Cerebellar Ataxia and Overactive Bladder after Encephalitis Affecting the Cerebellum

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Key Words

Cerebellitis · Detrusor overactivity · Overactive bladder · Autonomic dysfunction

Abstract

The cerebellum is one of the regions that contribute to urinary dysfunction in humans. A 43-year-old woman at age 35 had an acute onset of encephalitis that led to fever, generalized convulsion and coma. Six months after the disease onset, she regained consciousness and developed generalized myoclonus, cerebellar ataxia and overactive bladder, e.g., urinary urgency, daytime urinary frequency, and urinary incontinence. Eight years after the disease onset, she was revealed to have cerebellar atrophy on MRI, cerebellar hypoperfusion on SPECT, and detrusor overactivity on urodynamic study. Selective inflammation in the cerebellum seemed to produce cerebellar ataxia and overactive bladder in our case.

Introduction

Specific brain areas, i.e., the medial frontal cortex, periaqueductal grey matter (PAG), pontine micturition center (PMC) and cerebellum, are constantly activated in response to urinary storage and micturition in humans during functional imaging studies [1]. Less constantly activated areas include the basal ganglia. Of these structures, PAG and PMC serve as the relay center of the spino-bulbo-spinal micturition reflex, and the frontal cortex and the basal ganglia are considered to control (or inhibit) the micturition reflex [2]. In experimental animals, stimulation of the cerebellum and fastigial nucleus either

inhibited or facilitated the reflex [3–7], whereas lesioning mostly facilitated the reflex [3, 4, 8]. There are fiber connections between the bladder and the cerebellar vermis both morphologically [9, 10] and electrophysiologically [3, 4]. In addition, patients with late cortical cerebellar atrophy [11] and those with cerebellar stroke [12] have shown urinary dysfunction and detrusor overactivity. Thus, the cerebellum is thought to control the micturition reflex. Here we report a case of a woman who, after recovery of acute encephalitis affecting the cerebellum, presented with cerebellar ataxia as well as overactive bladder.

Case Report

A 43-year-old Japanese woman during her stay in the USA at age 29 had an episode of transient delirium and hallucination (details not known). There was no abuse of alcohol or drugs, and the patient had no motor or urinary disturbance at the time of the episode. At age 35, she suddenly developed acute onset of fever, generalized convulsion and coma, and she was brought to a local neurology hospital. The cerebrospinal fluid examination was normal, virus antibodies were negative, and antibody against cerebellar Purkinje cells was negative. However, encephalitis of autoimmune etiology was the tentative clinical diagnosis. Intubation, mechanical ventilation and preservative therapies, including valproic acid administration for less than a month, gradually ameliorated her disturbance of consciousness over a period of 6 months. She did not undergo phenytoin administration. However, after she regained consciousness, she developed generalized myoclonus, ataxia and overactive bladder, e.g., urinary urgency and frequency. She was discharged from a local hospital with a wheelchair. Her condition did not change for the following 8 years, except for the disappearance of myoclonus. She then visited and was admitted to our hospital.

On admission, she seemed alert, cooperative, and intelligent. No aphasia, apraxia, agnosia, or hemineglect was found. Her Mini-Mental State Examination score was 28. Extraocular movement was saccadic and hypometric, and she had gaze-evoked nystagmus and rebound nystagmus. She had ataxic dysarthria, whereas no dysphagia was found. Other cranial nerve functions were normal, and Horner's signs were not seen. Coordination of the upper and lower extremities was poor, and she had dysidiadochokinesis. She could stand and walk with a Lofstrand elbow crutch, with a wide-based stance. Tendon reflexes in her 4 extremities were normal. She had no muscle weakness in the extremities, and there was no Babinski sign. No muscle rigidity was seen. A sensory examination showed normal findings. She had urinary urgency, twice nocturnal urinary frequency, daytime urinary frequency of more than 15 times, and urgency incontinence. She did not have constipation or postural dizziness. Blood chemistry and urinalysis were normal, including thyroid function and autoantibodies against the thyroid gland. The cerebrospinal fluid was normal. Electroencephalography showed normal findings. Axial slices of brain magnetic resonance imaging (MRI) on admission showed atrophy of the cerebellar hemisphere and the vermis (fig. 1a). No lesions were seen in the medial frontal lobe, PAG, PMC, or other areas of the brain. Axial and sagittal slices of ^{99m}Tc -labeled L,L-ethyl cysteine dimer (ECD) single-photon computed emission tomography (SPECT) showed hypoperfusion in the cerebellum, as detected by MRI, without apparent diaschisis within the brain (fig. 1b). These findings suggest that the lesions in the cerebellum accounted for the patient's cerebellar ataxia. She did not have urinary tract infection, stones, or uterine prolapse, all of which can cause urinary dysfunction. She was not taking drugs that might affect the lower urinary tract function. She had no postural hypotension in the head-up tilt test. Her cardiac ^{123}I -labelled metaiodobenzylguanidine uptake was normal.

