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Deep brain stimulation improves cerebellar tremor symptoms in paraneoplastic cerebellar degeneration: a case report

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Abstract

Paraneoplastic cerebellar degeneration (PCD) is a rare neurological syndrome caused by a remote effect or immune response involving the cerebellum due to tumor. Here, we report a rare case of PCD secondary to ovarian cancer, presenting clinically with cerebellar tremor. The patient presented with involuntary movements affecting the head, neck, and limbs, along with ataxia and horizontal nystagmus. After conventional medical treatments proved ineffective, the patient underwent a multidisciplinary assessment and received approval from the Institutional Review Board at Affiliated Nanjing Brain Hospital, Nanjing Medical University, to consent to deep brain stimulation (DBS) targeting the ventral intermediate nucleus (VIM) of the thalamus. During the 18-month follow-up, the frequency and amplitude of the tremor significantly improved, with the TRS (1–9) total score decreasing to 23, a 64.06% improvement compared to preoperative levels. The ADL scale score increased from 10 preoperatively to 35, indicating a significant improvement in quality of life. Additionally, the patient's cognitive and ataxic symptoms did not worsen. These results suggest significant improvement in symptoms compared to baseline, with enhanced daily life activities and improved quality of life.

Keywords Paraneoplastic neurological syndrome, Paraneoplastic cerebellar degeneration, Deep brain stimulation, Cerebellar tremor, Case report

Introduction

Paraneoplastic cerebellar degeneration (PCD) is one of the common types of paraneoplastic neurological syndromes (PND) [1]. It is caused by the remote effects of tumors or autoimmune reactions affecting the cerebellum, and clinically manifests as cerebellar involvement symptoms such as ataxia, spontaneous nystagmus, and cerebellar tremor, often accompanied by abnormal autoantibodies in serological tests [2, 3]. The diagnosis of PCD is primarily based on the diagnostic criteria for PND proposed by Graus et al. [4] in 2004. Currently, the diagnosis and treatment of PCD face numerous challenges, with a high risk of misdiagnosis in the early stages. Even after diagnosis, there is a lack of clear clinical

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evidence for the effectiveness of symptomatic treatment and immunotherapy targeting the autoimmune response.

Case Presentation

This case report describes a 55-year-old patient with ovarian cancer who presented with dizziness, unsteady gait, and right-sided paroxysmal headache, accompanied by nausea, vomiting, and slurred speech on January 10, 2023, without any obvious cause. Initially diagnosed with "viral encephalitis," she was treated with anti-inflammatory steroids, immunomodulatory gamma globulin, clonazepam, and buspirone, but her symptoms of dizziness and unsteady gait did not improve. Subsequently, the patient developed involuntary movements of the head, neck, and limbs, and was eventually referred to the neurology department of our hospital. Her past medical history, personal history, and family history were unremarkable.

Neurological examination revealed motor tremors in the head, neck, and limbs, spontaneous horizontal nystagmus, and hypotonia(Video 1). The patient exhibited clumsy alternating hand movements, unstable finger-to-nose and heel-to-shin tests, and was unable to walk independently. When assisted, she displayed a wide-based and unsteady gait. The total score on the Fahn-Tolosa-Marin Tremor Rating Scale (TRS 1–9) was 64. Further investigations after admission included a PET-CT scan, which indicated malignant ovarian cancer with multiple systemic metastases. The patient subsequently underwent sequential lines of molecularly targeted therapies; however, no significant clinical improvement was observed. Following a multidisciplinary consultation and comprehensive evaluation, the patient met the international diagnostic criteria for PND [6], with significant neurological involvement (cerebellar symptoms), the presence of a relevant tumor antibody (anti-Yo antibody), and a diagnosis of malignant tumor (ovarian cancer) within five years, leading to a definitive diagnosis of PCD.

