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CASE REPORT

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Guillain-Barré syndrome accompanied by central nervous system lupus in a patient with juvenile rheumatoid arthritis

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Abstract We describe a 17-year-old female with juvenile rheumatoid arthritis accompanied by Guillain-Barré syndrome (GBS) during the course of central nervous system (CNS) lupus. She initially developed CNS lupus, including headache and convulsion. A high-signal area in a magnetic resonance scan of her brain with T2-weighted images was noted, and her cerebrospinal fluid exhibited increased levels of IgG and interleukin-6. Eighteen days after the onset of CNS lupus, polyneuropathy in the lower extremities developed, and a diagnosis of GBS was made. No obvious preceding infections in the upper respiratory or gastrointestinal systems were noted before the onset of GBS, indicating that GBS might be part of the symptoms of CNS lupus.

Key words Autoimmune · Central nervous system lupus · Guillain-Barré syndrome · Magnetic resonance image

Introduction

Guillain-Barré syndrome (GBS) is an acute demyelinating polyneuropathy characterized by areflexic motor paralysis with mild sensory disturbance, coupled with an acellular increase in total protein concentration in cerebrospinal fluid (CSF). The etiology of GBS has not been clarified. However, an autoimmune response has been implicated, at least as part of the pathogenesis. We describe a patient with systemic lupus erythematosus (SLE) who presented GBS shortly after the onset of central nervous system (CNS) lupus, and discuss some possible mechanisms concerning the etiology of GBS.

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Case report

A 17-year-old Japanese female was admitted to our hospital with a second episode of fever, headache, appetite loss, and proteinuria. No specific family history of the illness was noted.

At 15 years of age, she had developed polyarthritis. She was diagnosed as having a polyarticular type of juvenile rheumatoid arthritis (JRA). She was prescribed prednisolone, 5 mg/day, and loxoprofen.

At 16 years of age, she was admitted to our hospital because of exacerbation of the polyarthritis. A radiological examination of the hands exhibited a narrowing of intercarpal joint spaces, presumably due to cartilage destruction. Laboratory examinations showed a weak positive fluorescent antinuclear antibody (ANA, 1:20, speckled pattern) and anti-DNA antibody (11 IU/ml). However, she presented no obvious symptoms of lupus. She was prescribed 15 mg/day prednisolone, and her joint symptoms were resolved.

On the latest admission, her body temperature was 37.6°C, and apparent facial erythema and a dry mouth were noted. Active arthritis was present in both wrists, knees, and ankle joints. No positive findings were noted after a complete examination of the nervous system. Laboratory examinations showed an increased erythrocyte sedimentation rate (ESR) (96 mm/h) and a slight increase in WBC (8900/mm^3) (Stab 2%, Seg 89%, Lym 8.5%, Mono 0.5%). Increased levels of lactate dehydrogenase (428 U; normal 170–370), C-reactive protein (4.6 mg/dl), rheumatoid factor (1:80 in a hemagglutination test), and IgG (2004 mg/dl; normal 850–1800) were also observed. Creatine kinase, blood urea nitrogen, and creatinine were normal, but moderate proteinuria was observed. CH50 was in the normal range, but the immune complex levels were slightly increased (4.4 mcg/ml (normal <2.9 in C1q assay) and 20.8 mcg/ml (normal <9.2 in C3d assay)). Autoantibodies were detected, including anti-DNA antibody (11 IU/ml), anti-SS-A antibody (1:16), and anti-SS-B antibody (1:8). However, IgG-anticardiolipin, anti-Sm, anti-RNP, antitopoisomerase

