Movement Disorders
CLINICAL PRACTICE
CASE REPORT

ADCY5-Induced Dyskinetic Storm Rescued with Pallidal Deep Brain Stimulation in a 46-Year-Old Man

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ADCY5 mutations cause early-onset hyperkinetic movement disorders.[1] A wide range of phenotypic presentations has been described in pediatric and adult patients including delayed psychomotor development and axial hypotonia as well as generalized myoclonus, dystonia, and chorea with prominent facial involvement.[1–4] It is reported that hyperkinesia typically starts with episodic attacks before the movement disorder becomes persistent. Hyperkinesia usually exacerbates upon falling asleep and awakening and as a result of infections.[1–4]

Case Report

Here we report the case of a 46-year-old male patient with a known *ADCY5*-related movement disorder who was transferred to our intensive care unit after he had been intubated and sedated because of uncontrollable hyperkinesia following an acute respiratory tract infection. Recurrent trials of extubation failed as a result of severe relapses of the hyperkinesia, whenever the treatment with midazolam and sufentanil combined with propofol or isoflurane was reduced.

The first signs of the disease in our patient were a delayed motor development with walking at the age of 3 and recurrent falls, possibly attributed to axial hypotonia. Soon after, he presented with episodic chorea of his face and limbs while waking up. Dyskinetic episodes were misclassified as epileptic seizures and were nonresponsive to various anticonvulsive medications (clonazepame, levetiracetam, lamotrigine, zonisamide). The hyperkinetic spells progressively worsened in frequency and severity during the following years until he had up to 15 episodes per night, each lasting 5 to 10 minutes (Video S1). The episodes involved violent uncontrolled movements of the limbs that led to falls and self-injuries. After sleep deprivation, the frequency of events increased. During the day, the patient reported continuous choreiform movements of his face and dystonic neck posture. Writing was difficult because of dystonia of his hands and arms. Repeated electroencephalograms and magnetic resonance imaging were unremarkable. In January 2019, genetic testing was performed and showed a mutation in the *ADCY5* gene (c.1252C>T; p.Arg418Trp). Thereafter, a treatment with trihexiphenidyl and clonazepame resulted in a modest benefit only.

At our intensive care unit, treatment of pneumonia was continued with intravenous antibiotics. Even after treatment of the infection, attempts to reduce the sedation were unsuccessful because of uncontrollable whole-body hyperkinesia that led to self-injuries and compromised mechanical ventilation. Additional treatment trials with caffeine, clonazepam, tetrabenazine, and dexmedetomidine remained ineffective, so we decided to use deep brain stimulation(DBS) as a further treatment option.

Frame-based stereotactic implantation of DBS electrodes (DB 2201-30AC; Boston Scientific, Marlborough, MA) into the posteroventral pallidum was performed with intraoperative electrophysiological monitoring using microelectrode recording and macrostimulation for the evaluation of side effects. Within the same operation, electrodes were connected to an implantable rechargeable neural stimulator (Boston Scientific Vercise Gevia). Lead placement was visualized by postoperative imaging using Lead-Dbs (see Fig. 1).[5] The day after the procedure, anesthesia was carefully reduced, and neurostimulation was started. We observed an immediate complete suppression of hyperkinesia after the activation of stimulation within seconds (Videos S2 and S3). After adjusting the final stimulation

