

CASE REPORT

Subacute cerebellar ataxia and atrophy developed in a young woman with systemic lupus erythematosus whose cerebrospinal fluid was positive for antineuronal cell antibody

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Subacute cerebellar ataxia in combination with cerebellar atrophy has rarely been reported as one of the manifestations of lupus in the central nervous system (CNS). We describe a 27-year-old woman with systemic lupus erythematosus who developed subacute cerebellar ataxia. Computed tomography and magnetic resonance imaging of her brain showed cerebellar atrophy in both hemispheres, particularly on the right side. Moreover, increased antineuronal cell antibody levels were detected in her cerebrospinal fluid. The cerebellar ataxia improved markedly following high-dose corticosteroid administration. This suggests that a relationship exists between autoantibodies and subacute atrophic processes in CNS lupus. *Lupus* (2012) **21**, 324–328.

Key words: APS; cerebellar ataxia; cerebellar atrophy; CNS lupus

Introduction

Although neuropsychiatric manifestations are present in 50–70% of patients with systemic lupus erythematosus (SLE),¹ cerebellar involvement occurs in less than 2% of cases.² Among them, cerebellar atrophy has rarely been reported, although cerebral cortical atrophy has been detected by magnetic resonance imaging (MRI) in no less than 70% of patients with SLE.³ In the case of cerebellar ataxia, cerebellar symptoms have often been associated with signs of brainstem or corticospinal tract disease.² This suggests that crossed cerebellar diaschisis plays an important role in these symptoms. In the present report, we describe a young woman with SLE who developed cerebellar ataxia and bilateral cerebellar atrophy. An MRI of her brain showed no lesions other than cerebellar atrophy. Treatment with high dose (1 mg/kg) oral prednisolone was effective, resulting in an improvement in

her neurological symptoms, although her atrophied cerebellar hemisphere did not change.

Case report

A 27-year-old Japanese woman was diagnosed with SLE in 2002 (at 19 years old) on the basis of arthritis, photosensitivity, and positivity for antinuclear and anti-double-stranded DNA (anti-dsDNA) antibodies. Shortly before her SLE diagnosis, she developed deep vein thrombosis in her left lower leg and was diagnosed with antiphospholipid syndrome and displayed positivity for lupus anticoagulant (LAC) and anti cardiolipin (aCL) and β 2 glycoprotein-I (β 2GPI) antibodies. Soon after her SLE diagnosis, she received oral corticosteroid therapy (starting with 30 mg/day of prednisolone) and has remained well after daily treatment with 5 mg of prednisolone since 2006. She was also given warfarin, and her PT-INR was controlled at 2–3.

In December 2008, she complained of gait instability and was admitted to our hospital in April 2009. On examination, she was found to have truncal ataxia. Bilateral dysdiadochokinesia

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Figure 1 Coronal computed tomography at onset of symptoms in patient showing a lesion in the right middle cerebellar peduncle.

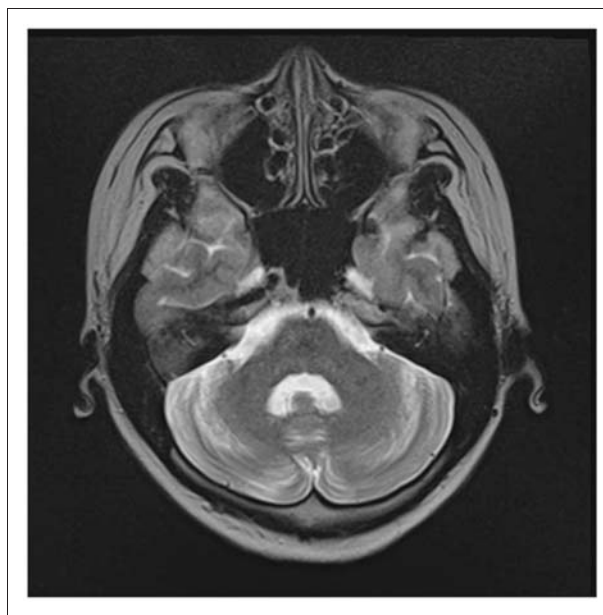


Figure 2 Coronal magnetic resonance imaging at onset of symptoms in patient. Bilateral cerebellar atrophy, dominant in the right side, was detected. No lesion was observed in the right middle cerebellar peduncle.

was detected, and heel–shin test impairment was found to be more marked on the right side. She also displayed fixation nystagmus to the right. No scanning speech was detected. Computed tomography of the brain showed bilateral (although it was dominant on the right side) cerebellar atrophy and a low-density area of about 9 mm in diameter in the right middle cerebellar peduncle (Figure 1). An MRI of the brain also showed bilateral cerebellar atrophy, but no lesion was detected in the right middle cerebellar peduncle (Figure 2). There was no evidence of demyelination. A magnetic resonance angiography of the brain did not reveal any evidence of arterial occlusive lesions or arterial stenosis, although a single photon emission computed tomography of the brain showed decreased vascular flow, which ranged from mild to severe in the right cerebellum and was slight on the left side. An electroencephalogram showed mild diffuse slow waking activity with occasional high voltage delta activity on either side.

