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Juvenile Parkinsonism Misdiagnosed as Dopa-responsive Dystonia: A Case Report

Su Ji Lee[1*], Seungbeen Hong[1], Myungsang Kim[3], Sung-Rae Cho[1,2†]

Yonsei University College of Medicine, Department of Rehabilitation Medicine and Research Institute[1], Yonsei University College of Medicine, Brain Korea 21 PLUS Project for Medical Science[2], Gangnam Severance Hospital, Rehabilitation Institute of Neuromuscular Disease, Yonsei University College of Medicine, Department of Rehabilitation Medicine[3]

Introduction
Juvenile parkinsonism(JP) may present atypical features such as dystonia, unlike elderly-onset parkinson's disease. Thus, JP is often misdiagnosed as other diseases, including dopa-responsive dystonia. The aim of this report is to present a case of JP misdiagnosed as Dopa-reponsive dystonia.

Case Reports
A 32-year old female visited our outpatient clinic with gait disturbance. She had no specific past history or family history. When she was at 19 years old, clawing toes emerged and genu recurvatum was progressed. In December 2007, Electromyography(EMG) was performed at other institution to rule out hereditary myopathy. However, EMG findings were not compatible for any types of myopathies so she was considered to have hereditary spastic paraplegia. In physical examination, bilateral lower extremities showed normal except for left hip flexor (Grade 4) on manual muscle test. Muscle tone was increased in both legs and hyperactive patella tendon reflexes were noted. There were no clasp-knife response or cogwheel rigidity. When she walks, in-toeing gait pattern in both legs, genu recurvatum in left knee and toe walking in right foot were observed. These patterns showed diurnal variation and got worsen in the afternoon. In January 2010, we conducted direct sequencing after Polymerase Chain Reaction to confirm mutation of Spastin (SPG4), the causative gene of familial spastic paraplegia, no mutation for SPG4 was found. We tried low-dose levodopa-carbidopa administration considering possibility of DRD and most of her symptoms and patterns of diurnal variation were disappeared. In April 2010, we conducted a trial to compare before and after low-dose levodopa-carbidopa administration. Before low-dose levodopa-carbidopa administration, the Dystonia Movement Scale(DMS) was 10 out of 120 points and the Disability scale(DS) was 5 out of 30 points, whereas the DMS and DS after administration was 2 and 1. (Figure 1) In September 2012, direct sequencing of the GCH1 gene, which is known to be a cause of DRD, was performed, however, there was no mutation in coding region of GCH1 gene. We

regarded her diagnosis as DRD and continued levodopa treatment because GCH1 gene mutation is not positive in all of the DRDs (more than 50% positive) and clinical symptoms of the patient were consistent with DRD. In February 2018, PARK2 exon 4 deletion was identified through Next-Generation Sequencing(NGS) (Figure 2) and decreased F-18 FP-CIT uptake in the bilateral putamina and posterior caudate nuclei in dopamine transporter imaging with fluorine-18-FPCIT. (Figure 3) Finally, she was diagnosed with JP.

Conclusion

We report a case of juvenile parkinsonism previously regarded as dopa-responsive dystonia. If abnormal muscle tone or movement is observed in the younger patients, it is necessary to consider these various medical condition and make a differential diagnosis.

	Before	After
Dystonia Movement Scale	10	2
Disability Scale	5	1

Figure 1. Comparison of Dystonia Movement Scale and Disability Scale between before and after low-dose levodopa-carbidopa administration

Variants of Interest

ACMG Classification	Gene	Accession	Nucleotide	Amino acid	Zygosity	dbSNP	Disorder (OMIM, HGMD)	Inheritance	Global (ExAC)	Korean (KRGDB)	Comments
Likely pathogenic	PARK2	NM_004562.2	Exon 4 deletion		Homo		Adenocarcinoma of lung, somatic, 211980 (3); Adenocarcinoma, ovarian, somatic, 167000 (3); {Leprosy, susceptibility to}, 607572 (3); Parkinson disease, juvenile, type 2, 600116 (3); Autosomal recessive	AR			variant validation
VOUS	NLGN1	NM_014932.3	c.2147G>A	p.Arg716His	Hetero	rs118079207			0.0004	0.00884244	
VOUS	DCAF17	NM_025000.3	c.-111G>T		Hetero	rs80336595	Woodhouse-Sakati syndrome, 241080 (3), Autosomal recessive	AR	0.0006	0.0096463	

* dbSNP, The Single Nucleotide Polymorphism Database; OMIM, Online Mendelian Inheritance in Man; ExAC, population frequency from The Exome Aggregation Consortium; KRGDB, population frequency from the Korean Reference Genome DB; VOUS, Variants of unknown significance; AD, autosomal dominant; AR, autosomal recessive; XD, x-linked dominant; XR, x-linked recessive

Figure 2. PARK2 exon 4 deletion was identified through Next-Generation Sequencing(NGS)

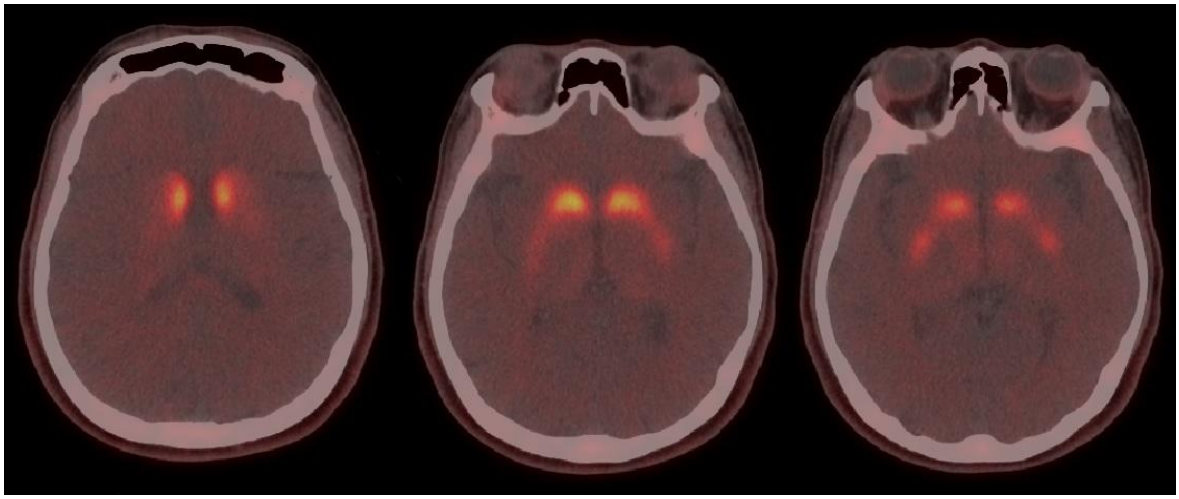

Figure 3. Hypometabolism in the bilateral bilateral putamina and posterior caudate nuclei was noted in fluorine-18-FPCIT PET-CT images.