Low-dose Methylphenidate Monotherapy for Features of Attention-Deficit/Hyperactivity Disorder Secondary to Hereditary Cerebellar Ataxia

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Cerebellar contribution to nonmotor functions including cognitive and affective conditions via the cerebral cortex has been supported by anatomical, physiological, and functional neuroimaging studies. Cerebellar diseases, in general, may be accompanied by cerebellar cognitive affective syndrome (CCAS), which presents with disturbances of executive functioning, spatial cognition, linguistic capacities, and affect [1,2]. Psychiatric conditions that develop secondary to cerebellar lesions include psychosis [3], bipolar mania [4], and depressive disorder [5]. Although the literature on these secondary psychiatric conditions consists mainly of clinical cases, treatment options for psychiatrists have been seldom provided. As a result, psychiatrists have to decide between antipsychotics, mood stabilizers, antidepressants, or noninvasive brain stimulation on a case-by-case basis [5,6]. To the best of our knowledge, features of attention-deficit/hyperactivity disorder secondary to hereditary cerebellar ataxia (ADHD/CA) have never been reported before. Here, we present the case of a patient with CCAS suffering from sudden-onset features of ADHD.

A 16-year-old unmarried female student presented to our outpatient department with acute onset of easy distractibility, hyperactivity, hypertalkativeness, decreased need for sleep, and distorted interpersonal behaviors, including lack of respect for interpersonal boundaries or appropriate social limits for 2 weeks. She was taken to a local medical doctor, who initially suspected the presence of a manic episode of bipolar disorder. Thereafter, the patient was brought to our psychiatric outpatient clinic for a second opinion. The sudden onset of psychiatric symptoms men-

tioned above in the absence of a psychiatric history indicated an atypical presentation. Therefore, she was admitted to the psychiatric ward for further evaluation and treatment.

During the examination, she was well oriented in time, space, and person but had trouble focusing during the interview. No markedly elevated moods such as euphoria, elation, ecstasy, or increased irritability were observed. Her psychomotor activity had accelerated and increased. She had rapid and impulsive speech. Delusions and/or hallucinations were either lacking or could not be elicited.

In addition, neurological evaluation showed normal sensory system, muscle power, and cranial nerves. There was no nystagmus, truncal ataxia, or limb ataxia. She had mild scanning speech. Mild dysmetria was present in the bilateral upper limbs during finger-nose testing. She walked with a slightly wide-based gait and demonstrated difficulty with tandem gait and one-leg stand. Her blood pressure and pulse were normal. There were no Kayser-Fleischer rings. There was a history of poor balance and slightly slurred speech since childhood, with insidious onset of unsteady gait with occasional falls in junior high school. There was no history of brain injury, encephalitis, fever, convulsions, incontinence, swallowing difficulty, or visual problems. She had never consumed alcohol or illicit drugs. Her great-grandfather had been diagnosed with CA at 90 years of age. Moreover, her parents insisted that no features of ADHD were observed by them or her school teachers prior to this incident.

Brain magnetic resonance imaging showed mild bilateral atrophy of the cerebellum. The following laboratory and imaging

examinations were also conducted to rule out acquired causes of CA and to exclude some of the possible organic causes of the sudden-onset psychiatric condition. Urine examination, blood examination including liver and renal functions, electrolytes, thyroid function, vitamin B12, folic acid, and ammonia levels were all within the normal limits. The venereal disease research laboratory test and human immunodeficiency virus screening test were non-reactive. Based on the patient's slowly progressive ataxia since childhood, positive family history of CA and no specific acquired cause of the CA having been found from the physical examination, laboratory tests, and brain imaging study stated earlier, the cause of the CA was more likely to be hereditary than acquired. However, the patient and her parents refused to accept molecular genetic testing.

Because of her sudden-onset psychiatric symptoms, ADHD/CA was suspected and we prescribed methylphenidate (MPH, 5 mg twice a day). The patient showed dramatic improvement in her features of ADHD after starting on the low-dose MPH monotherapy. On the first day of treatment, the patient's parents reported improvement, stating that the patient's inattention and impulsive behaviors such as not listening to others and frequently interrupting ongoing conversation were less disturbing. On the next day, the nursing staff also observed the rapid and substantial improvement, stating that the patient could follow the rules of group activities in the ward for the first time and that "she is different as if she were not the same person." Over the following days, the patient's parents reported improvement almost every day, and 1 week after MPH treatment, she was discharged with very considerable improvement.

In this case, the features of ADHD did not appear until the patient was 16 years of age. The psychiatric presentation was not typical of ADHD because of the late onset. However, it was not typical for a manic episode either, because the core features of elevated or irritable mood were not present. The features were better characterized as being those of ADHD. However, because these features were not present during the developmental years, a diagnosis of primary ADHD could not be made.

An association between cerebellar lesions and the features of ADHD has not previously been established. It has recently been suggested that patients with ADHD might have an increased risk of developing subsequent cerebellar lesions [7]. However, as far as we are aware, ADHD/CA has not previously been reported in the

literature and, consequently, there are no recommended treatment strategies.

The multifaceted neuropsychiatric phenomena following lesions to the cerebellum indicate that these clinical conditions are not likely to be related to the cerebellar lesions itself but probably result from disruption of the cerebellar circuits at various levels in the central nervous system (CNS). In 1998, Schmahmann and Sherman [8] first described "cerebellar cognitive affective syndrome" and suggested that the syndrome was caused by the disruption of the cerebellar modulation of neural circuits that link the prefrontal, posterior parietal, superior temporal and limbic cortices, with the cerebellum. Although most patients with ADHD have no evidence of gross structural damage in the CNS, current advances in neuroscience and neuroimaging have provided evidence that features of ADHD are the result of complex interactions of neuroanatomical and neurochemical systems. In addition, the prefrontal cortex has received considerable attention as being relevant to the understanding of ADHD. The prefrontal cortex also has many reciprocal connections with other brain regions, including the striatum, parietal cortex, and cerebellum [9]. Therefore, networks within the brain may play a vital role in both CCAS and ADHD. Based on these factors, we hypothesize that the ADHD/CA was the result of similar disruption of the cerebro-cerebellar circuits. The dramatic response to MPH might have been through normalization of the activity of the relevant cognitive neuronal networks connecting to the cerebellum [10].

No firm conclusions can be drawn from a single case report. However, these findings might alert clinicians to be aware of the possibility that features of ADHD might accompany hereditary cerebellar ataxia and also to the possibility that ADHD features might respond to treatment with low-dose MPH in this situation.

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Conflict of Interest

The authors declare no conflict of interest.

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