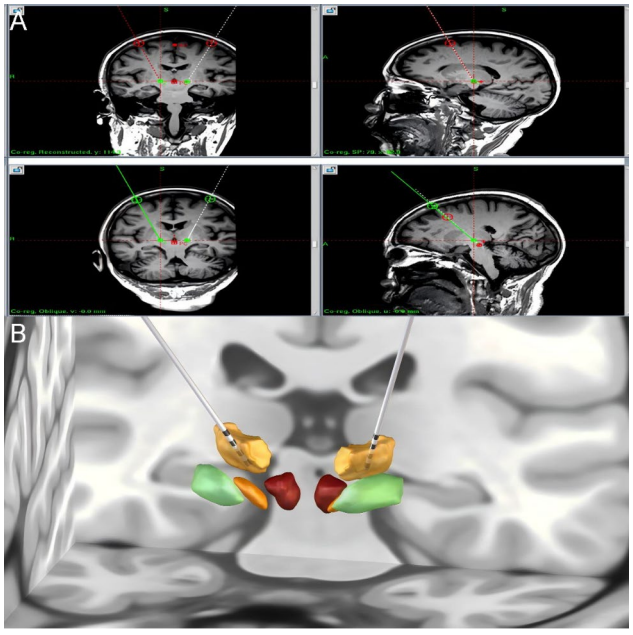

Fig. 1 (**A**) Preoperative Fusion and Needle Path Visualization in Surgi-Plan; The image in the lower left corner indicates that the patient has a mild degree of cerebellar atrophy, but it does not affect the implantation of the electrodes. (**B**) Fusion of patient's postoperative CT with MRI using Lead DBS software, enabling three-dimensional reconstruction of electrode positions; yellow cluster represents the ventral intermediate nucleus (VIM) of the thalamus

Considering the phenomenological similarities between the patient's tremor and essential tremor, we believe that VIM-DBS can improve the patient's tremor symptoms. After a multidisciplinary evaluation and discussion, and with informed consent from the patient and her family, the patient underwent bilateral VIM-DBS under general anesthesia. Due to the lack of direct visualization of the ventral intermediate nucleus (VIM) on neuroimaging, empirically determined VIM coordinates were employed for surgical targeting (Left VIM: X = 96.5 mm, Y = 80.1 mm, Z = 118.5 mm; Right VIM: X = 96.5 mm, Y = 80.1 mm, Z = 118.5 mm). The procedure was performed under general anesthesia using the Leksell stereotactic system. Bilateral electrode implantation (L301 PINS model) was conducted according to preoperative planning. Intraoperative electrophysiological monitoring using the Omega recording system identified characteristic VIM neuronal activity patterns. On the left side, electrophysiological signals extended from 7.3 mm superior to 1.5 mm inferior relative to the target coordinate, while right-sided signals spanned from 6.5 mm superior to 2.0 mm inferior. Final electrode placement positions were determined at 1.0 mm below the target coordinate on the left hemisphere and 1.7 mm inferior to the target on the right hemisphere. Bilateral electrodes (L302; PINS, Beijing, China) were accurately implanted into the VIM. Postoperative CT scans showed no complications, and preoperative MRI fusion confirmed the accurate placement of the electrodes (Fig. 1).

Based on the patient's clinical manifestations, electrode contacts 2 and 6 located in downwards positions were selected for therapeutic stimulation. The pulse generator was activated 10 days postoperatively, with initial settings as follows: left C + 6-, voltage 2.7 V, frequency 150 Hz, pulse width 60ms; right C + 2-, voltage 3.0 V, frequency 150 Hz, pulse width 60ms. The patient's tremor symptoms improved immediately after stimulation. As the patient's involuntary movement symptoms improved significantly, and the relevant imaging reexaminations did not detect any signs of tumor recurrence or metastasis, the patient discontinued the personalized sequential oncological treatment for ovarian cancer. Throughout the 18-month follow-up period, the patient did not take any

related medications or receive any relevant treatments. During the 18-month follow-up, the frequency and amplitude of the tremor significantly improved, with the TRS (1–9) total score decreasing to 23, a 64.06% improvement compared to preoperative levels. The ADL scale score increased from 10 preoperatively to 35, indicating a significant improvement in quality of life(Table 1)(Video 2). Additionally, the patient's cognitive and ataxic symptoms did not worsen. During the follow-up period, the patient spontaneously turned off the DBS stimulation. As a result, the patient's tremor symptoms appeared immediately. The tremor symptoms improved rapidly after we turned the device back on. The corresponding timeline chart of the patient is shown in Fig. 2.

Discussion

Holmes et al. have identified tremor as a core symptom of cerebellar lesions [5, 6]. Previous literature reports that PCD patients often exhibit various types of motor tremors [7]. These motor tremors, also known as cerebellar tremors, differ from the resting tremors seen in Parkinson's disease, presenting more as intention and postural tremors. The mechanism underlying these motor tremors remains unclear, with some studies suggesting that cerebellar dysfunction leads to defective feedforward control, causing inappropriate contraction and hierarchical activity of antagonistic muscles [8]. However, these motor tremors significantly impact patients' quality of life, worsening as the disease progresses. Therefore, there is an urgent need for effective methods to alleviate these symptoms, improve patients' quality of life, and reduce their suffering.

