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Case Report

Delayed Onset Eye Opening Apraxia due to Progression of Brain Atrophy following Subthalamic Nucleus Deep Brain Stimulation: A Case Report

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Eye opening apraxia (EOA) has been described in literature as a complication of deep brain stimulation (DBS), especially after electrode implantation in the subthalamic nucleus (STN). EOA can be either worsened or alleviated by DBS depending on the etiology. Herein, we report a rare case where the progression of brain atrophy may have contributed to the delayed onset of EOA. The patient, a 73-year-old woman, had previously undergone bilateral STN-DBS for advanced Parkinson's disease (PD), which was performed by another DBS team, at the age of 68 years. She initially experienced a dramatic improvement in her motor symptoms, with no adverse events. However, she had difficulty in opening her right eye 3 years after the DBS surgery. Imaging studies showed that the brain atrophy had progressed over the past 5 years, and that the DBS electrodes were implanted through the far anterior entry points. We considered that the relative movement of the DBS might have been caused by the progression of the brain atrophy to the posterior limb of the internal capsule (IC) where the corticobulbar tract exists, and this was enhanced by the lower implantation angle. The present case illustrates the importance of the DBS insertion angle considering the a+ trophic effect and the follow-up imaging studies after DBS.

Keywords: eye opening apraxia; deep brain stimulation; corticobulbar tract; adverse event

Introduction

Eye opening apraxia (EOA) has been described in literature as a complication of deep brain stimulation (DBS), especially after subthalamic nucleus (STN) DBS,[1–3] and a 1.8–30% prevalence has been reported.[4] Two potential mechanisms of this complication are off dystonia due to the progression of Parkinson's disease (PD) and spread of electrical stimulation to the corticobulbar tract.[2] The EOA can be either worsened or alleviated by DBS depending on the etiology, but this complication usually occurs immediately after surgery in either cases. Herein, we report a rare case where the progression of brain atrophy as well as the DBS implantation technique contributed to the delayed onset of EOA.

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Case Report

The patient was a 60-year-old woman when she was diagnosed with PD, and started on antiparkinsonian medications. Her PD symptoms gradually progressed over time to the point where wearing-off and on/off motor fluctuations aggravated her quality of life. She was, therefore, underwent bilateral simultaneous STN-DBS implantation at the age of 68. Preoperatively, the diagnosis of PD was confirmed by a levodopa challenge test and metaiodobenzylguanidine (MIBG) scan. A preoperative levodopa challenge test showed dramatic improvements in her motor symptoms as her Unified Parkinson's Disease Rating Scale (UPDRS) Part III scores were 4 and 35 in on and off medication states, respectively. The cardiac MIBG uptake was significantly decreased as the heart to the upper mediastinum ratio were 1.39 and 1.26 at early and delayed phases, respectively. She initially experienced a dramatic improvement in her motor symptoms, with no adverse events. However, she gradually developed difficulty opening her right eye 3 years after the DBS surgery. At that time, she was diagnosed with senile ptosis at another institution, and subsequently underwent plastic surgery that did not resolve the problem. She was, therefore, referred to our institution for further evaluation 5 years after DBS surgery at the age of 73.

At our institution, she was evaluated by our multidisciplinary team. She showed continuous eye closure with intermittent high-frequency eye blinks on the right without abnormal movements of the mouth or neck in the DBS state. To test whether her eye opening difficulty was stimulation-induced or not, we evaluated her facial symptoms under off DBS condition. This test revealed that her facial symptoms disappeared when only the left DBS was turned off, and the condition of the right DBS did not affect the eyelid symptoms. Additionally, the severity of EOA symptom did not fluctuate with on/off medication states, and the levodopa equivalent dose of her medication was 430 mg. It should be also noted that she did not have cognitive declines.

