Multiple Sclerosis with Caudate Lesions on MRI
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Abstract
A 31-year-old woman displayed sleepiness and impairment of recent memory. T2-weighted MRI revealed high signal intensity lesions in the bilateral basal ganglia, thalamus, and brainstem. Although remission was achieved with corticosteroid therapy, she again displayed memory dysfunction and emotional disturbance one year later, at which time MRI disclosed new lesions in the right caudate nucleus and left frontal white matter. Corticosteroid therapy led to improvement, and she suffered no recurrence on maintenance steroid therapy. These findings suggest that caudate lesions do occur in multiple sclerosis, the manifestations of which can be abulia and memory dysfunction, as in the present case.

Key words: caudate nucleus, abulia, memory dysfunction, emotional disturbance

Introduction
The role of the basal ganglia in cognitive function and social behavior in humans is not well understood. Lesions in the thalamus or basal ganglia have rarely been reported in patients with multiple sclerosis (MS). It has recently been established that between 40% and 60% of MS patients suffer cognitive impairment of significant magnitude (1). In addition, Thornton and Raz (2) identified a more global pattern of memory deficits in MS than had previously been thought.

We treated a case of MS in which MRI revealed lesions in the caudate nuclei. The relationship between the patient’s cognitive changes and caudate lesions is discussed.

Case Report
A 31-year-old right-handed woman with no previous psychiatric, relevant medical, or family psychiatric history presented with paroxysmal sleepiness and memory dysfunction one month after a non-specific upper respiratory tract infection associated with a low-grade fever. She developed anorexia in January 1996, and diplopia appeared thereafter. She was admitted to our hospital on February 1, 1996.

On admission, she was alert. Her body temperature was 37.5°C and there were no abnormalities on general physical examination. Uveitis was not found by an ophthalmologist. No skin rash was observed. There was no lymphadenopathy. No meningeal signs were noted. She had impairment of recent memory, although no aphasia, apraxia or agnosia was found. The visual fields were normal to confrontation test and the pupils reacted equally to light. A right sixth cranial nerve palsy was observed with diplopia on right lateral gaze. Motor examination revealed mild weakness in all extremities with generalized hyperreflexia but no pathologic reflexes. Sensory examination revealed no abnormalities. She had no extrapyramidal or cerebellar signs, and urinary function was normal.

Blood cell counts, urinalysis and blood chemistry test results were normal. Serum angiotensin-converting enzyme was within normal limits. The erythrocyte sedimentation rate (ESR) was 7 mm/h. CRP, STS and serum ANA were negative. Lymphocyte subsets were within normal ranges, with CD4 32.7% and CD8 41.9%. Antibody titers to Epstein-Barr virus, Japanese encephalitis, herpes simplex, cytomegalovirus and varicella-zoster viruses were all negative. Antibodies to human T-lymphotrophic virus were also negative. Needle reaction was negative. The tuberculin test was positive. Needle reaction was negative. The tuberculin test was positive. A lumbar puncture revealed a normal pressure, 1 white blood cell (100% mononuclear cells)/μL, protein of 24 mg/dl, IgG 2.0 mg/dl, IgG index 0.47 (normal: 0.34–0.85), and glucose of 56 mg/dl. CSF oligoclonal bands and myelin basic protein (MBP) were not found. The chest X-ray film was normal. Visual evoked potentials (VEP) were normal. Auditory brainstem responses (ABR) were normal bilaterally. Median nerve somatosensory evoked potentials were normal. On admission, brain CT disclosed no abnormality.

She suffered deterioration characterized by bilateral blepharoptosis, defective upward gaze, facial diparesis, dysphagia, and diminished right palatal reflex over the three-week period following admission. During this period, she responded to commands, but was drowsy. The first MRI examination, performed 21 days after admission, revealed no abnormalities on T1-weighted images and high signal intensity lesions bilat-
Figure 1. MRI (0.5 Tesla) performed on February 21, 1996. Axial spin-echo T2-weighted image (repetition time 2,000 msec, echo time 100 msec) reveals high signal intensity in both medulla oblongata (A), midbrain (B), basal ganglia (C, D), and thalamus (C, D) (arrows).
Hashiguchi et al generally in the caudate nucleus, putamen, globus pallidus, the anterior limb of the internal capsule, thalamus, and brainstem on T2-weighted and proton-weighted images (Fig. 1). Intravenous prednisolone treatment (40 mg/day) was started on hospital day 22. On the 30th day after initiation of this treatment, MRI demonstrated that the multifocal lesions had almost completely disappeared. By two months later, her level of consciousness and neurological symptoms had improved dramatically except for gustatory disturbance, and she was discharged. The dose of prednisolone was gradually tapered without a recurrence. Prednisolone was discontinued in December 1996.

