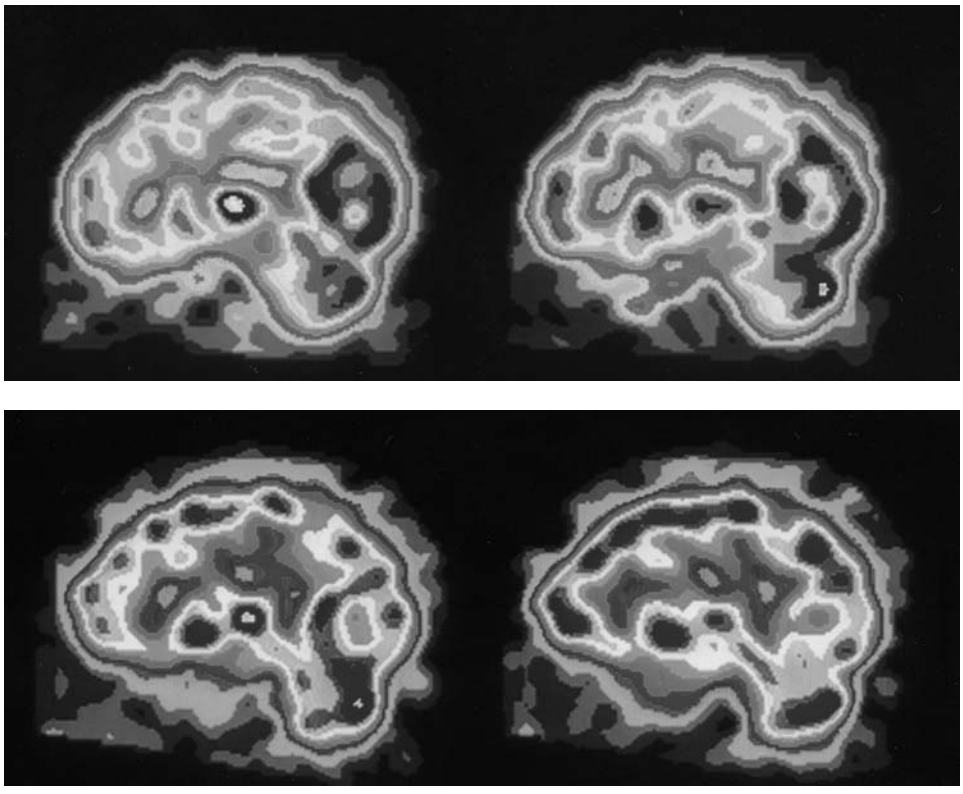

Fig. 3. **A** Single-photon emission computed tomography (SPECT) taken when the neuropsychiatric symptoms appeared. The blood flow was diffusely decreased in the cerebrum compared with the cerebellum. **B** The SPECT image had returned to normal on December 18, 2002

Serum complement and platelet counts, which normalized after the first pulse therapy, decreased again coincident with the manifestation of psychiatric symptoms, and returned to normal after the second pulse therapy. The cerebrospinal fluid obtained 2 weeks after the second pulse therapy showed normalized levels of IgG index (0.568) and IL-6 (1.4 pg/ml). The patient was discharged on December 4, 2001, and her SPECT returned to a normal image on December 18, 2002 (Fig. 3B). Her condition is now under control with 10 mg PSL daily.

Discussion

The American College of Rheumatology (ACR) has documented 12 common nueropsychiatric symptoms which have been observed in SLE patients.[2] Cerebrovascular disease, seizure disorder, and psychosis are the three major symptoms, and our patient presented with a typical psychosis with depression, paranoia, poriomania, and visual/auditory hallucinations. The present case of lupus psychosis developed after steroid pulse therapy for lupus peritonitis.

The differential diagnosis between lupus psychosis and steroid-induced psychosis is critical in such case, because the therapies are opposite to each other. The symptoms of steroid-induced psychosis are usually dose-dependent and appear during the first month of steroid treatment. However, the onset of lupus psychosis may overlap with the period when the steroid therapy becomes effective on the acute symptoms, because steroids may possibly induce the psychiatric symptoms of a latent CNS lupus.[3]

Lupus psychosis is classified into two major types: organic brain syndrome and nonorganic psychosis.[4] The basic pathogenesis of organic brain syndrome is thought to be due to small-vessel angiopathy,[5] which can often be detectable by CT or magnetic resonance imaging (MR) angiography, although patients with nonorganic psychosis usually lack these apparent findings. SPECT or positron emission tomography (PET) well reflect the progression of diffuse changes in the brain, a decreased blood flow, or the metabolism of the entire brain. Indeed, SPECT of our patient showed a decreased blood flow in the cerebrum during her acute phase of CNS lupus.

Further investigations are needed in the field of diagnostic imaging of steroid-induced psychosis, and especially in comparative studies in relation to CNS lupus.

Although systemic indices of the disease activity of SLE, including white blood cell count and the levels of anti-DNA Ab or complement, do not reflect the neuronal disease activities in SLE,[6] either antiribosomal P antibody (Anti-P) in the serum[7] or antibody against neuronal cells in cerebrospinal fluids (CSF anti-N)[8] have been reported to correlate with psychosis of CNS lupus. Specifically, an increase in IgG index,[6] IL-6,[9] or interferon-alpha[10] in cerebrospinal fluids is a valuable diagnostic test for neuronal involvement. Inflammatory cytokines such as IL-6 or interferon-alpha are particularly high in the cerebrospinal fluids of lupus psychosis patients. In our case, both IgG index and IL-6 in cerebrospinal fluids had increased in association with the acute

symptoms of psychosis, and disappeared promptly when the patient's behavioral abnormalities were normalized.

The introduction of steroid plus therapy has significantly improved patients' prognoses for CNS lupus. However, careful observations are still needed until the recovery is complete because the psychiatric symptoms of lupus psychosis usually remain longer than the acute phase of the disease. The monitoring of cytokine levels in the cerebrospinal fluid is an established tool for the diagnosis of lupus psychosis. However, these indices sometimes prove negative, or do not correspond to the acute progress of the symptoms. In such a case, a prompt diagnosis using PET or SPECT is also required. Here, we have reported a case of CNS lupus where there was a difficulty in the differential diagnosis between lupus psychosis and steroid-induced psychosis. This case suggests the importance of the appropriate use of both cerebrospinal indices and diagnostic images for a precise and prompt diagnosis of lupus psychosis.

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