The UPDRS motor scores were also evaluated under off medication condition to confirm whether the left DBS was had an effect on her motor symptoms in the off medication state. While the left DBS was responsible for the right EOA, the left STN-DBS was attributable for motor symptoms as the total UPDRS motor score was 35 and 20 with off and on the left DBS conditions, respectively. Her pulse generators (Soletra, Medtronic, Minneapolis) were originally programmed at the previous institution as follows: 3 (–), Case (+),

60 μsec, 180 Hz, 2.5 volts on the left and 2 (–), 3 (+), 60 μsec, 160 Hz, 2.5 volts on the right.

Imaging studies revealed that the brain atrophy had progressed over the past 5 years (Fig. 1). Besides, stereotactic measurement of the DBS electrode locations revealed an extremely low insertion angle relative to the anterior commissure (AC) - posterior commissure (PC) line. We used a stereotactic working station (iPlan, Brainlab, Germany) for measurement, and the data are described in Table 1. In her case, model 3389 lead (Medtronic, Minneapolis) was implanted.

We tried a variety of stimulation settings. Threshold testing of the stimulation-induced side effects using monopolar settings (60 μsec, 160 Hz) revealed that the stimulation of the dorsal contacts (2 and 3) was more likely to induce EOA at lower voltage than the stimulation of ventral contacts (0 and 1). However, more intensive stimulation than the threshold level of EOA was required to improve the motor symptoms in the right hemibody. Lower stimulation intensity, thus, alleviated EOA symptoms but aggravated the overall motor symptoms. In the present case, replacing the left STN lead with a globus pullidus interna (GPi) lead might have been a treatment option as reported by another group;[5] however, she was not willing to undergo additional surgery to solve her problem. We, therefore, instructed her to turn off the left DBS device and take additional medications as needed in a social situation that she would like to suppress the EOA. As the bipolar settings were less likely to induce EOA than monopolar settings, we also reprogrammed the left IPG as follows: 1 (–), 2 (+), 60 μsec, 180 Hz, 3.0 volts.

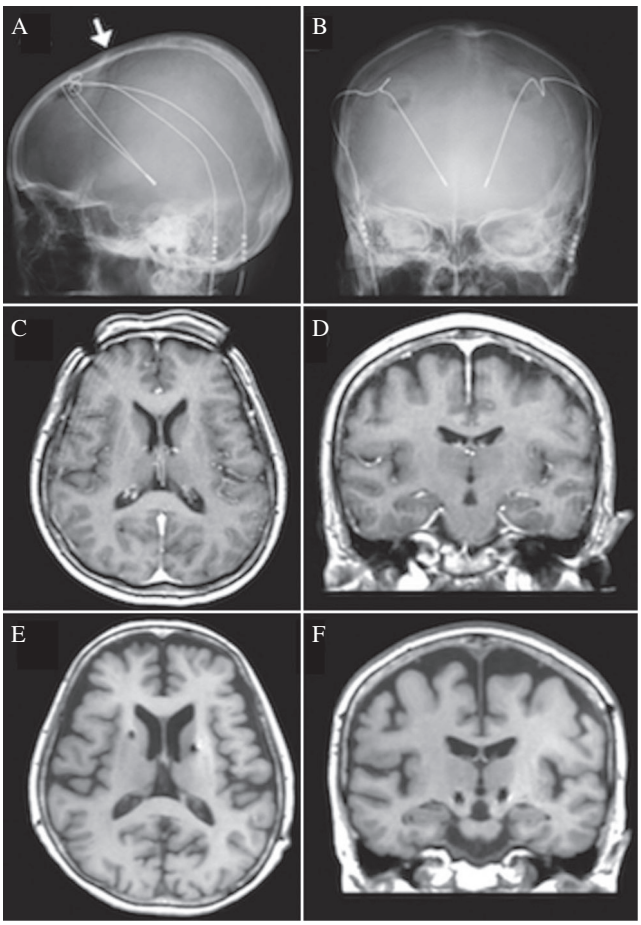

Fig. 1 Imaging studies of the patient. A and B. Skull X-ray images showing the intracranial electrodes with the far anterior entry points. C and D. T_1-weighted images with contrast for stereotactic planning at the age of 68 years. E and F. T_1-weighted images without contrast 5 years after DBS surgery. These MRI images show the atrophic change in the brain over a period of 5 years.

