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SHORT REPORTS

Focal Leg Dystonia Associated with Cerebellar Infarction and Application of Low-Frequency Cerebellar Transcranial Magnetic Stimulation: Evidence of Topographically Specific Cerebellar Contribution to Dystonia Development

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Abstract
The cerebellum has recently been highlighted as a key neural substrate responsible for dystonia. A 57-year-old female presented with isolated focal leg dystonia that developed 8 years after acute cerebellar infarction. Brain magnetic resonance imaging showed an old cerebellar infarct in the right anterior cerebellum. Low-frequency cerebellar repetitive transcranial magnetic stimulation on the right cerebellum partially improved dystonia in this patient. This case provides valuable evidence on cerebellar mechanisms related to the development of dystonia in a topographically specific manner. Cerebellar brain stimulation can be a potential therapeutic strategy for patients with dystonia.

Keywords Dystonia · Cerebellum · Transcranial magnetic stimulation

Introduction

The cerebellum has recently been highlighted as a key neural substrate responsible for dystonia [1–8]. In contrast to the previously accepted concept that distinct motor circuits exist for the basal ganglia and the cerebellum, more recent studies have shown that these two structures communicate within a functional network [1, 2, 4, 5]. Various neuroimaging, neurophysiological, and neuroanatomical studies have put forth the novel concept of dystonia being a network disorder involving the basal ganglia and other brain regions, especially the cerebellum [6, 9]. Reports of late-onset focal or segmental dystonia related to various abnormalities in the cerebellum and linked anatomy support this concept [8, 10–12]. Among the forms of dystonia, focal leg dystonia due to cerebellar lesion has not been reported. We describe a patient with focal right lower limb dystonia, whose brain MRI showed a focal ipsilateral cerebellar infarction, and who showed improvement of dystonic symptoms after low-frequency cerebellar repetitive transcranial magnetic stimulation (rTMS).

Care Report

A 57-year-old female was admitted to the Neurology department due to gait difficulty and discomfort in the right leg that had persisted for 6 months. The patient had a 10-year history of hypertension. She had experienced acute onset dysarthria and disequilibrium to the right side 5 years earlier before admission and was diagnosed with an ischemic stroke in the right cerebellum, from which she recovered with lingering mild dysarthria only. She had no family history of dystonia and took aspirin, atorvastatin, and valsartan. Ten months before admission, the patient experienced a sprain, and the pain from this injury on the right calf and ankle resolved over 3 months. However, she reported feeling that her right leg was "twisted and stiff" while walking. One month after the onset of ambulatory discomfort in the right leg, she reported

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feeling the right leg "twisting" even at rest. Neurological examination revealed mild cerebellar dysarthria. A cerebellar function test showed no abnormal findings in the finger-to-nose test, rapid alternating hands movement test, or heel to shin test. At rest, her right leg showed dystonia with slow writhing movements. Dystonia in her right leg became prominent while walking, showing dorsiflexion and inversion of the ankle (Supplementary video). Burke-Fahn-Marsden dystonia rating scale (BFMDRS) was 16. Motor strength and sensory functions including pain sensation, temperature, position, and vibration sensory functions were also normal in both the upper and lower extremities. She did not show bradykinesia and rigidity. Deep tendon reflexes were normoactive in all extremities. Brain Fluid Attenuated Inversion Recovery (FLAIR) MRI showed focal hyper-intense signal in the right anterior cerebellar hemisphere (Fig. 1a). The signal intensities of the lesion were low on the T1-weighted image (Fig. 1b). There were no abnormal lesions in other brain areas. Spine MRI showed a non-specific degenerative change in the lumbar spine. Nerve conduction study (NCS) and electromyography (EMG) showed normal findings. All laboratory findings including those from blood cell counts, routine chemistry, thyroid function test, and analysis of ceruloplasmin and electrolytes levels were normal.

Low-Frequency Cerebellar Transcranial Magnetic Stimulation

Resting motor threshold (RMT) was measured on the right abductor pollicis brevis muscle. RMT as defined as the lowest stimulus intensity required to produce motor-evoked potentials (MEPs) of at least 50 μV in at least 5 of the 10 consecutive trials [13]. Stimulation intensity for the rTMS procedure was set at 90% of the RMT. RMT of the patient was 89%. The stimulation site for the right cerebellum was 3 cm lateral and 1 cm inferior to the inion. For 5 days, 600 stimulations per day were applied with the stimulation intensity of 80% at a frequency of 1 Hz. Each session of rTMS consisted of 20 trains with a duration of 30 s each, separated by 10 s. After the 5 sessions, BFMDRS improved from 16 to 7. The patient showed improvement of dystonia at rest; however, dystonia during gait persisted after rTMS application.

