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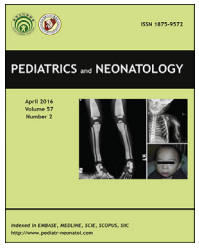

BRIEF COMMUNICATION

Dramatic Improvement in Juvenile Parkinsonism after Levodopa Treatment in a Patient Negative for the *PANK2* Mutation

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1. Introduction

Juvenile parkinsonism is a rare movement disorder. In pediatric patients, the manifestations are more complex and varied, which makes the diagnosis challenging. It may occasionally manifest as another disease such as dopa-responsive dystonia, Wilson disease, or neurodegeneration with brain iron accumulation (i.e., Hallervorden–Spatz disease).[1,2] This paper reports a 14-year-old girl who experienced a variety of movement disorders such as parkinsonism and dystonia. Her symptoms changed and worsened within a few years, but dramatically improved with levodopa treatment.

2. Case Report

A 14-year-old girl was first brought to the outpatient clinic because of progressively slowing gait, tremors, and limbs dystonia. During infancy, she was relatively quiet and less energetic in comparison to other babies. She started walking at the age of 1 year and 8 months, but only started talking at 3 years old. Her parents observed the developmental delay, but did not have her undergo further evaluations. At the age of 9 years, she had intermittent tremors, upper extremity dystonia, and dysarthria.

By the time she was 13 years old, her symptoms had worsened and repetitive stereotyped behaviors began. Soon after, she began to experience fecal and urine incontinence, and she lacked facial expression, drooled uncontrollably, and screamed loudly and meaninglessly. She was administered various medicines such as anticholinergic drugs, dopamine antagonists, and antipsychotics, but these all failed to stop the deterioration of her symptoms. When she presented to the outpatient service at the age of 14 years, she could neither walk nor stand.

Neurologic and physical examinations revealed marked generalized spasticity and extreme postural instability. Her range of eye motion was full, but she had facial masking, hand dystonia, increased deep tendon reflexes, and knee jerks. Muscle power in all extremities was full and sensation was intact. Routine blood tests such as complete blood count, differential count, copper, ceruloplasmin, iron, ferritin, lactate, amino acids, organic acids, and thyroid function were within normal limits. Chromosome analysis and tests for the methyl CpG binding protein 2 (*MECP2*) gene and pantothenate kinase 2 (*PANK2*) gene were also normal.

Electroencephalography showed no epileptiform discharges but showed a slow background. Brain magnetic resonance imaging obtained at 13 years of age demonstrated bilateral symmetric low-intensity signals in the T2 images of the globus pallidus. Proton magnetic resonance spectroscopy (MRS) revealed a decreased N-acetylaspartate

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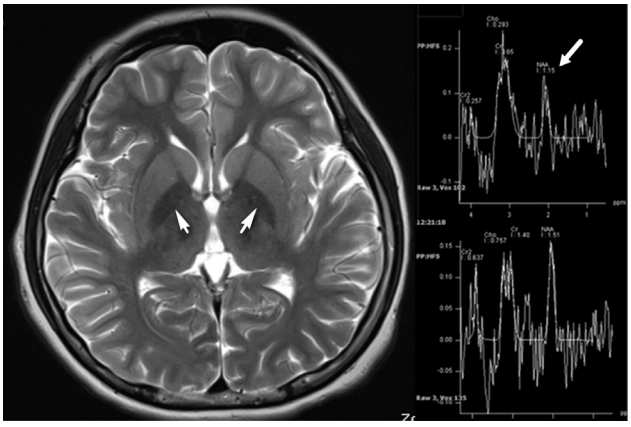

Figure 1 Brain magnetic resonance T2 image of the patient at 13 years old reveals bilateral symmetric low-intensity signal in the globus pallidus (left, arrow). The proton magnetic resonance spectroscopy image reveals an abnormally decreased n-acetylaspartate peak in the basal ganglia (upper right, arrow) in contrast to the normal n-acetylaspartate peak (lower right) in the contralateral gray matter area.

peak in the basal ganglia at 14 years of age (Figure 1). The Tc99m-ECD brain perfusion single-photon emission computed tomography (SPECT), also obtained at 14 years of age, revealed hypoperfusion of the left basal ganglia.

Her parents do not remember any history of movement or neurodegenerative disorders. Tracing her previous medical record showed she received dopamine antagonists and antipsychotics, which worsened her clinical condition.

This time, she was administered levodopa at 1 mg/kg/day that was gradually increased to twice daily. Soon after, her slow gait and dystonia dramatically improved. Her tremors were also successfully controlled. Within 1 week after starting levodopa treatment, she was able to walk and her hand tremors and dystonia improved significantly.

3. Discussion

Parkinsonism is common in adults; it typically manifests in middle and late life. However, a juvenile form can occur before the age of 20 years.[3] In pediatric patients, juvenile parkinsonism is often difficult to diagnose and manage. The variable symptoms and etiologies make it difficult to identify juvenile parkinsonism; because of the possible adverse effects of levodopa, many clinicians hesitate to use it in the early stage of the disease.[4]

In this patient, parkinsonism combined with dystonia is a more accurate description of her symptoms. However, some monamine neurotransmitter metabolism disorders (e.g., dopa-responsive dystonia, sepiapterin reductase deficiency) may present with similar features. Based on her SPECT scanning (e.g., hypoperfusion of the left basal ganglia) and neuroimaging findings (e.g., basal ganglia T2 hypointensity), the most likely etiology was neurodegeneration with iron accumulation in the brain.[5] In recent years, similar disorders of brain iron content without *PANK2* mutations such as aceruloplasminemia, neuroferritinopathy, and infantile neuroaxonal dystrophy have been classified as disorders of neurodegeneration with brain iron accumulation.[6] However, because of the availability of genetic testing and because *PANK2* accounts for nearly one-half of cases, *PANK2* was chosen for genetic testing. The results showed she had no mutation in the gene.

Levodopa is the most effective drug in the treatment of parkinsonism[7]; however, its effectiveness in pediatric patients remains unclear. This report underscores how the early and decisive use of levodopa can effectively improve juvenile parkinsonism with unknown cause, perhaps even as a diagnosis of exclusion by treatment.

Conflicts of interest

The authors have no conflicts of interest to declare relevant to this article.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.pedneo.2015.06.002.