The laboratory work-up included a sedimentation rate of 83 mm/h and a C-reactive protein level of 0.18 mg/dl (normal: 0–0.3 mg/dl). A complete blood count revealed lymphopenia (white blood cell count: 6500/mm³, neutrophils: 79.5%, lymphocytes: 13.6%). Serological tests revealed an IgG level of 3146 mg/dl (normal: 870–1700 mg/dl) and an IgM level of 89 mg/dl (normal: 35–220 mg/dl).

Her antinuclear antibody titer was 1:2560 (speckled) (normal: less than 1:40), her anti-dsDNA antibody level was 31 IU/ml (normal: less than 10 IU/ml), and her anti-ssDNA antibody level was 104 AU/ml (normal: less than 20 AU/ml). The anti-RNP antibody index was 153.5 (normal: less than 21), while the anti-Sm antibody was not detected. The anti-SS-A antibody index was 137.8 (normal: less than 29) and the anti-SS-B antibody index was 20.4 (normal: less than 24). Although she had a high level of IgG and positive anti-SS-A/B antibody indexes, she had no sicca syndrome. The serum anti-ribosomal P antibody was present (normal: negative). The glutamate receptor autoantibody, anti-NR2 antibody, was detected. The levels of C3, C4, and CH50 were normal. At this time, tests for LAC and aCL antibody were negative, although aβ2GPI antibody was weakly positive (16 U/ml; normal: less than 10 U/ml). An examination of her cerebrospinal fluid (CSF) revealed a cell count of 8 cells/ml (monocytes: 99%), a protein concentration of 67 mg/dl, a glucose concentration of 52 mg/dl, an IgG level of 345.5 mg/μl (IgG index: 1.38), and an interleukin 6 level of 2.9 pg/ml (normal: less than 4.3 pg/ml). The CSF culture did not reveal any signs of infection. An enzyme-linked immunosorbent assay (ELISA) showed that the antineuronal cell antibody level in her CSF was elevated to 1.27 U/ml (normal: less than 0.27 U/ml), although

no anti-NR2 antibody was detected in the CSF. No anti-Yo, anti-Hu, or anti-Ri antibodies were found in her serum or CSF.

Lupus activity was suspected, because her anti-dsDNA antibody showed continuous elevation from less than 10 IU/ml in 2003 to 31 IU/ml in 2008. A diagnosis of central nervous system (CNS) lupus was made, and 1 mg/kg body weight per day prednisolone (55 mg/day) was started. As a result, she showed gradual improvements in her signs and symptoms, and her dysdiadochokinesia and gait improved markedly. After 6 weeks, she was placed on 45 mg/day prednisolone, and a further spinal fluid examination revealed improvement, a cell count of 2 cells/ml, a protein concentration of 61 mg/dl, an IgG index of 1.22, and an interleukin 6 level of 1.6 pg/ml. Her anti-dsDNA and anti-ssDNA antibody levels were also decreased to 5 IU/ml and 18 AU/ml, respectively. However, a repeat MRI of the brain showed no change in her bilateral cerebellar atrophy (Figure 3). In 2011, about 2 years after the onset of her cerebellar signs, she is currently on low-dose prednisolone (6 mg/day) and remains well. She displays minimal cerebellar signs.

Discussion

The cerebellar ataxia and atrophy in our case can be explained by an autoimmune mechanism associated with the exacerbation of SLE because these symptoms occurred in combination with serological abnormalities compatible with SLE flare and improved after treatment with high-dose prednisolone therapy. The increases in the CSF antineuronal cell antibody level and in the serum anti-ribosomal P antibody level were compatible with CNS lupus.⁴ The anti-NR2 antibody level was increased in the serum, but not in the CSF. The significance of the increase in the serum anti-NR2 antibody level is unclear because serum NR2 autoantibodies are detectable in more than a third of patients with SLE, and the correlation between the antibody and neuropsychiatric complications of SLE remains controversial.^{5,6} It is also possible that antiphospholipid antibodies directly damage neuronal cells by cross-reacting with epitopes on CNS phospholipids.^{7,8} Considering her good response to corticosteroid therapy, it is unlikely that her antiphospholipid antibodies are related to cerebellar atrophy through microvascular occlusion.