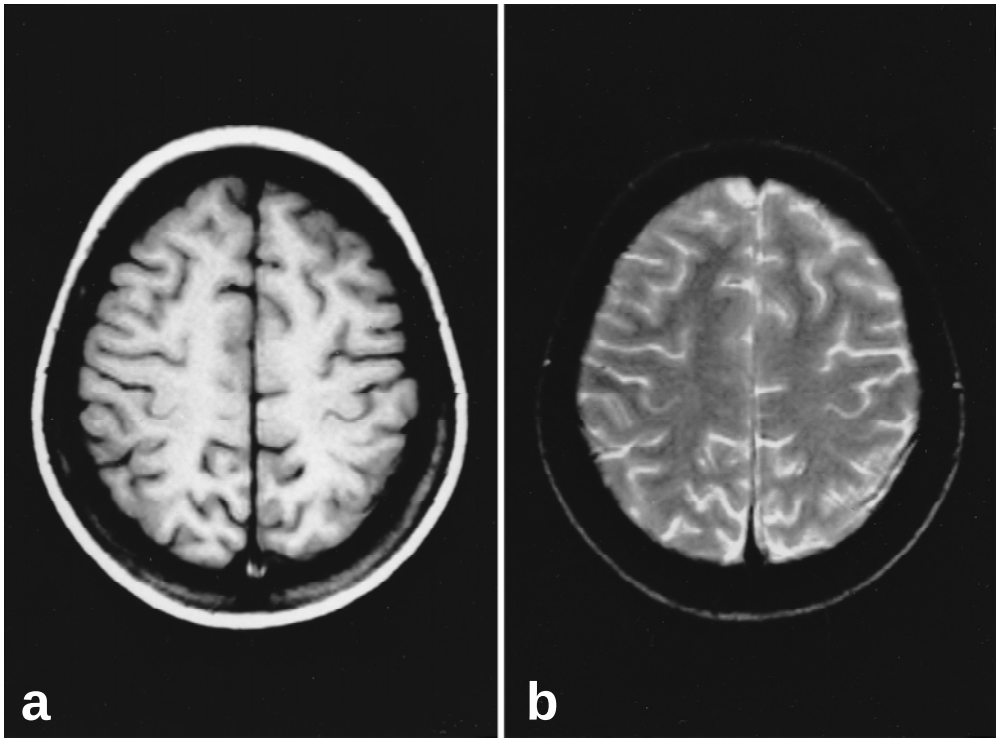

Fig. 1. Magnetic resonance (MR) of the brain on (**a**) T1- and (**b**) T2-weighted images during the clinical course. MR imaging on the day of admission. No abnormal lesions were noted in either T1- or T2-weighted images

I, and anti-Jo-1 antibodies were not detected. Lupus anticoagulant was also negative.

On admission, the patient complained of a severe headache. However, T1- and T2-weighted magnetic resonance (MR) images of the brain showed no abnormalities (Fig. 1), and examination of the CSF was normal (protein, 40 mg/dl; IgG-index, 0.8; interleukin-6, 0.58 pg/ml). On the second day after admission, she suddenly exhibited a convulsion. There was no paresis, muscle weakness, or sensory loss, and no abnormal findings were noted in the cranial nerves or deep tendon reflexes. An electroencephalogram showed predominantly slow waves. On day 9, MR images of the brain were taken, and showed a high-signal area in the bilateral occipital lobe which spread through the cortical part to the white matter on T2-weighted images (Fig. 2). Examination of the CSF indicated increased levels of IgG and interleukin-6 (28.0 pg/ml), the IgG-index was 6.2, but protein was normal (41 mg/dl). All these data indicated CNS lupus. A renal biopsy was performed to evaluate the persistent proteinuria. The histological examination revealed a proliferation of mesangium, and segmental widening of the mesangial area in the focal glomerulus. No distinct hypertrophy of the basement membrane was noted. These findings were compatible with lupus nephritis (WHO-II b).

Methylprednisolone pulse therapy (1000 mg/day for 3 days) was administered for the CNS lupus and lupus nephritis starting on day 12 after admission, followed by 60 mg/day oral prednisolone. The symptoms of headache, fever, and anorexia disappeared. T2-weighted MR images of the brain on day 17 showed that the high-signal area had disappeared, as seen on the last MR imaging (Fig. 3). An electroencephalogram, also showed an improvement. Despite these improvements, she presented progressive muscle weakness, which was dominant in proximal muscles of the limbs on day 17. She also complained of numbness of the glove and stocking type. Deep tendon reflexes disappeared, but no abnormal findings were noted in the cranial nerve system.

These symptoms rapidly worsened, and complete paralysis of the upper and lower extremities emerged by day 22, but still with no cranial nerve involvement. Laboratory examinations, including creatine kinase, aldolase, myoglobin, electrolytes, and thyroid hormone, were all normal. T1- and T2-weighted MR images of the brain on day 24 still showed no abnormal lesions. However, examinations of the CSF on the same day showed an increased level of protein (355 mg/dl) without pleocytosis or augmentation of the IgG-index (0.4) or interleukin-6 (4.84 pg/ml). No oligoclonal bands were noted. An electroneurographic examination of a left median nerve showed a delay in conduction velocity with a deterioration of amplitude, which was dominant in the motor nerves. All these findings were consistent with the development of GBS. No obvious preceding infections in the upper respiratory or gastrointestinal systems were noted before the onset of GBS. No antibodies against pathogenic microorganisms, including cytomegalovirus, Epstein–Barr virus, *Mycoplasma*, and *Campylobacter jejuni*, were detected in serum or CSF. Furthermore, no antiganglioside antibodies, including IgG-anti-GM1, IgM-anti-GM1, antiacialo-GM1, anti-GD1b, and anti-GQ1b antibodies, were detected in serum.

