

Effect of acetazolamide for long-lasting paroxysmal dystonia in a patient with multiple sclerosis: a case report and review of literature

Pei-Chun Hsieh¹
Shu-Min Chen¹⁻³
Yao-Hong Guo¹
Ta-Shen Kuan^{1,2}
Wei-Jang Yen¹
Wen-Chen Chang¹
Yu-Ching Lin¹⁻³

¹Department of Physical Medicine and Rehabilitation, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan, Republic of China; ²Department of Physical Medicine and Rehabilitation, College of Medicine, National Cheng Kung University, Tainan, Taiwan, Republic of China; ³Medical Device Innovation Center, National Cheng Kung University, Tainan, Taiwan, Republic of China

Abstract: Dystonia is a rare manifestation of multiple sclerosis (MS), but it always interferes with the functional performance and quality of life. We report a rare case of long-lasting paroxysmal dystonia associated with MS. The patient was a 40-year-old woman with relapsing-remitting MS for 6 years. During the latest attack of MS, she suffered from long-lasting paroxysmal dystonia in her left hand. Despite treatment with pulse high-dose intravenous methylprednisolone, interferon, and baclofen, along with occupational therapy, the dystonia persisted and significantly bothered her daily activities. Finally, she was treated with oral acetazolamide (250 mg, three times a day for 4 days), which was very effective for the control of her dystonia. The dystonic movement subsided without recurrence in a follow-up of 17 months. We advocate this effective and safe treatment for patients with paroxysmal dystonia associated with MS.

Keywords: multiple sclerosis, dystonia, acetazolamide, movement disorders, rehabilitation

Introduction

Multiple sclerosis (MS) is known as an immune-mediated multifocal demyelinating disorder, which consists of components of neuroinflammation and neurodegeneration.¹ It mostly occurs between the ages of 18 and 45 and has a substantial economic and social burden.^{1,2} The most common symptoms include spasticity, fatigue, balance problems, weakness, sensory disturbance, neurogenic bladder and bowel, cognition impairment, depression, pain, sexual disorder, emotional lability, blurred vision, and speech difficulties, in the order of their frequency of occurrence.^{1,2} Compared with the 60%–80% prevalence rate of spasticity due to the involvement of the pyramidal system, the involuntary movement disorders due to the lesion of the extrapyramidal system, such as myoclonus, spasmodic torticollis, paroxysmal dystonia, chorea, and ballism are very rare in patients with MS.² In this case report, we describe a woman with relapsing-remitting MS, complicated with disabling paroxysmal dystonia, which responded very well to the 4-day administration of acetazolamide.

Case description

This 40-year-old woman had unremarkable past medical, family, and movement disorder history. In July 2005, at age 34, the patient initially presented with blurred vision, slurred speech, dysphagia, gradual onset of left hemiparesis, and ataxia. There were no significant biochemical findings in laboratory examinations of serum and cerebrospinal fluid. Surveys of infectious diseases were all negative, including rapid plasma regain, venereal disease research laboratory, human immunodeficiency

Correspondence: Yu-Ching Lin
Department of Physical Medicine and Rehabilitation, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, 138 Sheng-Li Road, Tainan 704, Taiwan, Republic of China
Tel +886 62 353 535 ext 2666
Fax +886 62 766 106
Email richelin@mail.ncku.edu.tw

virus, and cultures. The visual and somatosensory evoked potential indicated a right optic nerve lesion and right thoracolumbar myelopathy, respectively. Magnetic resonance imaging revealed multiple lesions at the cerebellum, brainstem, corpus callosum, as well as at the cervical and thoracic spinal cord. The above symptoms were fully recovered after pulse high-dose intravenous methylprednisolone therapy. There were several relapses with complete remission in the following years. The above findings in this patient met the criteria for the diagnosis of multiple sclerosis. The patient received interferon beta-1b from August 2009.

