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CASE REPORT

Subthalamic Nucleus Deep Brain Stimulation Treatment for Generalized Off-Period Dystonia in Parkinson's Disease : Case Report

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Currently, deep brain stimulation (DBS) is the safest and the most effective surgical treatment for Parkinson's disease (PD). However, there is no general consensus on whether subthalamic nucleus (STN) or globus pallidus internus (GPi) is the best target for PD. Generally, bilateral GPi-DBS is the preferred rational surgical strategy for dystonic symptom in PD. However our case proved that bilateral STN-DBS could significantly improve off-dystonia symptoms for PD having severe generalized off-dystonia symptoms with dopamine response. Therefore, STN-DBS can be considered as treatment for generalized off-dystonia in PD patients with levodopa response.

KEY WORDS: Deep brain stimulation · Off-period dystonia · Subthalamic nucleus · Globus pallidus internus.

INTRODUCTION

Parkinson's disease (PD) patients who are responsive to levodopa with appropriate motor fluctuation are potential candidates for deep brain stimulation (DBS) known to have electrical, chemical, and other neuronal-network influence on brain tissue.[12)15)] Over the last two decades, two specific sites in the brain have been most commonly targeted for DBS in PD : the subthalamic nucleus (STN) and the globus pallidus internus (GPi). Both STN and GPi are nuclei in the basal ganglia as key parts of the neuronal network, where much of the degenerative change in PD occurs. STN is part of the indirect basal ganglia pathway while GPi is part of the direct pathway. Hence, stimulating each of these targets can improve PD motor symptoms.[9)12)15)] Historically, the target of choice for DBS in management of PD patient with dystonia has been GPi. However, recent trend for off-period dystonia treatment is to delay levodopa introduction and in smaller daily dose for reduced dystonic phenomena. In addition, STN has been proposed as a target for patients with off-period focal dystonia. Those with young onset PD (YOPD) characterized by severe akinesia with a high degree of sensitivity to levodopa and a tendency to develop dyskinesia, especially painful off-period focal dystonia, seem to be ideal candidates for bilateral STN-DBS.[7)9)13)] In addition, mostly off-period dystonia usually appears in focal dystonia and most frequently affects the foot.[7)] However, our case had unusual dystonic features. Here we report a rare case of a man with YOPD who developed very severe and uncommon dystonia feature combined with varying generalized off-dystonia appearance simultaneously who was treated with bilateral STN-DBS.

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CASE REPORT

The patient was a 47-year old man with a nine-year history of Parkinson's disease manifested by tremor, rigidity, bradykinesia, and off -period dystonia. He has been taking Parkinson's medication since 2004. When he visited our center, he was treated with 843.5mg levodopa equivalent daily dose (LEDD). Although he was on PD therapy of medication with physical therapy, the treatment was ineffective in reducing motor impairment or disability as time went by. His initial symptom was right hand tremor. It progressed to tremors of both hands and legs. In the off period, he showed marked bradykinesia. His speech was slurred. In addition, he had severe cogwheel rigidity in both limbs and the neck. Thus, this patient had markedly different dystonia feature of generalized dystonia with PD and levodopa-responsive form of dystonia. Preoperatively, dystonic movement observed both upper limb and left leg. Symptoms appear during drug off state, without any par-

ticular area or time when the symptoms become severe, but the patient has been observed to show dystonic symptoms depending on movement. The following dystonic movement was found on resting, action, and waking. When he was at resting state, his right shoulder showed abduction and elevation, showing right elbow flexion in front of chest. His left shoulder showed adduction, having left elbow flexion on the lateral chest. Even on action, his face turns to the left side with left laterocollis. The patient had truncal dystonia. The patient had dystonia at both hands and forearms, thus limiting writing and eating tasks. Foot dystonia in the patient had flexion of the left toe II-V and extension of the big toe such as striatal foot. These phenomena and dystonia pain were not only increased in the morning, but also throughout the day. In addition, his dystonia features was similar to those of early childhood onset dopamine-responsive dystonia because his dystonia had dramatic levodopa response. While walking, his arm swing was absent due to severe dystonia symptoms and gait freezing appearance. He also showed either both upper limb dystonia or left big toe dystonia. His posture was leaning to the left side. In addition, he complained wearing-off phenomena.The findings on computed tomographic (CT) and magnetic resonance image (MRI) were with normal limits. Fluorine-18 labeled FP-CIT positron emission tomography (PET) images represent symmetrically decreased radiotracer uptake in bilateral basal ganglia (BG), especially lentiform nuclei. He underwent surgery in July 2013. There were no intraoperative complications. His generator settings were stable with good capture of his PD symptoms by a contacts 1, 60μs pulse width of 2.5V at 130 Hz on both sides. His dystonia, tremor, rigidity, and bradykinesia were all greatly improved. His unified Parkinson's disease Rating Scale (UPDRS) motor score was improved from 43 to 8 and his Hoehn & Yhar scale was improved from 3 to 1 (Table 1). His Burke-Fahn-Marsden rating Scale (BFMRS) sub-scores showed marked improvement from 72 to 2 (Table 2) and initial postoperative period LEDD reduced from 843.5mg to 498mg. Furthermore, his off-period dystonia and pain have relieved complete since the immediate postoperative period.

