Fahr's Disease Presenting as Late-Onset Levodopa-Responsive Parkinsonism

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A 75-year-old man with no significant past medical illness or pertinent family history presented with insidious onset, gradually progressive, asymmetrical parkinsonism of 1 year's duration. He had no history of mood disorders, psychosis, or cognitive decline. On neurological examination, his Unified Parkinson's Disease Rating Scale motor score was 25/108 with asymmetrical rest tremor, rigidity, and bradykinesia, predominantly involving right-sided extremities. He had a slow shuffling gait and reduced right arm swing. The remainder of his neurological examination was normal. He was started on levodopa-carbidopa (100/25 mg) 1 tablet by mouth four times per day. On follow-up 6 months later, his Unified Parkinson's Disease Rating Scale motor score reduced by 64% to 9/108 with a global improvement in parkinsonism. After a fall, noncontrast computed tomography (CT) scan of the brain revealed calcification involving bilateral basal ganglia, thalamus, subcortical white matter, and cerebellum (Figure 1). Laboratory workup showed normal serum parathyroid hormone, calcium, and phosphate. Genetic testing revealed a heterozygous mutation c.1507G > A (p.Gly503Ser) in exon 8 of the SLC20A2 gene, suggestive of idiopathic basal ganglia calcification (IBGC), also known as Fahr's disease or primary familial brain calcification, a form of bilateral striopallidodentate calcinosis (BSPDC).[1,2] BSPDC can be autosomal dominant, sporadic, familial (occurrence in multiple family members by chance), or secondary.[2] The first three subtypes belong to Fahr's disease or IBGC, a rare neurodegenerative disorder.[2] Secondary BSPDC, known as Fahr's syndrome, is linked to calcium and phosphate metabolism defects, infectious or neoplastic brain disorders, previous head trauma, and systemic lupus erythematosus[2]; therefore, laboratory workup is essential when assessing a possible IBGC patient. Our patient had the sporadic subtype.

IBGC usually manifests in third through sixth decades,[1,3] with a median age of onset at 31 years.[1] Men are affected more commonly than females.[1,3] Mutations in three genes including SLC20A2, PDGFRB, and PDGFB, are identified in 50% of cases, indicating the possibility of involvement of other genes yet to be reported.[4] SLC20A2 mutations account for nearly half of the

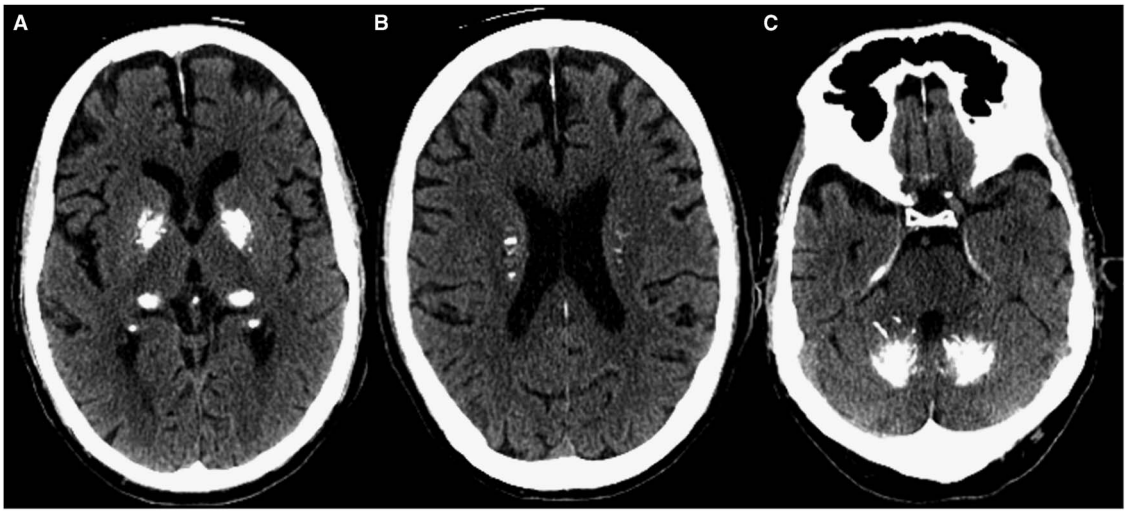

Figure 1: *Noncontrast CT of the brain showing bilateral calcifications in the basal ganglia and thalamus (A), subcortical white matter (B), and cerebellum (C).*

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identified cases.[1] IBGC usually presents with psychiatric features (75.8%), movement disorders (60.6%), and cognitive impairment (57.8%).[1] Movement disorders are more frequent in patients with SLC20A2 mutations, with parkinsonism being the most common (92%).[1] Although psychiatric features and cognitive decline are common in early-onset cases (before 18 years of age), movement disorders predominate in late-onset cases (after 53 years of age).[1] Other neurological manifestations including speech disorder, gait abnormality, cerebellar ataxia, pyramidal features, and seizures may be seen in patients with IBGC.[1,3] Up to one-third of patients may remain asymptomatic.[1,3]

The clinical status correlate with the total calcification score (a visual rating scale of calcification on CT of the brain), with symptomatic patients having a higher score.[1,3] The total calcification score increases with age and is higher in males and those having mutations involving SLC20A2 gene.[1] Symptomatic drug therapy for various neuropsychiatric features may be helpful, and levodopa-responsiveness has been reported in up to two-thirds of patients of IBGC with parkinsonism in two separate studies.[1,5] Although the likelihood of co-occurrence of Parkinson's disease and IBGC cannot be excluded, brain calcification on CT scan along with SLC20A2 mutation in our case highlights the possibility of IBGC presenting as late-onset levodopa-responsive parkinsonism.

Statement of Authorship

NK undertook conception, design, and writing of the first manuscript. MJ undertook manuscript review and critique.

Disclosures

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References

1. Nicolas G, Charbonnier C, de Lemos RR, et al. Brain calcification process and phenotypes according to age and sex: lessons from SLC20A2, PDGFB, and PDGFRB mutation carriers. Am J Med Genet Part B Neuropsychiatr Genet. 2015;168:586-94.
2. Savino E, Soavi C, Capatti E, et al. Bilateral strio-pallido-dentate calcinosis (Fahr's disease): report of seven cases and revision of literature. BMC Neurol. 2016;16:165.
3. Manyam BV, Walters AS, Narla KR. Bilateral striopallidodentate calcinosis: clinical characteristics of patients seen in a registry. Mov Disord. 2001;16:258-64.
4. Lemos RR, Ramos EM, Legati A, et al. Update and mutational analysis of SLC20A2: a major cause of primary familial brain calcification. Hum Mutat. 2015;36:489-95.
5. Manyam BV, Walters AS, Keller IA, Ghobrial M. Parkinsonism associated with autosomal dominant bilateral striopallidodentate calcinosis. Park Relat Disord. 2001;7:289-95.

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