In April 2011, she suffered from left optic neuritis, weakness in four extremities with spasticity, left paresthesia, neuropathic pain over her chest and back, and impaired proprioception. After pulse steroid therapy, she was transferred to an acute rehabilitation ward for further training. Seven days after the onset of this MS relapse, involuntary movement developed in her left hand, which consisted of nonrhythmic posture of alternative flexion and extension of the fingers, abduction and adduction of the thumb, opponens of the thumb and little finger, flexion, and extension of the wrist. Each episode of dystonia lasted several hours. The involuntary posture was usually aggravated by voluntary motion, attenuated at rest, and might subside temporarily while she slept. It did not involve the proximal upper limbs, lower limbs, trunk, face, and neck. There were no other neurological deficits, such as conscious disturbance, aura, and fatigue, indicating seizure disorders. The psychiatric evaluation was unremarkable. The paresis, spasticity, and neuropathic pain improved after the treatments with steroid, interferon beta-1b, baclofen, and imipramine; however, the paroxysmal dystonia persisted despite the above treatments and occupational therapy. The dystonia impaired her hand function significantly. After discussing the details with the patient, she accepted the prescription of oral acetazolamide (250 mg, three times a day) 17 days after the onset of dystonia. The patient felt progressive reduction in the amplitude of the disabling dystonic movement at first, then in the frequency of symptoms. Finally, dystonic movement subsided 4 days after treatment with acetazolamide. In consequence, she could continue the rehabilitative programs, and her hand functions were resumed to premorbid status. The total treatment time of acetazolamide was 4 days. She was successfully discharged home and was able to participate in most activities. There was no recurrence of dystonia in the following 17 months of follow-up.

Discussion

Paroxysmal dystonia is characterized by intermittent onset of sustained muscle contractions causing patterned twisting and repetitive movements or abnormal postures that might last seconds to hours.^{1,3} The idiopathic paroxysmal dystonia can be subdivided into kinesigenic, nonkinesigenic, hypnogenic, and exercise-induced forms.³ There were also some acquired paroxysmal dystonia, induced by the lesions involving the basal ganglion, extrapyramidal tract system, or thalamus.^{3,4} A widely accepted mechanism of dystonia is the increased motor cortical excitability by altered thalamic signaling.⁵ Paroxysmal dystonia is rare in patients with MS. The pathogenesis of paroxysmal dystonia in patients with MS remains unknown.⁴ Several mechanisms have been proposed, including axonal irritability secondary to the release of inflammatory mediators,⁴ a transversely spreading ephaptic activation of axons within the partially demyelinated lesion at any level in the motor fiber tracts, which was supported by a transcranial magnetic stimulation study.⁵ Beyond the typical localizations, there were some sporadic case reports disclosing the demyelinated plaques in the cervical spinal cord, midbrain, medulla, internal capsule, cerebral peduncle, and even some cases without anatomic evidence in patients with MS.^{1,2,4,5} Some investigators explained that the nature of lacking anatomic evidence for MS may be caused by secondary immune components, such as antibasal ganglia antibodies.⁶

The reported features of paroxysmal dystonia in MS were frequent attacks (several times daily), short duration (seconds to minutes mostly), and stereotyped posture of unilateral dystonia of the arm, leg, and sometimes the face and neck, which could not be attributed to an epileptic origin.^{2,5,7-12} There were some typical trigger factors, such as startle reaction, hyperventilation, stress, and fatigue.³ Paroxysmal dystonia in some patients may subside within a few weeks spontaneously or after treatment.⁷ The most commonly prescribed medication was carbamazepine, but some patients did not have a satisfying response.^{2,4,12} A few cases reported trying to suppress symptoms with acetazolamide,⁹⁻¹¹ phenytoin,¹² adrenocorticotropic hormone,¹³ cannabis,¹⁴ and botulinum toxin.¹⁵ The therapeutic effects varied, and acetazolamide was considered to be the one with fewer side effects. In 1992, Sethi et al⁹ first adopted acetazolamide alone or in combination with carbamazepine in treating three patients with central demyelinating disease and paroxysmal dystonia. Nardocci et al¹⁰ noted that paroxysmal dystonia completely receded with a 4-day treatment of acetazolamide