Lower-Urinary Tract Function (8 Years after Disease Onset)

An urodynamic study [13] (Urovision, Lifetec, Inc., Houston, Tex., USA; Neuropack M2, Nihon Kohden, Inc., Tokyo, Japan) was performed to measure post-void residual (PVR) volume and medium-fill (50 ml/min) water cystometry with pressure-flow analysis. Simultaneously, sphincter electromyography (EMG) was carried out using a concentric needle electrode in the external anal sphincter muscles. Sixty min after her last void in a toilet, she could not void in the laboratory; therefore, free flow could not be obtained. However, transurethral catheterization showed a PVR of only 22 ml (normal <30 ml). The first sensation of bladder filling occurred at a smaller-than-normal volume, i.e., 48 ml (100 < normal < 280 ml), her bladder capacity was smaller than normal, 133 ml (245 < normal < 600 ml), and she had detrusor overactivity. She did not have uninhibited sphincter relaxation during the storage phase. On coughing, she did not leak. When the patient tried to start

voiding, she showed normal detrusor contraction as indicated by a maximum Watts Factor of 26.7 W/m² (normal >10 W/m²). The pressure-flow analysis showed an unobstructed pattern. Sphincter EMG showed no detrusor-sphincter dyssynergia. Analysis of motor unit potentials of the external sphincter muscle revealed normal findings.

She was started on 0.2 mg/day imidafenacin (a cholinergic agent) for overactive bladder, and taltirelin hydrate (thyrotropin-releasing hormone analogue) for cerebellar ataxia. At 2 months after administration of these agents, although ataxia did not change significantly, urinary incontinence disappeared and urinary urgency and frequency markedly improved.

Discussion

Our patient initially had acute encephalitis that led to high fever, generalized convulsion, and coma. Our patient was unique in that after recovery of acute encephalitis, she presented with cerebellar ataxia and overactive bladder together. To the best of our knowledge, no such case has previously been reported. Urodynamic study revealed the presence of detrusor overactivity. She did not have urinary tract infection, stones, or uterine prolapse, all of which may cause urinary dysfunction. The findings of the brain MRI and SPECT scans suggested that the cerebellum was selectively affected in the patient at the time of the urodynamic study. The results of the present study correspond well to the previous experimental studies [4–10]. Clinically, patients with late cortical cerebellar atrophy [11] or those with cerebellar stroke [12] have shown urinary dysfunction and detrusor overactivity. A functional SPECT study of multiple system atrophy, in which detrusor overactivity is common, showed reduced tracer activity in the cerebellar vermis during urinary storage and micturition in the patient cohort as compared with a control cohort [14]. In addition, an MRI study of lesion sites in multiple sclerosis revealed a correlation between urinary dysfunction and the cerebellum [15]. The above clinical and experimental studies, including ours, suggest that the cerebellum has an inhibitory influence on the micturition reflex. Loss of the cerebellum's inhibition might have led to the detrusor overactivity in our case.

In conclusion, we have described a case of a woman who, after recovery of acute encephalitis affecting the cerebellum, presented with cerebellar ataxia and overactive bladder.

Fig. 1. MRI and SPECT of the patient at the time of the urodynamic study. **a** T2-weighted MRI image of the axial plane (left) showed atrophy of the hemisphere and vermis of the cerebellum, and slight enlargement of the fourth ventricle. T1-weighted image of the sagittal plane (right) showed atrophy of the cerebellar vermis (arrowheads). **b** Axial (upper) and sagittal (lower) planes of ECD-SPECT images showed hypoperfusion in the cerebellum (arrowheads) without apparent diaschisis within the brain. R = Right; L = left; P = posterior; A = anterior.

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