Movement Disorders
CLINICAL PRACTICE

CASE REPORT

Stroke Mimicking Thalamotomy in Primary Familial Brain Calcification

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Beneficial spontaneous brain lesions have been pivotal in discovery of many of the currently used targets for functional neurosurgery, but such cases are rare. We describe the first such case of primary familial brain calcification (PFBC) with complete, lasting resolution of rest tremor after an ischemic stroke.

Case Report

A 75-year-old man without previous neurological complaints had a 1–2-month history of rest tremor in his left hand. Only days before his scheduled first visit to neurology outpatient clinic, he developed acute stroke symptoms with left-sided sensorimotor hemiparesis and dysarthria (NIHSS 5). Brain computed tomography (CT) revealed no acute changes but showed prominent bilateral calcifications of the basal ganglia and thalami (Fig. 1A). He received intravenous thrombolysis treatment with alteplase, which clearly improved the symptoms with only a mild residual left-sided motor weakness without drift (total NIHSS score 1 from minor lower facial palsy the following day). Immediately after the stroke, the patient also noticed a complete resolution of his left-hand rest tremor. At clinical examination, he had mild-to-moderate bradykinesia, more prominent on the left side. Brain magnetic resonance imaging (MRI) 24 hours after the onset of stroke demonstrated a new, residual lacunar infarct in the right internal capsule (Fig. 1B).

At follow-up visits, the patient's left hand was still tremor-free with minor residual motor hemiparesis (modified Rankin scale 1). However, he showed slowly progressive parkinsonian symptoms, including bilateral left-dominant bradykinesia and rigidity, right-sided rest tremor, freezing of gait, and restless legs.

Striatal dopamine transporter imaging using 123I-FP-CIT single-photon emission computed tomography (SPECT) showed substantial bilateral striatal presynaptic dopamine deficit (Z-score below −3.3 in all striatal subregions, Fig. 1C). Laboratory tests, including serum calcium, phosphate, and parathyroid hormone, were normal. Levodopa was gradually increased to 300 mg per day without benefit and discontinued due to its side effects. Targeted next-generation sequencing revealed a heterozygous mutation of *SLC20A2* gene (c.760C>T), confirming the diagnosis of primary familial brain calcification (PFBC). Although the patient's parkinsonism progressed (Unified Parkinson's Disease Rating Scale [UPDRS] motor score reaching up to 38 with continuous right-sided rest tremor and bilateral left-dominant bradykinesia rigidity), the left-sided rest tremor remained completely absent up to the last follow-up at 16 months after the stroke.

The patient's stroke lesion was localized to the right non-decussating dentatorubrothalamic tract (ndDRTT), but not to its better-known decussating part (dDRTT), using the LEAD-DBS anatomy tool and DBS Tractography Atlas (Fig. 1D).[1,2]

Discussion

Spontaneous brain lesions leading to improvement of preexisting symptoms are a rare but well-described clinical phenomenon.[3] These beneficial brain lesions can be uniquely valuable in identifying new treatment targets, and such cases have played a pivotal role in identifying many of the currently used targets in functional neurosurgery.[4] To our knowledge, this is the first reported case of such paradoxically beneficial lesion in a PFBC patient.

PFBC, previously also known as Fahr's disease and familial idiopathic basal ganglia calcification, is a rare genetic neurodegenerative disease usually inherited in autosomal dominant fashion.[5] PFBC is radiologically characterized by prominent intracerebral calcifications predominantly in the basal ganglia.[5] Clinical presentation varies but usually involves gradually progressive symptoms starting at middle or late adulthood. Neuropsychiatric symptoms are often the first manifestation followed by movement