(250 mg, three times a day), and paroxysmal tremor was also attenuated by a 1-month treatment in a patient. Waubant et al¹¹ reported that the symptoms stopped in a few hours post-acetazolamide treatment (250 mg, twice a day) in their patients. Waubant et al prolonged the treatment for 1 month, and the symptoms did not recur. In addition, acetazolamide was also proven to be effective in hereditary episodic ataxia type 2, another kind of movement disorder.^{3,16}

The exact mechanism of acetazolamide for paroxysmal dystonia in MS remains unclear. Acetazolamide is a carbonic anhydrase inhibitor, which fosters metabolic acidosis across the blood-brain barrier, thereby lowering the intracellular pH that reduces the potassium channels' conductance and might alter the transmembranous potential and neuron excitability.¹⁶⁻¹⁸ In addition, it could alternate the efflux of intracellular bicarbonate through γ -aminobutyric acid (GABA)-activated channels.¹⁹ An animal study gave evidence that showed acetazolamide exerts antidystonic effects in the *dt^{SZ}* mutant hamster via inhibiting bicarbonate regeneration and reducing GABA-mediated excitation without affecting GABA-mediated inhibition.¹⁹ Therefore, the neuronal hyperexcitability might be reduced, and the paroxysmal dystonia improved consequently.

To the best of our knowledge, this type of MS with long-lasting paroxysmal dystonic posture of the hand is extremely rare in the previous literature. The common trigger factors of dystonia, such as startle reaction, hyperventilation, stress, and fatigue, did not induce the patient's dystonia. The occurrence of dystonia endangered independence in the daily basic activities of this patient. Her dystonia did not respond to treatment with steroid, interferon, and baclofen. Because of the good responses and few side effects of acetazolamide in previous case reports for typical short-lasting paroxysmal dystonia in MS,⁹⁻¹¹ we treated our patient with this drug with a dosage of 250 mg, three times a day. The bothersome dystonia subsided after 4 days of treatment with acetazolamide. There was no recurrence of dystonia in the next 17 months of follow-up. This dramatic effect of acetazolamide in our patient with MS and dystonia was an inspiring finding that would be of great interest for further study.

Conclusion

Paroxysmal dystonia is rare in patients with multiple sclerosis, but it significantly endangers the independence of patients in basic daily living activities. It is worthwhile for the physician to identify this disabling but treatable movement disorder. Paroxysmal dystonia in MS may subside without treatment.

In addition to the policy of "wait and see," medications with few side effects, such as acetazolamide, might be one of the treatment alternatives. We shared our clinical experience and advocate this effective and safe treatment option with acetazolamide for individuals with multiple sclerosis and dystonia.

Acknowledgments

We thank Professor Chang-Zern John Hong for his assistance in reviewing this manuscript. This article was supported by a research grant from the National Science Council (NSC 100-2321-B-006-006) in Taiwan, Republic of China.

Disclosure

The authors report no conflicts of interest in this work.