Given the tremor symptoms in such patients, neuromodulation techniques like DBS hold promise as effective tools for improving PCD symptoms. A study by Kvernmo et al. [9]demonstrated that VIM and PSA stimulation significantly improve both resting and motor tremors. However, a common postoperative side effect of VIM-DBS is ataxia, which may further deteriorate the patient's coordination. Nonetheless, a case report by Moritz et al. [10]on DBS treatment for hereditary ataxia with tremor showed that appropriate stimulation patterns can significantly improve tremor symptoms while avoiding the risk of ataxia. Therefore, we are exploring such stimulation patterns to maximize patient recovery and minimize complications. The 18-month follow-up of this case preliminarily confirms the safety and efficacy of VIM-DBS in improving tremor symptoms. However, research on PCD patients remains limited, and invasive neuromodulation therapies are still in the exploratory stage. Future studies need to delve deeper into the mechanisms of tremor and neural circuits in PCD to determine the optimal implantation targets and postoperative programming.

Table 1 TRS and ADL scale

Time Point	PRE-DBS	POST-DBS 10Day	POST-DBS 1 month	POST-DBS 6 months	POST-DBS 12 months	POST-DBS 18 months
TRS(1–9)	64	44	40	23	24	23
ADL	10	20	35	35	35	35
MoCA	26	25	25	25	26	26
MMSE	25	24	24	25	25	25
mRS	4	3	3	3	3	3

TRS: Fahn-Tolosa-Marin- The essential tremor Rating Assessment Scale(TRS)project 1–9, ADL: activities of daily living. MOCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; mRS, Modified Rankin Scale