Discussion

The abnormal movement in this patient was consistent with isolated focal leg dystonia. The old infarct in the right cerebellum without other brain lesions and normal findings of the spinal MRI and NCS/EMG suggest that focal leg dystonia was caused by the cerebellar lesion. In addition, the 5-year interval between acute stroke and the development of dystonia is consistent with the common temporal course of post-stroke movement disorder [14]. The possibility of a genetic etiology for dystonia in this patient was not excluded. However, the age of onset, negative family history, and clinical course of the disease suggested that a genetic cause was unlikely. Focal or segmental dystonia due to cerebellar lesions mostly occurs in the neck and cranial area and rarely occurs in the upper limb [11], though one case report described lower limb dystonia due to syringomyelia and cerebellar ectopia in the cervical spinal cord [15]. Although cerebellar mechanisms of dystonia related to the ectopic lesion were suggested, spinal contributions could be associated with lower limb dystonia in that patient [11]. Functional neuroimaging studies have revealed

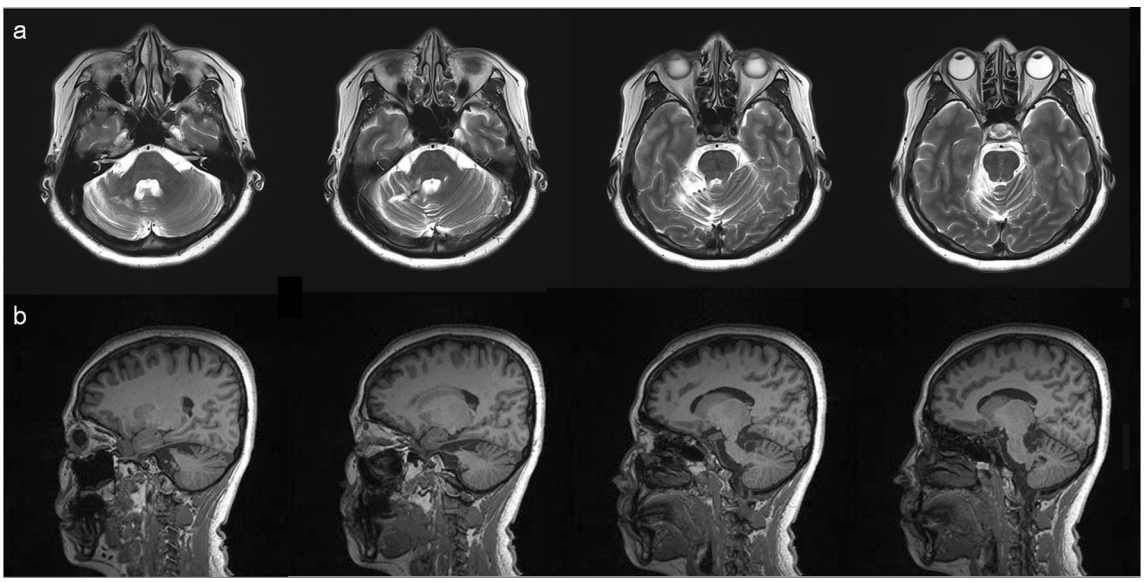

Fig. 1 Brain MRI shows high signal intensities on FLAIR-weighted image **a** and low signal intensities on T1-weighted image **b** in the right anterior cerebellum

that the anterior cerebellum is connected to sensorimotor cortices, and that cerebellar lobules II and III are responsible for foot and leg movements [16, 17]. The cerebellar lesion in this patient was associated with the area for lower limb movements.

It is unclear whether trauma prior to the development of dystonia played a role in the symptoms [18]. The patient did not have any leg pain when dystonia developed, and there was no obvious musculoskeletal traumatic injury. In addition, the dystonia was mobile in form, as opposed to the fixed-form dystonia typically associated with trauma. These findings suggest that the trauma experienced by this patient was likely not directly associated with the focal leg dystonia. Instead, it is possible that the minor trauma may have triggered dystonia in a state of balance without symptoms, even though there was an underlying dysfunction in the basal ganglia-cerebellum-motor network due to the existing cerebellar lesion. If this is the case, then the minor trauma preceding the development of dystonia may have contributed to the movement disorder by taxing an already overburdened neuromuscular system, and disrupting whatever compensatory mechanisms had been at work allowing the patient to remain asymptomatic until this point.

We applied low-frequency cerebellar rTMS on the ipsilateral side of the cerebellum to the old ischemic lesion. Adding to the evidence for cerebellar contribution to dystonia, non-invasive brain stimulation including TMS and transcranial direct current stimulation (tDCS) studies have shown that cerebellar connectivity and plasticity are impaired, and cerebellar stimulation may have a promising effect in patients with dystonia [19–22].In addition, the lesion in the cerebellum responsible for focal leg dystonia was obvious in our patient. The patient showed a partial improvement of dystonia after application of 5 sessions of cerebellar rTMS. Due to limitations in the technology for targeting of the stimulation, we could not select the location of rTMS application over the right anterior cerebellar lesion, which could have caused the limited effect of cerebellar stimulation in this patient. Since rTMS only temporarily changes plasticity in the human brain, it might not be sufficient to normalize distorted functional changes caused by an obvious structural lesion.

This case showed unusual focal leg dystonia as a post-stroke movement disorder due to cerebellar infarction. It may provide valuable evidence on cerebellar mechanisms related to the development of dystonia in a topographically specific manner. However, as the present study only comprised a single case, clinical studies with comparatively larger number of patients are needed to obtain more significant evidence of cerebellar contribution to dystonia. Cerebellar brain stimulation may be a potential therapeutic strategy for patients with dystonia.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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