After a one-year remission, in early March 1997, the patient again developed anorexia, and was readmitted on June 9, 1997. This time, mental status testing revealed normal intelligence and full orientation, but recent memory was impaired. She was apathetic and had decreased spontaneous speech. The remainder of her neurological examination was normal. MRI revealed no abnormalities on T1-weighted images but there were new lesions in the right caudate nucleus and left frontal white matter on T2-weighted images (Fig. 2). After oral prednisolone (30 mg daily) was restarted, her symptoms resolved rapidly. On the 14th day after initiation of this treatment, the multifocal lesions observed on MRI had completely disappeared. The clinical and radiological course, and favourable response to corticosteroids were consistent with the diagnosis of MS. Three years after discharge, in 2000, she remained well while taking prednisolone at a reduced dose of 5 mg, and follow-up MRI examination results were normal (Fig. 3).

Discussion

In this case, negative CSF laboratory studies and electrophysiological investigation results appeared inconsistent with the diagnosis of MS. However, these results do not exclude the diagnosis of MS, since CSF oligoclonal bands are positive in only 43%, MBP in 44%, VEP in 75%, and ABR in 46% of Japanese MS patients (3, 4).

The diagnosis of MS in this case was initially problematic since differentiation from acute disseminated encephalomyelitis (ADEM) was difficult. Whereas ADEM is usually a monophasic illness, MS is by definition a multiphasic disease which frequently results in stepwise or steadily progressive deterioration in neurological function. When ADEM is recurrent, its differentiation from MS becomes difficult (5). Kesselring et al (5) described unusual locations of lesions in the basal ganglia, including the hypothalamus, in one case of ADEM studied by MRI, and emphasized that this finding is rare in MS. Involvement of the basal ganglia and thalami was subsequently reported to occur in ADEM (6). Since MS is primarily a disease of the white matter, basal ganglia-associated signs and symp-

Figure 2. MRI (1.5 Tesla) performed on June 5, 1997. Axial spin-echo T2-weighted image (repetition time 3, 600 msec, echo time 100 msec) reveals new lesions in the right caudate nucleus and left frontal white matter.
First admission  Second admission
11  12  1  2  3  4  3  4  5  6  7  8  7
8  5mg  40mg
Prednisolone

Sleepiness
Memory dysfunction
Anorexia
Emotional disturbance
Diplopa
Facial diparesis
Dysphagia
Gustatory disturbance

Figure 3. Clinical course of the present case.

Symptoms are quite rare. However, thalamic involvement has been reported in MS (7). In the present case, although differentiation of MS from ADEM by MRI was difficult, because of the separation of her two episodes in time and central nervous system location, our patient should be regarded as having MS rather than ADEM.

The differential diagnosis of this patient must also include neuro-Behçet syndrome, granulomatous diseases such as sarcoidosis, CNS vasculitis, encephalitis and brain tumors such as lymphoma. Laboratory findings such as increased ESR, positive CRP and CSF pleocytosis suggest a more inflammatory process in neuro-Behçet syndrome than in MS (8). In the present case, the eyes and skin were not affected, and laboratory studies were normal. Neuro-Behçet syndrome and sarcoidosis were therefore ruled out. In patients with primary angitis of the CNS, infarcts are multiple, bilateral, supratentorial, and more common in the deep white matter on MRI findings (9), which do not fit those in the present case. Primary cerebral malignant lymphoma was excluded because the lesions exhibited neither edema nor mass effect on MRI and because the clinical course was free of recurrence for three years after discharge. Other diseases of the CNS, such as leukodystrophy, subacute sclerosing panencephalitis, and progressive leukencephalopathy could be excluded because of her clinical course, viral titers, CSF findings, and improving MRI findings. Thus, the diagnosis of clinically definite MS was made according to the criteria of Poser and colleagues (10).

The cognitive and behavioral disturbances resulting from basal ganglia dysfunction are often complex and difficult to localize and classify. The present case is unique in that bilateral lesions of the caudate nuclei were present at the first admission and a right caudate nucleus lesion was subsequently found on second admission. In the brain of patients with MS, plaques may also be found in the striatum, pallidum, and thalamus (11). MRI T2 shortening has been studied in the basal ganglia of patients with MS (12, 13). MRI and PET studies of MS patients have shown that basal ganglia lesions are associated with cognitive dysfunction (14). Mendez et al (15) reported the behavioral and cognitive characteristics of 12 patients with caudate lesions. Patients fell into three groups according to predominant behavioral characteristics. One group was apathetic and had reduced spontaneity and initiative. We will refer to this state as abulia, after Fisher (16). On second admission, our patient exhibited abulia that appeared to be a significant consequence of right caudate damage. The caudate may also play a distinct role in memory. In monkeys, stimulation of the caudate may impair memory (17). Results of single-unit recording from monkey caudate suggest that caudate cells function in the integration of visual information and memory (18). Stein et al (19) studied 12 patients with hemorrhage in the head of the caudate nucleus. In five of these 12 patients, memory was impaired. The impairment of recent memory in our patient thus appears to have been due to a disorder of caudate function. However, at the first admission, thalamic lesions may have been a cause of the patient’s lethargia, abulia and amnesia (20, 21).
To our knowledge, this is the first report of a patient with MS with caudate lesions who displayed abulia and memory dysfunction. Our findings strongly suggest that the onset of neurological signs in a subacutely psychotic patient should be investigated with MRI, the findings of which can diagnose MS. Future evaluation of patients with focal caudate lesions should further characterize the behavioral and cognitive functions of the caudate nuclei.

References