References

- Shneyder N, Harris MK, Minagar A. Movement disorders in patients with multiple sclerosis. *Handb Clin Neurol*. 2011;100:307-314.
- Thompson AJ, Toosy AT, Ciccarelli O. Pharmacological management of symptoms in multiple sclerosis: current approaches and future directions. *Lancet Neurol*. 2010;9(12):1182-1199.
- Dressler D, Benecke R. Diagnosis and management of acute movement disorders. *J Neurol*. 2005;252(11):1299-1306.
- Usmani N, Bedi G, Lam BL, Sheremata WA. Association between paroxysmal tonic spasms and neuromyelitis optica. *Arch Neurol*. 2012;69(1):121-124.
- Trompetto C, Avanzino L, Bove M, Buccolieri A, Uccelli A, Abbruzzese G. Investigation of paroxysmal dystonia in a patient with multiple sclerosis: a transcranial magnetic stimulation study. *Clin Neurophysiol*. 2008;119(1):63-70.
- Delgado S, Baez S, Singer C, Sengun C, Sheremata WA, Papapetropoulos S. Parkinsonism/dystonia syndrome secondary to multiple sclerosis with anti-basal-ganglia antibodies. *Mov Disord*. 2009;24(2):309-311.
- Schmidt FR, Costa FH, Silva FM, et al. Paroxysmal dystonia and neuromyelitis optica. *Arq Neuropsiquiatr*. 2012;70(4):271-272.
- Aguirre-gomez M, Ramió-Torrentà L, Gich J, Quiles A, Genís D. Paroxysmal dystonia and pathological laughter as a first manifestation of multiple sclerosis. *Mult Scler*. 2008;14(2):262-265.
- Sethi KD, Hess DC, Huffnagle VH, Adams RJ. Acetazolamide treatment of paroxysmal dystonia in central demyelinating disease. *Neurology*. 1992;42(4):919-921.
- Nardocci N, Zorzi G, Savoldelli M, Rumi V, Angelini L. Paroxysmal dystonia and paroxysmal tremor in a young patient with multiple sclerosis. *Ital J Neurol Sci*. 1995;16(5):315-319.
- Waubant E, Alizé P, Tourbah A, Agid Y. Paroxysmal dystonia (tonic spasm) in multiple sclerosis. *Neurology*. 2001;57(12):2320-2321.
- Berger JR, Sheremata WA, Melamed E. Paroxysmal dystonia as the initial manifestation of multiple sclerosis. *Arch Neurol*. 1984;41(7):747-750.
- Minagar A, Sheremata WA, Weiner WJ. Transient movement disorders and multiple sclerosis. *Parkinsonism Relat Disord*. 2002;9(2):111-113.
- Deutsch SI, Rosse RB, Connor JM, Burket JA, Murphy ME, Fox FJ. Current status of cannabis treatment of multiple sclerosis with an illustrative case presentation of a patient with MS, complex vocal tics, paroxysmal dystonia, and marijuana dependence treated with dronabinol. *CNS Spectr*. 2008;13(5):393-403.

15. Rüegg SJ, Bühlmann M, Renaud S, Steck AJ, Kappos L, Fuhr P. Cervical dystonia as first manifestation of multiple sclerosis. *J Neurol*. 2004;251(11):1408–1410.
16. Strupp M, Zwergal A, Brandt T. Episodic ataxia type 2. *Neurotherapeutics*. 2007;4(2):267–273.
17. Michel V, Riant F, Tournier-Lasserre E, et al. Long-term improvement of paroxysmal dystonic choreathetosis with acetazolamide. *J Neurol*. 2006;253(10):1362–1364.
18. Olson WL Jr. Acetazolamide relieves concurrent episodic movement disorders encountered in Southern states. *South Med J*. 1999;92(2):228–232.
19. Richter A, Hamann M. The carbonic anhydrase inhibitor acetazolamide exerts antidystonic effects in the dt(sz) mutant hamster. *Eur J Pharmacol*. 2004;502(1–2):105–108.

Neuropsychiatric Disease and Treatment

Dovepress

Publish your work in this journal

Neuropsychiatric Disease and Treatment is an international, peer-reviewed journal of clinical therapeutics and pharmacology focusing on concise rapid reporting of clinical or pre-clinical studies on a range of neuropsychiatric and neurological disorders. This journal is indexed on PubMed Central, the 'PsycINFO' database and CAS.

The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <http://www.dovepress.com/neuropsychiatric-disease-and-treatment-journal>