DISCUSSION

More than 120,000 patients had taken DBS worldwide. Previous data have proven the efficacy and safety of DBS. Thus, DBS has become particular useful in the therapeutic strategy for PD. Despite the increasingly widespread use of this surgical technique, there is no general consensus on whether GPi or STN is a better target for PD. This question remains unclear.[3)15)] Before performing DBS, the crucial issue is : which brain target should be chosen to optimize the patient's outcome? Previous studies have proved that GPi-DBS is an effective treatment for various types of dys-

Table 1. Unified Parkinson's disease Rating Scale with 5-year follow-up

	Pre-operation		Post-operation	1 year	3 year	5 year
	Drug on	Drug off	On	On	On	On
I. Mentation, Behavior and Mood	2	2	0	1	1	1
II. Activities of Daily living (ADL)	13	25	10	10	10	10
III. Motor scale	15	43	8	10	11	12
IV. Dyskinesias	0	0	0	0	0	0
V. Hoehn & Yahr	1	3	1	1	1	1
VI. Schwab & England ADL score	80	50	90	90	90	90

Table 2. The Burke-Fahn-Marsden rating Scale with 5-year follow-up

	Pre-operative	Post-operative	1 year	3 year	5 year
Eye, mouth, speech/swallowing (0−32)	4	2	2	2	2
Neck (0−8)	8	0	0	0	0
Right arm (0−16)	16	0	0	0	0
Left arm (0−16)	16	0	0	0	0
Trunk (0−16)	12	0	0	0	0
Right leg (0−16)	0	0	0	0	0
Left leg (0−16)	16	0	0	0	0
Total	72	2	2	2	2

tonia as well as PD. In addition, it has lower risk of complication than pallidotomy. Since GPi-DBS has larger brain targets than STN, it can be more effective for stimulation with more safety.[5)11)15)] On the other hand, a meta-analysis has found that STN-DBS is more effective on akinesia. It can improve all types of levodopa induced dyskinesia (LID) at various degrees. It has the most dramatic effect on off-period focal dystonia because off period dystonia is associated with parkinsonian signs caused by dopamine depletion. It can improve with the same therapeutic measures used for motor fluctuation.[1)7)13)] The effect of DBS is due to its inhibition of neuronal cell body and excitation of neighboring fibers. Thus, it can change the firing rate and pattern of neurons in BG. It can also stimulate astrocytes to release calcium that may lead to the release of glutamate and adenosine, resulting in local increase in cerebral blood flow and stimulated neurogenesis. All these actions influence multiple thalamcortical circuits, downstream pathways, and other brain structures. Thus, it has electrical, chemical, and neuronal-network influence on brain tissue.[12)] Both STN and GPi are key parts of the neuronal network. They can stimulate sensorimotor subregions and reduce PD motor symptoms. However, there are differences in basal ganglia-thalamo-cortical circuit and morphology.[15)] The indirect BG pathway of STN contains neuropeptide enkephalin and dynophin while the direct pathway of GPi neurons carry neuropeptides substance P. These two pathways can be inhibited by neurotransmitter GABA but excited by glutamine.[6)] Furthermore, sizes of both targets are obvious different. The GPi has a large size of motor region, thus requiring large electrical fields for effective stimulation and easier programming. In addition, it has less manipulation by medications than STN.[10)15)] On the other hand, STN allows for lower battery consumption with much more reduction in dopaminergic medication because stimulation of the STN can activate nigrostriatal (increasing release of dopamine) fiber tracts which may benefit those with all types of LID at varying degrees. The most dramatic effect has been observed for off period focal dystonia because STN stimulation can lead to inhibition of thalamus, thus promoting a decrease of unwanted motor activity such as drug-induced dyskinesia.[6)10)15)]

PD-related dystonia is associated with frequent and long duration of levodopa treatment. It involves a complete spectrum of focal dystonia. The most frequent site for off-period dystonia is the foot. For peak dose dystonia, neck and face are commonly involved. Diphasic dystonia usually affects both distal and proximal lower limbs as well ipsilateral arm.[4)14)] Our case had unusual dystonia features, including foot dystonia, neck dystonia, and digital and proximal lower limbs dystonia with good levodopa response. In addition, it usually occurred at drug off period. Thus, these dystonic phenomena elicited generalized off-period dystonia. These motor complications caused severe disability and impaired his quality of life. Dopamine depletion seen in PD can lead to a reduction in selectivity and special focalization of cortico-BG circuitry. The primary goal of PD treatment is to elevate the level of dopamine in the brain. However, treatment with dopamine may lead to hypersensitivity of postsynaptic dopamine receptors. After 5−10 years of treatment, most patients with PD have motor fluctuation.[8)9)] Thus, when medical treatment fails, DBS is usually considered.[3)] Selecting the best DBS target for PD is still controversial. Previous studies have already proven that bilateral GPi stimulation can ameliorate dystonia symptoms.[4)7)9)] In contrast, Detante, et al.[2)] reported that four patients with generalize dystonia underwent STN-DBS was ineffective. However, STN-DBS of PD with dopamine sensitive generalized off-period dystonia could be a favor treatment target of DBS.

CONCLUSION

In conclusion, our case suggests that the STN may become the preferred target for DBS in PD with young onset and levodopa-responsiveness generalized off-period dystonia along with severe disability and akinesia.

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