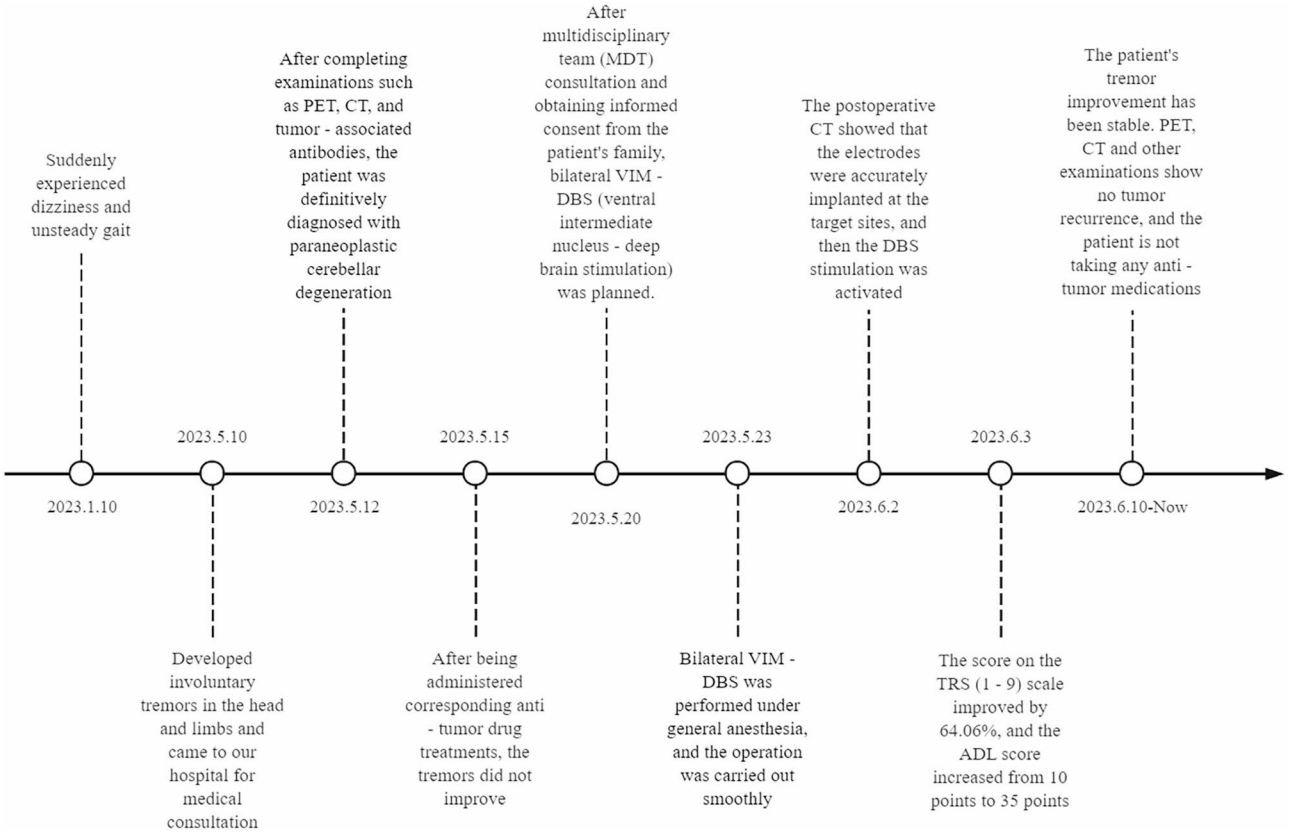

Fig. 2 A corresponding timeline chart for the onset of the patient's symptoms, diagnosis, cancer treatment, DBS surgery, DBS program settings, tremor assessment, etc

When it comes to using deep brain stimulation (DBS) to treat tremor symptoms associated with paraneoplastic cerebellar degeneration related to malignant tumors, there are both risks and benefits, and numerous challenges lie ahead in the future. For patients with malignant tumors, radiotherapy and chemotherapy are extremely crucial for controlling the symptoms of primary tumors. A reasonable treatment plan can effectively control tumor progression and improve the corresponding clinical symptoms of patients. However, we believe that for patients who have received a clear diagnosis through multidisciplinary consultations and meet the relevant indications for DBS surgery, the benefits obtained from DBS may far exceed expectations. Therefore, making a clear pre - operative diagnosis and evaluating whether the patient meets the surgical indications are extremely important steps. In addition, complications and immune damage related to malignant tumors can affect postoperative wound healing and increase the risk of infection. Thus, the peri - operative management of patients with malignant tumors is also one of the challenges we face. According to our 18 - month postoperative follow - up of the patients, significant benefits were achieved after the surgery. Therefore, we conclude that after a detailed evaluation and multidisciplinary discussion to confirm the diagnosis and rule out relevant surgical contraindications, DBS can significantly improve the movement disorder symptoms of patients with paraneoplastic cerebellar degeneration (PCD).

Conclusion

In this case report, the patient presented with significant cerebellar tremor preoperatively, prompting us to target the VIM nucleus. Follow-up over one and a half years post-DBS surgery showed marked improvement in tremor symptoms compared to baseline, with improvement varying according to stimulation parameters. Currently, there is limited research specifically on PCD, and invasive neurostimulation therapies are still exploratory. Future research should delve deeper into the mechanisms underlying tremor in PCD and its neural circuits to identify optimal implantation targets and refine postoperative programming protocols. Moreover, conducting multicenter clinical trials is a crucial strategy for validating the efficacy and safety of PCD-DBS. Such trials play an important role in selecting the optimal target and developing specific programming protocols.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-025-04196-3.

Supplementary Material 1

Supplementary Material 2: Video 1. Pre-DBS activation. DBS, deep brain stimulation. Video 2. 1-year post DBS. DBS, deep brain stimulation.

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Author contributions
Conceptualization: Xiang Wei, Jingxuan Liu, Guanghan Lu; Methodology: Xiang Wei, Jingxuan Liu, Jiuqi Yan, Chang Qiu; Formal analysis and investigation: Xiang Wei, Wenwen Dong, Liang Zhao, Chang Qiu; Writing - original draft preparation: Xiang Wei; Writing - review and editing: Wenbin Zhang, Jun Yan; Funding acquisition: Wenbin Zhang; Resources: Wenbin Zhang; Supervision: Wenbin Zhang, Chang Qiu, Liang Zhao;

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of the Affiliated Nanjing Brain Hospital, Nanjing Medical University, and informed consent was obtained from the patient.

Consent to publish
This manuscript has obtained the informed consent of the patient and his/her daughter for publication and the written informed consent forms have been obtained from the patient and their family members.

Conflicts of interest
The authors declare that there are no conflicts of interest relevant to this work.

Competing interests
The authors declare no competing interests.

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