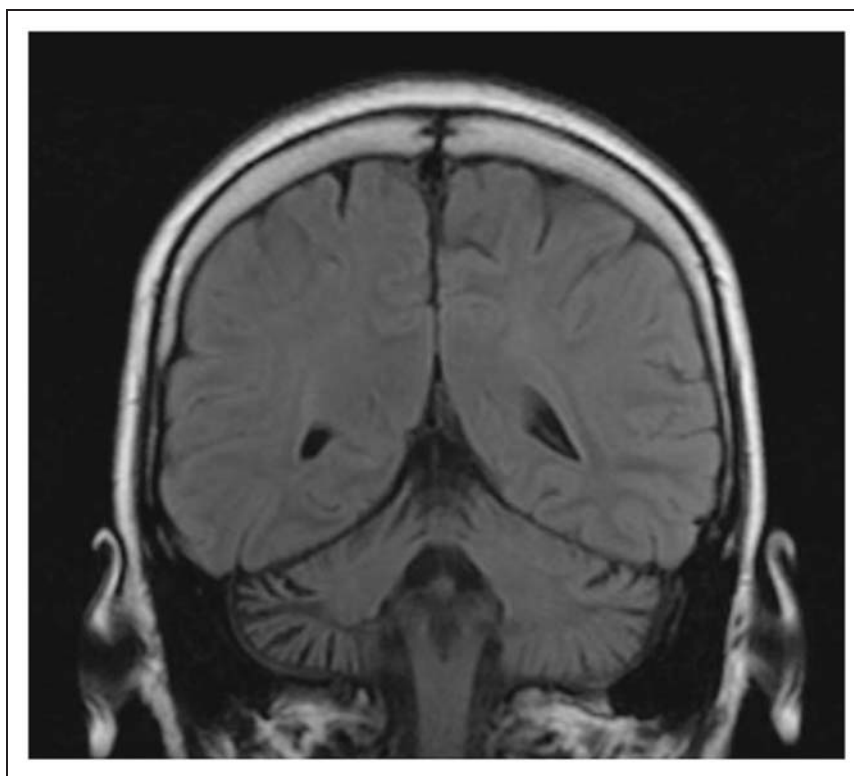


Figure 3 Axial magnetic resonance imaging at follow-up of patient showing no improvement of her atrophic cerebellar hemisphere.

Table 1 Comparison of SLE cases involving both cerebellar ataxia and atrophy

| Age | Sex | CT/MRI scan | APS | Neuronal cell specific antibodies | Treatment | Treatment effect | Ref. |
|-----|-----|---|-----|--|---|---|---------------|
| 56 | F | Diffuse cerebellar atrophy | NE | NE | no treatment | (improved) | ¹⁰ |
| 47 | F | No abnormal lesions in the cerebellum at the onset of ataxia | No | Antibody to human Purkinje cells, antibody against a 75 kDa protein in the cerebellar cortex | mPSL pulse therapy followed by 50 mg of oral PSL | Slight improvement in ataxia, progression of cerebellar atrophy | ¹¹ |
| 40 | F | Mild cerebellar atrophy in both hemispheres combined with moderately severe atrophy of the vermis | No | NE | 1 mg/kg/day oral PSL and 150 mg/day AZA | Improvement of ataxia, unchanged atrophy | ¹² |
| 27 | F | Pancerebellar atrophy without evidence of demyelination | No | Negative for serum and CSF anti-Yo, anti-Hu, and anti-Ri | mPSL pulse therapy followed by 1 mg/kg/day of oral PSL, 150 mg/day AZA was added when PSL was tapered to 5 mg daily | Improvement of ataxia, unchanged atrophy | ¹³ |

NE, not examined; mPSL, methylprednisolone pulse therapy; AZA, azathioprine; PSL, prednisolone

Although cerebellar ataxia is an uncommon symptom in patients with SLE, cases of cerebellar ataxia presenting with cerebellar atrophy are much rarer. We found only four such cases after searching the PubMed database (Table 1). In these cases, moderate to high doses of corticosteroid therapy including methylprednisolone pulse therapy (intravenous methylprednisolone 1 g daily for 3 days) were the main treatments and obtained a relatively good response. Previous reports revealed that brain MRI of acute cerebellar ataxia SLE patients showed reversible edematous lesions in the brain, suggesting acute blood–brain barrier changes secondary to small-vessel vasculopathy.⁹ There might be pathogenetic differences between acute and subacute cerebellar ataxia. In our case, the clinical response to corticosteroid therapy was rapid, although MRI showed no changes in the patient's cerebellar atrophy. We achieved reductions in the patient's CSF IgG index and serum anti-dsDNA and anti-ssDNA levels. It has been suggested that antibody-mediated reactions could explain her cerebellar symptoms. Although cerebellar ataxia may occur secondary to paraneoplastic syndromes associated with anti-Hu and anti-Yo antibodies, the clinical course is usually acute. Our case is characteristic in that autoantibody-mediated subacute cerebellar ataxia was suggested. We could not confirm the binding of her antineuronal cell antibody to cerebellar tissues by immunohistochemical analysis. The autoantigen of her antineuronal cell antibody should be identified to clarify the processes of observed subacute cerebellar ataxia.

Our case highlights the importance of performing MRI for SLE patients with cerebellar signs. Although the significance of specific antineuronal

antibodies in manifestations of CNS lupus is still unclear, high-dose corticosteroid therapy is expected to improve the neurological symptoms of patients suffering from this condition, probably by suppressing the production of pathogenic autoantibodies or cytotoxic processes mediated by cellular and humoral immunity.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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