Table 1 Coordinates of the tip of the electrodes relative to the mid-commissural point

	X	Y	Z	Center-line angle	AC-PC angle
Left	−10.1	−4.9	−6.76	19.87	44.27
Right	10.52	−5.03	−7.36	17.05	52.18

Discussion

The EOA symptom in the present case started in a delayed fashion. In this case, clinicians should be aware that there were at least two differential diagnoses including off dystonia and DBS side effects.[2] A simple solution to differentiate these two conditions is just turning off the DBS. If EOA aggravated under an off DBS condition, stimulation intensity may be increased. Our patient was considered to have stimulation-induced side effects as the off DBS condition clearly improved the EOA symptom. The severity of the EOA may fluctuate with medication dosages, but the mechanisms have not been understood completely.[6]

Interestingly, the onset of EOA was delayed for 3 years following DBS surgery in the present case. One possible explanation was that the relative movement of the DBS lead moved closer to the posterior limb of the internal capsule (IC) where the CBT exists due to brain atrophy. Even though the early progression of brain atrophy like our case is rare, it has been reported that the patients PD had significantly higher annual atrophy rate (0.8%) than normal subjects.[7] One group speculated that the brain atrophy may progress along the neuronal network where alpha-synuclein accumulates.[8] Recently, Martinez-Ramirez et al. reported three cases where brain atrophy had potentially contributed to the decrease in the threshold levels of stimulation-induced side effects over time.[9] We speculated that a similar case scenario had occurred in our patient as the MRI images showed clear progression of brain atrophy. Not every STN-DBS patient, however, has decreased threshold levels of the stimulation-induced side effects. In our case, a lower insertion angle with a far anterior entry point may be another factor. With this angle, DBS electrode is likely to be located closer to the IC compared with the higher insertion angle (Fig. 2).

Even though this is a report of only one patient, our case addressed the importance of on/off testing of the DBS devise for accurate diagnosis and appropriate insertion angle for better long-term outcomes considering the possible atrophy with aging. We advocate that DBS patients should be closely followed-up, and imaging studies should be performed regularly.

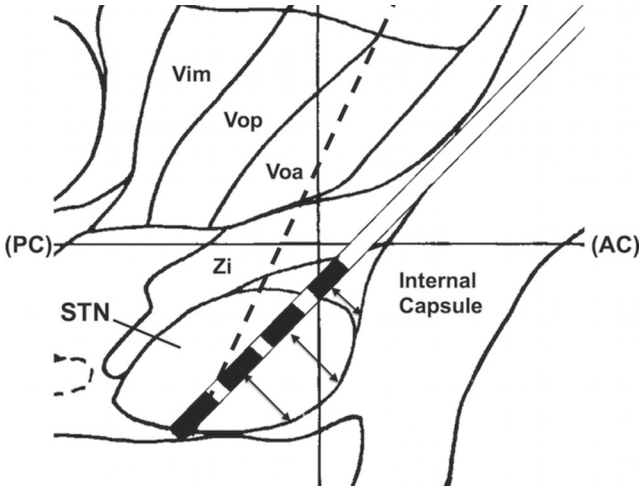

Fig. 2 Relationship between the implanted electrode and internal capsule. In this figure, the electrode is positioned at a 44° AC-PC angle, and the dotted line indicates DBS trajectory at a 65° AC-PC angle. The figure illustrates that the lower insertion angle may determine the distance between each DBS contact and internal capsule. Vim = ventral intermedius; Voa = ventralis oralis anterior; Vop = ventralis oralis posterior.

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Disclosure

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