Immunoadsorption plasmapheresis using an IMMUSORBA TR-350 column (Asahi Medical Co., Tokyo, Japan) was performed six times from day 31, and a

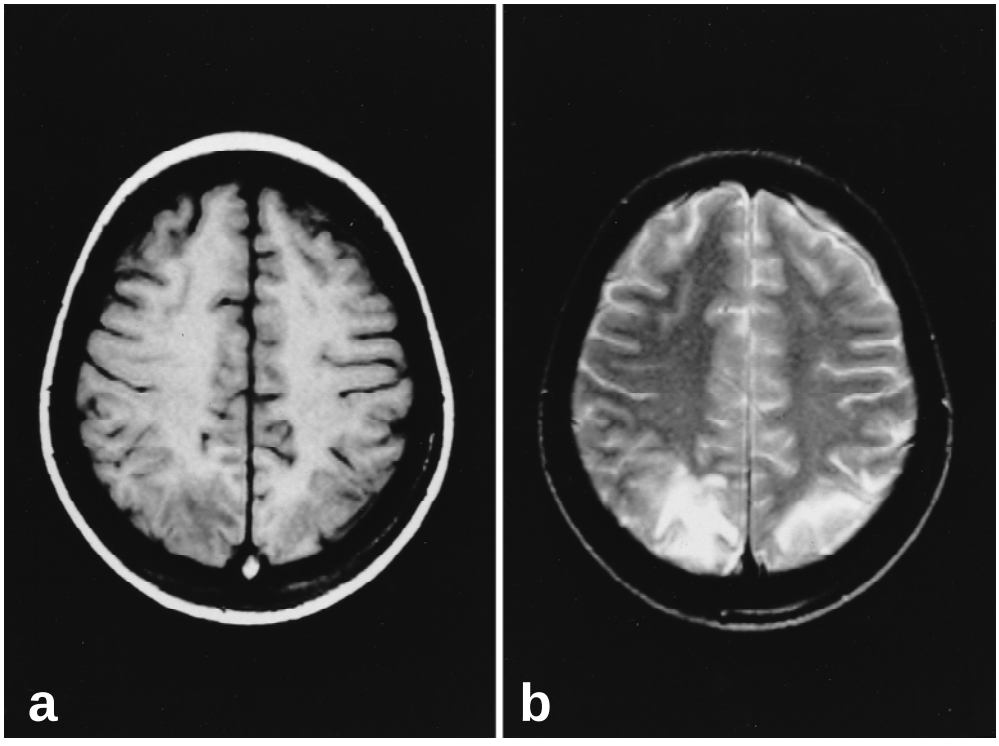

Fig. 2. MR imaging on day 9. A high-signal area in the bilateral occipital lobe, which spread through the cortical part to the white matter on a T2-weighted image, was noted. **a** T1-weighted image. **b** T2-weighted image

