Idiopathic Basal Ganglia Calcification Presented with Progressive Supranuclear Palsy-like Features

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Fahr's disease, or idiopathic basal ganglia calcification (IBGC), is a rare neurological syndrome characterized by abnormal calcified deposits located mostly in bilateral basal ganglia and dentate nucleus, and also in cerebral cortex, thalamus, hippocampus, cerebellar, and subcortical white matter. Clinically, it presents various symptoms, including parkinsonism (presented in 57% of the patients), chorea (19%), tremors (8%), dystonia (8%), athetosis (5%), and orofacial dyskinesia (3%).[1]

Postural instability and frequent falls, dysarthria, bradykinesia, and supranuclear gaze palsy, are the main clinical manifestations of progressive supranuclear palsy (PSP), but those that are associated with striopallidodentate calcification, have been rarely reported. Here, we present a sporadic case with bilateral calcified deposits in brain demonstrated with progressive gait disturbance, dementia, slurred speech, and oculomotor abnormalities.

Case Report

A 48-year-old female showed recent memory decline for 5 years, dysarthria for 3 years and progressive gait disturbance with freezing and unbalance for 6 months. She presented a slurred speech, had hesitation when initiating gait and could not walk without assistance. She felt walking like glued to the floor, but she could step across the barrier in front of her feet. General neurological examination showed difficulty in calculating, recent memory disturbance, hypophonia, and slurred speech. She showed difficulty to generate vertical upward and downward saccades and slow horizontal saccades.

She presented severe bilateral bradykinesia and moderate muscular rigidity, active deep-tendon reflexes, gait disturbance with freezing, and forward-bent posture with the absence of arm swings. Unified Parkinson's Disease Rating Scale-III motor scores are 43 before and 37 after acute levodopa challenge test, respectively. Hoehn and Yahr stage is 4/5. General cognition was lower (MMSE22/30). Her serum calcium, thyroid function, parathyroid hormonal assay, liver function, and kidney function were within normal limits. Her pseudohypoparathyroidism gene test showed no mutations. She was diagnosed with systemic lupus erythematosus 13 years ago, with positive antinuclear antibody titer (1:320) while anti-double stranded DNA (6.7 U/ml) most recently. In addition, she did not show signs of a headache, seizures, arthritis, vasculitis, or mental disturbance, which did not support the diagnosis of cerebral lupus. Brain computed tomography revealed symmetrical areas of calcification in bilateral basal ganglia, thalamus, centrum semiovale, midbrain, and cerebellum [Figure 1a-1d]. Magnetic resonance imaging showed the calcified deposit in the midbrain. *SLC20A2* gene mutation was screened, but there was no mutation found in this patient. Considering that this patient mainly suffered from the extrapyramidal symptom, she was prescribed levodopa 450 mg/d and selegiline 10 mg/d. Symptoms were slightly improved under medication in the 1st week but became worse after then.

This case exhibited extensive bilateral calcification in the brain, and showed progressive movement disorders such as clumsiness, fatigability, unsteady gait, and speech

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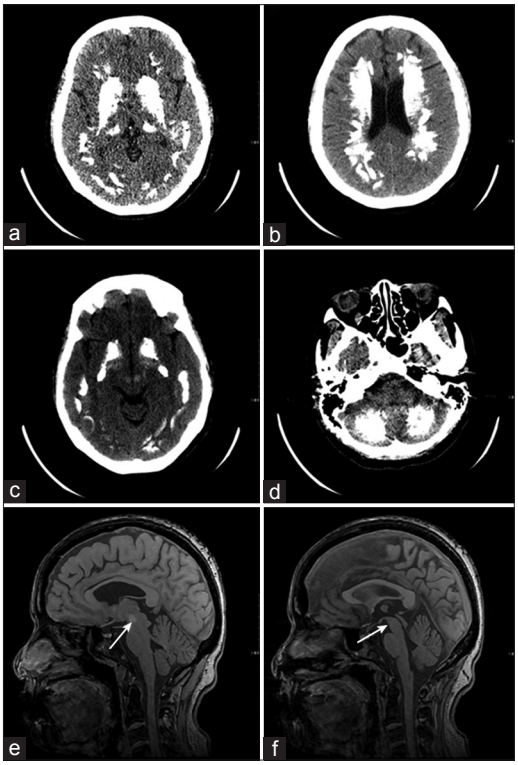

Figure 1: Computed tomography of the brain demonstrated extensive, bilateral calcification of basal ganglia, thalamus, centrum semiovale, midbrain, and cerebellum (a-d). Sagittal magnetic resonance imaging of the brain shows calcified deposits in midbrain and no atrophy in midbrain (e and f, arrows).

impairment. Considering the onset age and the absence of metabolic diseases, we initially diagnosed her with IBGC (Fahr's disease).

In our case, vertical supranuclear palsy, prominent postural instability, symmetric rigidity, dementia, and early dysathria are the main characteristics of PSP. All the direct evidence, including the onset age at 48 years, gradually progressive disorder, poor response of parkinsonism to levodopa, supported the diagnosis of PSP. However, we found that calcified deposit existed in her midbrain [Figure 1e and 1f], which was mentioned in the exclusion criteria (one of the mandatory exclusion terms in the NINDS-SPSP criteria of the diagnosis of PSP). Therefore, we ruled out the diagnosis of PSP in this case according to NINDS-SPSP demonstrated, though she presented a PSP-like clinical feature.

IBGC associated with the oculomotor disorder is rare. Kim *et al*.[2] presented a 77-year-old man, diagnosed as idiopathic hypoparathyroidism, suffering from PSP-like phenotype with bilateral calcification in the brain. The patient was not diagnosed PSP due to the absence of atrophy of midbrain tegmentum, superior colliculi, and pons. They assumed that oculomotor disturbance might be one of the symptoms in IBGC.

Unlike the cases reported by other researchers, which mainly presented as the oculomotor abnormality and frequent falling, our patient exhibited severe freezing of gait. Williams *et al*.[3] reported that pure akinesia with gait freezing may be associated with PSP-tau pathology and suggested that it might be the third clinical phenotype of PSP. We hypothesize that the freezing of gait and PSP-like features in our patient may be attributed to the calcification in the midbrain.

Mutations in *SLC20A2*, *PDGFRB*, *XPR1*, and *PDGFB* have been reported to cause primary familial brain calcification (PFBC). For patients that are considered the diagnosis of PFBC, other causes of brain calcification, such as disorders of calcium metabolism and heavy metal intoxication, should be eliminated before pursuing genetic testing, particularly in simplex cases. If no other primary cause for brain calcification is found or if the family history is suggestive of autosomal dominant inheritance, molecular genetic testing should be considered. Sequencing of *SLC20A2* should be conducted first. It accounts for approximately 40% of all *PFBC* gene mutations including some Chinese families.[4] The other three gene mutations are rare and have not been found in the Chinese population. Hence, we tested *SLC20A2* mutation. However, there is no gene mutation in this patient.

In conclusion, the patient in our case showed prominent movement disorders and oculomotor disturbance with bilateral calcification deposits in the brain, suggesting that IBGC can cause supranuclear vertical and horizontal ophthalmoplegia. It is possible that the calcified deposit in midbrain may be associated with the oculomotor disturbance. Since several cases had been reported to have striopallidodentate calcification with vertical ophthalmoplegia, we suggest that it is necessary to carefully examine the eye movement in patients who are diagnosed with striatopallidodentate calcification.

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Conflicts of interest

There are no conflicts of interest.

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