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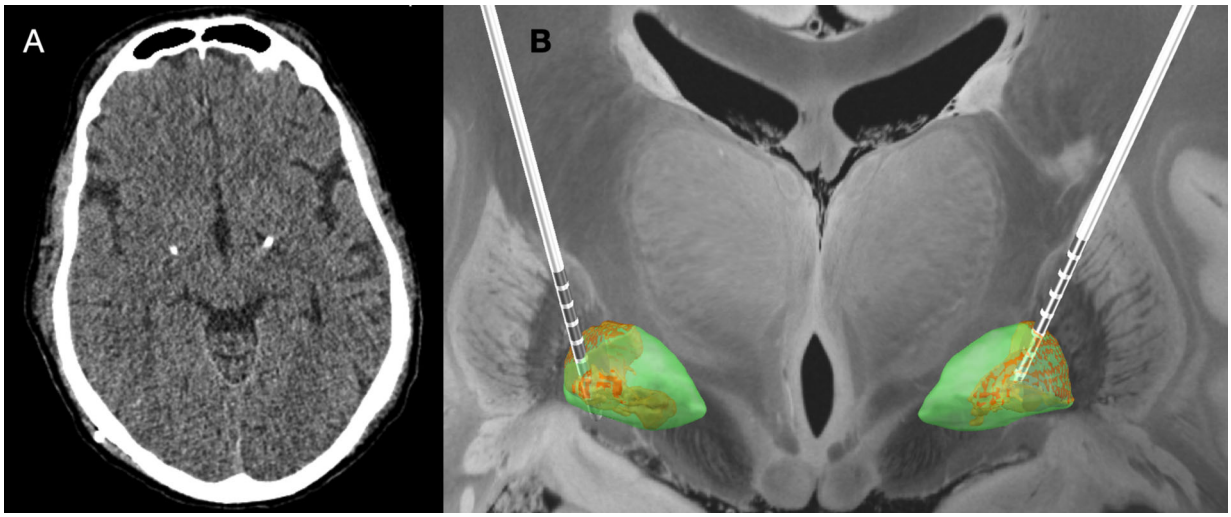

FIG 1. Postoperative imaging. (**A**) Postoperative computed tomography scan. (**B**) Reconstruction of electrodes in Montreal Neurological Institute space using LEAD-DBS software showing the lead inside the sensorimotor part (red) of the internal pallidum (green). Electrodes are projected onto a 7T brain atlas.[10]

settings (2-vs C+, 5.5 mA, 60 μs, 130 Hz), dyskinesia was permanently suppressed and analgosedation was stopped within 2 days except for sufentanil, which was tapered off during a period of 2 weeks combined with partly high dosages of dexmedetomidine because of vegetative signs of stress. Weaning from mechanical ventilation and decannulation were successful. The patient was transferred awake to a rehabilitation clinic 20 days after DBS implantation. At discharge the patient was able to speak and move all extremities at will. There were no more sleep-related events.

Two months after DBS implantation, the patient presented to our outpatient clinic. He described a pronounced improvement of his quality of life after the DBS operation compared with the years before, although he had a minor relapse of symptoms. Sleep-related hyperkinesia was reduced to 2 to 4 episodes per night, which lasted for only a minute and were drastically reduced in amplitude. At the latest visit of the patient to our outpatient clinic 7 months after the start of the DBS therapy, he only showed minor choreiform hyperkinesia of the face and extremities (Video S4).

Discussion

We present the first *ADCY5* patient with a life-threatening dyskinetic storm that was treated successfully with DBS. Our report adds to the growing evidence that confirms pallidal DBS as an effective therapy in various genetic conditions leading to dystonic storms.[6] DBS has recently been described as an effective therapy in *ADCY5*-related hyperkinesia, although clinical results seem to vary substantially.[7–9] Whether the heterogeneity of the benefit from DBS is attributed to additional genetic-related or operation-related factors (such as the exact electrode position) has to be explored in future clinical trials.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the first draft, B. Review and Critique.

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V.M.: 1A, 2C, 3B
D.M.: 1A, 2C, 3B
M.B.: 1B, 2C, 3B
M.B.G.: 1A, 1B, 2B, 2C, 3B
C.v.R.: 1A, 1B, 2B, 2C, 3A, 3B

Disclosures

Ethical Compliance Statement: The authors confirm that the approval of an institutional review board was not required for this work. We confirm that patient consent has been sought and allowed for this case and its publication. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Supporting Information

Supporting information may be found in the online version of this article.

Video S1. Preoperative video illustrating a nightly hyperkinetic spell filmed by the spouse of the patient.

Video S2. Postoperative video showing severe choreatiform hyperkinesia before and complete suppression of hyperkinesia after the activation of pallidal deep brain stimulation.

Video S3. Postoperative video showing the immediate clinical effect of pallidal deep brain stimulation on hyperkinesia.

Video S4. Video showing the patient on deep brain stimulation 7 months after the operation. Mild hyperkinesia of the face and extremities can be noted.