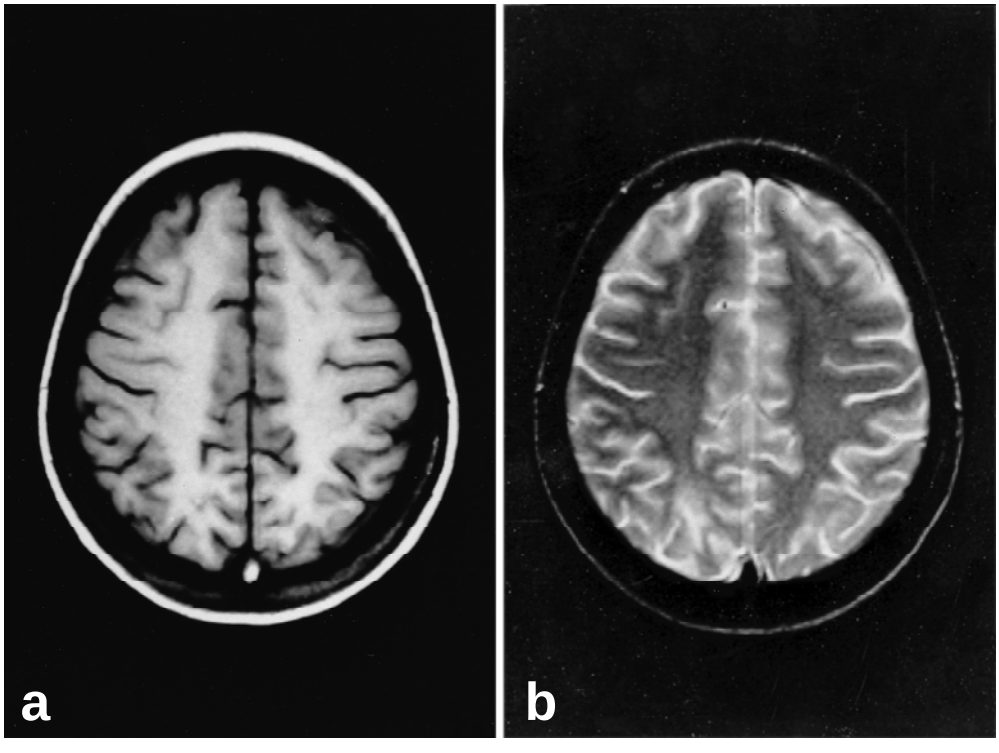

Fig. 3. MR imaging on day 17. The high-signal area on a T2-weighted image shown on day 9 has disappeared. **a** T1-weighted image. **b** T2-weighted image

gradual recovery of muscle strength was observed in distal muscles. GBS symptoms had almost disappeared approximately 2 months after onset.

The patient complained of dry mouth during her time in hospital, and a minor salivary gland biopsy of the lip showed a mild chronic sialadenitis, suggesting Sjögren's syndrome.

Discussion

We have presented a case of CNS lupus in a patient who had been suffering from JRA, followed by GBS.

Carol et al.[1] reported ten patients with JRA who progressed to SLE. As in this case, these patients were

characterized as polyarticular types with positive antinuclear antibodies (ANA). In their study, three patients had CNS lupus and two had proteinuria. Our patient exhibited a high-signal area on T2-weighted MR images of the brain after the onset of CNS lupus symptoms, which disappeared with an improvement in other symptoms. This is a typical MR imaging finding in patients with CNS lupus, and Sibbitt et al.[2] suggested that the high-signal area on a T2-weighted MR image indicates the presence of a local edema caused by the destruction of the blood-brain barrier due to vascular injury. Increased levels of the IgG-index and interleukin-6 in CSF also supported the diagnosis of CNS lupus.[3]

The characteristic feature in this case was the development of GBS shortly after the onset of CNS lupus. In approximately 70% of all patients, GBS develops shortly after the onset of infectious diseases, including pharyngolaryngitis and gastroenteritis. Cytomegalovirus, Epstein–Barr virus, *Mycoplasma*, and *Campylobacter jejuni* have been identified as preceding pathogens. Recently, the involvement of *Campylobacter* enteritis in the pathogenesis of GBS was suggested.[4] The presence of antiganglioside antibodies was reported in these patients. Ganglioside is widely distributed in the nervous system, and production of these antibodies might be involved in the onset of GBS, followed by *Campylobacter* infection.

Our patient exhibited neither clinical findings for preceding infections nor serological findings for antibodies against pathogenic microorganisms. The possibility of drug-induced GBS[5] was also excluded during her clinical course.

Therefore, we considered the possibility that GBS in this patient was an indigenous component of neuropathy in SLE. The development of GBS has been reported in patients with SLE, although it is not a common complication. Grigor et al.[6] reported one patient with GBS among 50 patients with SLE. Leneman[7] reported seven patients with SLE among 1100 with GBS. Several authors have reported neurological manifestations similar to GBS in patients with SLE.[8–14] Some claimed a possible involvement of immunological abnormalities in SLE in the pathogenesis of GBS. Robson et al.[14] reviewed these cases and suggested the mechanisms of GBS onset in SLE patients. These include the susceptibility of SLE patients to infection, autoantibody production, including myelin proteins, and destruction of the blood–brain barrier by CNS lupus. Consequently, autoantibodies against neuronal epitopes could be produced in local areas and may have a pathogenic action in the development of GBS.

Recently, the term "CNS lupus" has been claimed to be appropriate since the peripheral nervous system may also be involved.[15] The term "neuropsychiatric lupus" was an alternative proposal in order to encompass the range of manifestations.[15] Based on this definition, GBS can be recognized as part of the manifestations in neuropsychiatric lupus.

This case was characterized by the appearance of GBS 18 days after the onset of CNS lupus. Even though no antibodies to gangliosides were detected, destruction of the blood–brain barrier by CNS lupus could have induced autoantibody production to the nervous system in local areas. From these observations, we present this case as an intriguing clue in considerations of the pathogenesis of GBS.

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