

The effect of valproate on dystonic movement in a moyamoya patient: A case report

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Abstract

Moyamoya disease (MMD) is a progressive cerebrovascular disorder caused by narrowing of the arteries located at the base of the brain in the basal ganglia. Dystonia is a relatively rare symptom of MMD, and little is known about the treatment of this symptom in MMD patients. We report a case of dystonia in an MMD patient that was alleviated after valproate treatment. A 57-year-old female patient with MMD presented with new-onset dystonia of the left upper extremity and left hemifacial spasm. Although she already suffered from mild cognitive dysfunction, there was no exacerbation when dystonia presented. She was treated with valproate 300 mg b.i.d, and the symptoms were alleviated. We discuss the efficacy of valproate in terms of anatomy and neurotransmitters. In addition, the patient's symptoms are similar to those associated with LGI-1 encephalitis but are distinguished by the progression of the disease.

Keywords: Moyamoya disease, valproate, dystonia, LGI-1 encephalitis, FBDS

INTRODUCTION

Moyamoya disease (MMD) is an uncommon cerebrovascular disorder characterized by progressive occlusion of the supraclinoid internal carotid artery and its main branches within the circle of Willis.¹ Symptoms of MMD can vary widely from headache to ischemic symptoms. Common symptoms of MMD are ischemic episodes in children and intracranial hemorrhage in adults.² Dystonic movement is a relatively rare manifestation of MMD. Treatment of dystonia varies depending on the mechanism, but anticholinergic agents are generally the first choice. Here, we report the case of an MMD patient who showed dystonia symptoms but achieved favorable outcomes after using valproate.

CASE REPORT

A 57-year-old woman presented with dystonic movement of the left arm. She had suffered an ischemic stroke in bilateral frontoparietal lobe seven years prior and had been diagnosed with MMD. She had recovered almost completely, but mild cognitive dysfunction remained. Her

Mini-Mental State Examination (MMSE) score was 27, and her Clinical Dementia Rating (CDR) was 0.5 points. Seven years after the original ischemic attack, she exhibited repeated, intermittent muscle contractions in her left arm that caused abnormal movements and postures. She also had facial distortion on the left side, with the corner of her mouth pulled toward the ear. There were no other prominent neurologic deficits. MRI revealed moyamoya vessels in the basal ganglia (BG). MR angiography (MRA) and conventional angiography revealed moyamoya vessels near an occlusion of the supraclinoid portion of the bilateral internal carotid artery (ICA), multiple telangiectatic collaterals, and several poorly developed perforating vessels and anterior and posterior choroidal arteries (Figure 1). There was no significant change in the vessels compared with seven years prior. DWI showed no evidence of acute infarction. There was no epileptiform discharge on electroencephalography (EEG), and the results of a formal reading by an expert were normal. Single-photon emission CT (SPECT) after acetazolamide challenge showed mildly increased perfusion in the right frontal,

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Date of Submission: 11 August 2023; Date of Acceptance: 13 November 2023

<https://doi.org/10.54029/2024nwd>

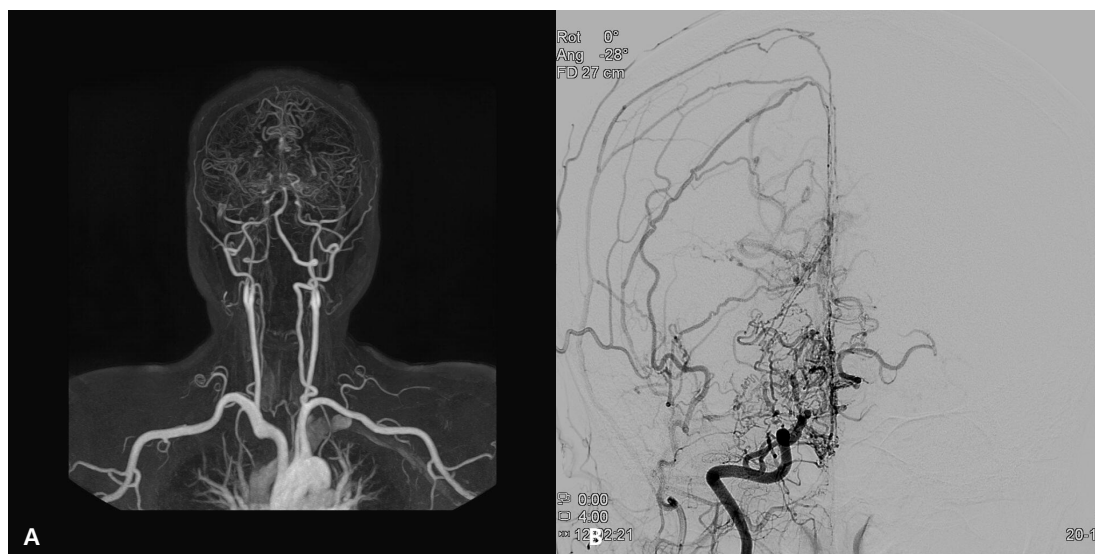


Figure 1. A 57-year-old female with bilateral moyamoya disease. A. MRA showed moyamoya vessels supplied by left and right internal carotid artery. B. Conventional angiography also showed moyamoya vessels supplied by right internal carotid artery.