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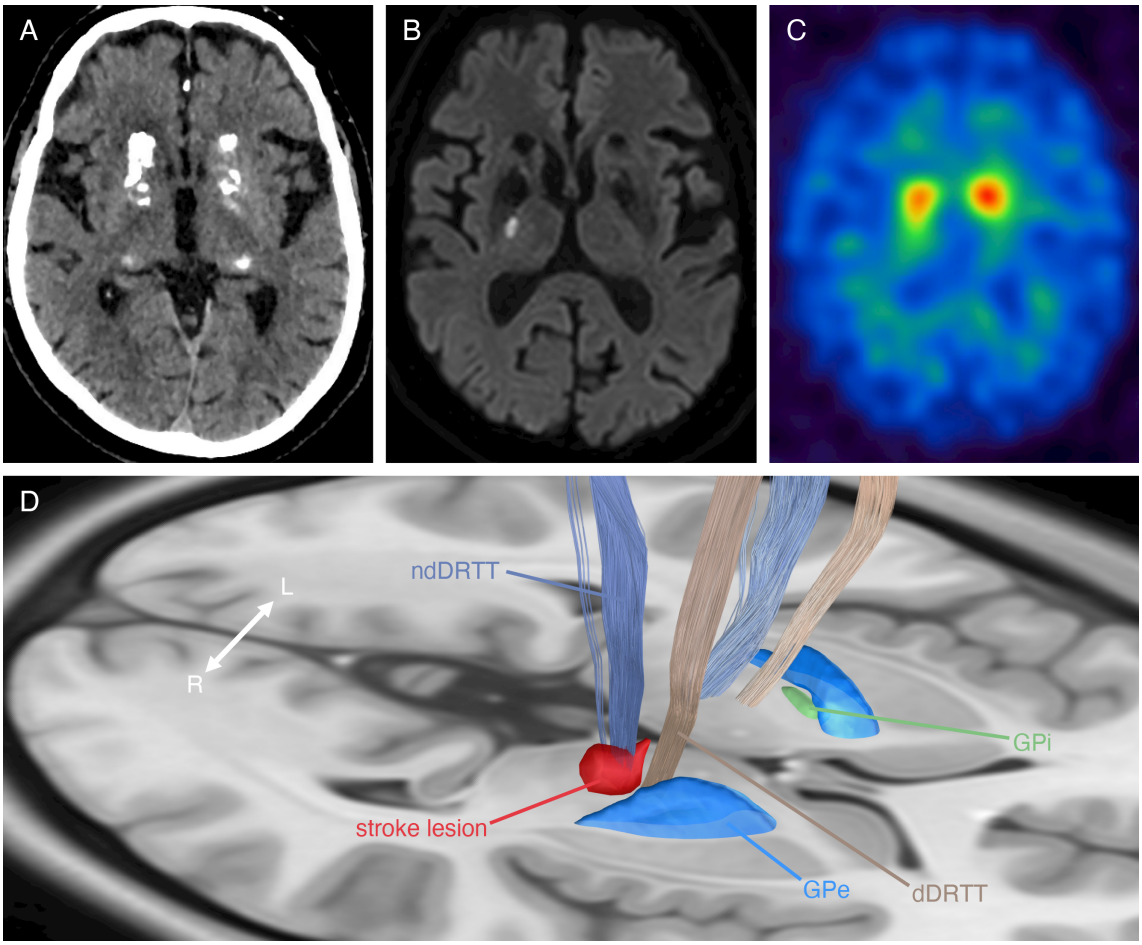

Fig. 1. (**A**) Brain computed tomography (CT) showing prominent bilateral intracerebral calcifications in the basal ganglia and thalami. (**B**) Trace diffusion-weighted imaging (DWI) sequence of brain magnetic resonance imaging (MRI) acquired 24 hours after stroke onset visualizing an acute infarct in the right internal capsule in proximity to the upper medial border of the GPe (center of gravity MNI coordinates of the lesion $x = 22.3$, $y = -13.3$, $z = 7.3$). (**C**) 123I-FP-CIT single-photon emission computed tomography (SPECT) revealed significant bilateral striatal presynaptic dopamine deficit. (**D**) Three-dimensional (3D) reconstruction of the infarct lesion and adjacent structures in MNI space created with LEAD-DBS anatomy tool. GPi, internal globus pallidus; GPe, external globus pallidus; dDRTT, decussating dentatorubrothalamic tract; ndDRTT, non-decussating dentatorubrothalamic tract.

disorders, most commonly including parkinsonism.[5] Case reports of PFBC patients with parkinsonism have demonstrated presynaptic striatal dopaminergic deficit but, unlike in Parkinson's disease, levodopa response is usually poor.[5,6]

Our patient's diagnosis of PFBC was confirmed with genetic testing. He also showed typical basal ganglia calcifications, striatal presynaptic dopaminergic deficit, and parkinsonism. Although coincidental Parkinson's disease cannot be ruled out, all findings were consistent with PFBC and the patient lacked levodopa response typical for Parkinson's disease. Our patient's age at symptom onset was older than commonly seen in PFBC, but other such cases with *SLC20A2* mutations and onset of symptoms, including parkinsonism, at over 70 years of age have been reported.[7] Improvement of tremor spontaneously reported by the patient at the time of stroke, and the absence of left-sided rest tremor despite otherwise left-predominant parkinsonism both support the interpretation that the lesion improved pre-existing rest tremor in our patient.

The lesion in our patient was outside the commonly used thalamotomy target for tremor and instead intersected the ndDRTT, which was identified in humans relatively recently, and its functions are not yet fully understood.[8] Although DRTT is primarily considered to be relevant for action tremor, the cerebello-thalamo-cortical circuit has been shown to be implicated in rest tremor in Parkinson's disease in addition to the basal ganglia.[9] Interestingly, with MR-guided focused ultrasound, the proximity of the lesion to ndDRTT has been suggested to be associated with limb tremor response.[10] This case provides additional evidence that ndDRTT may play an important role in limb tremor, encouraging more research on this tract as a

potential therapeutic target. Importantly, our case also demonstrates that PFBC patients with refractory tremor could potentially benefit from functional neurosurgery, such as thalamotomy or deep brain stimulation.

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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O.L.: 1C, 3B
A.B.: 1C, 3B
J.J.: 1A, 1B, 1C, 3A, 3B

Disclosures

Ethical Compliance Statement: The authors confirm that institutional review board or ethics committee approval was not required for this case report. The patient gave a written informed consent for publication of the case report. 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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Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions. ■

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