temporal, and parietal regions with an increased vascular reserve. We initially treated our patient with diazepam, a first-line drug for the treatment of dystonia; the dosage was started at 1 mg b.i.d. and increased to 2 mg b.i.d. However, the medicine did not relieve the symptoms. The patient was then treated with valproate 300 mg b.i.d., and her dystonic movement improved significantly within three days. We continued valproate therapy, but the symptoms recurred when the patient forgot to take her medication for a few days. After that, there was no further symptom recurrence as long as the patient continued taking valproate.

DISCUSSION

Dystonic movement is relatively rare as a manifestation of MMD, but there have been a few reported cases of recurrent dystonic movements as a manifestation of MMD.³⁻⁶ Baik⁷ reported movement disorder associated with MMD, but only 4 of the 42 patients enrolled in that study showed dystonia. Of the four patients with pure dystonia, one developed hemidystonia, while the other three developed focal dystonia affecting the leg, arm, or neck. However, none of them suffered facial dystonia.

In our patient, ipsilateral hemifacial dystonia occurred in addition to hemidystonia, which is rare compared to these reports. Because of this, although the patient had previously been diagnosed with MMD, we had to consider other differential diagnoses, such as LGI-1 encephalitis.

The patient had left-arm dystonia, ipsilateral facial spasms, and cognitive impairment. We considered the possibility that these symptoms were faciobrachial dystonic seizures (FBDSs) indicative of LGI-1 encephalitis. However, the patient's disease course did not match that of LGI-1 encephalitis; FBDSs usually precede full-blown encephalitis^{8,9}, which causes cognitive impairment. Our patient's dystonia improved with valproate, an antiepileptic drug. FBDSs usually respond to immunosuppressants^{9,10}, not antiepileptics. Therefore, the patient's dystonia and cognitive impairment were less likely to be caused by LGI-1 encephalitis. In the present case, the EEG results were normal. However, the presence of epileptiform discharges is not evidence of FBDS, and conversely, FBDS is often observed without EEG changes. Iyer *et al.*¹¹ suggested that FBDS may be a disease of the fronto-temporo-BG network. It is possible that angiogenesis in the BG interfered with the fronto-temporo-BG network and produced similar results. Unfortunately, the LGI-1 antibody test was not performed on our patient.

Khawaja *et al.*¹² reported a case of childhood MMD presenting with recurrent stereotyped episodes of generalized dystonia responsive to valproate. Lee *et al.*⁶ reported that a patient with MMD developed hemichorea responsive to anticonvulsants after revascularization. Dystonia is known to be caused by a pathology of the BG and GABA-producing Purkinje neurons that are involved in motor function. The effect of

valproate on dystonia can be explained as follows: valproate increases the activity of inhibitory GABA receptors in the BG and increases the GABA content of the brain by impeding the hydrolysis of two enzymes that inactivate GABA, namely, GABA transaminase and succinic semialdehyde dehydrogenase, while also affecting sodium channels.^{13,14} Another possibility is that GABAergic neurotransmission was affected by the change in blood flow caused by MMD. DuKart *et al.*¹⁵ found that cerebral blood flow may affect the activity of neurotransmitters. This seems to be the most convincing explanation for why our patient's dystonia responded to valproate, a drug with GABAergic effects.

However, the use of valproate in dystonia patients is controversial because dystonia is a symptom rather than a diagnosis. Moreover, the diseases that cause it are heterogeneous. Depending on the cause of the disease, the treatment may vary. Managing the cause of the disease can often improve dystonia. Brennan reported improvement in Meige syndrome with valproate and baclofen.¹⁶ They suggested reducing activity in the nigrostriatal dopaminergic pathway and inhibiting dopamine release from dopaminergic terminals in the striatum.

On the other hand, valproic acid was ineffective in several studies of DYT11 dystonia (myoclonus-dystonia syndrome).^{17,18} The underlying pathophysiology of myoclonus-dystonia still needs to be elucidated. However, it may relate to dysfunction of striatal monoamine neurotransmission or disruption of cerebellothalamic networks (possibly via a GABAergic deficit of Purkinje cells). Thus, the effect of valproate on dystonia and the associated mechanism is controversial, and further studies on this may lead to exciting research on brain networks in the future.

In this case report, we found that a moyamoya patient with dystonia responded to valproate. However, there is still no consensus on the treatment of dystonia symptoms in moyamoya patients. So far, there have been only a few reports. However, valproate could be a treatment for moyamoya patients, considering various mechanisms and drug action.

DISCLOSURE

Ethics: Informed consent was obtained from the patient for the study and for publication.

Financial support: None

Conflict of interest: None

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