

Familial Idiopathic Basal Ganglia Calcification

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Familial idiopathic basal ganglia calcification(FIBGC) is an inheritable neurological condition characterized by calcium deposits in the basal ganglia and extra-basal ganglia areas. The condition manifests as parkinsonism and other variable neuropsychiatric symptoms. FIBGC is a rare condition, and its pathophysiology has not yet been fully elucidated. Here we report the results of a clinical study of two related patients diagnosed with FIBGC.

KEY WORDS : Familial idiopathic basal ganglia calcification · Fahr's disease · Basal ganglia calcification.

Introduction

Familial idiopathic basal ganglia calcification(FIBGC) is a degenerative neurological disorder with characteristic calcium deposits in the basal ganglia and in other areas of the brain. FIBGC is a rare, inheritable condition, but its pathophysiology has not yet been elucidated. FIBGC is manifested by a variable combination of dystonia, parkinsonism, ataxia, cognitive impairment, and behavioral changes. Most cases display autosomal dominant transmission. Here we report the results of a clinical study of two related patients with FIBGC, along with a literature review.

Case Report

A 19-year-old woman presented with a one-year history of a progressive gait disturbance and general dystonia. She had a history of generalized tonic-clonic seizures since the age of one. The patient showed normal development until 18 years of age, at which time she developed a gait disturbance and mild dystonia. The patient's serum concentrations of calcium, phosphorus, magnesium, alkaline phosphatase, calcitonin, and parathyroid hormone(PTH) were all within normal limits. Routine hematologic and biochemical investigations did not disclose any specific abnormalities. Work-ups for metabolic, inflammatory, and infectious etiologies were also negative. A computerized tomography

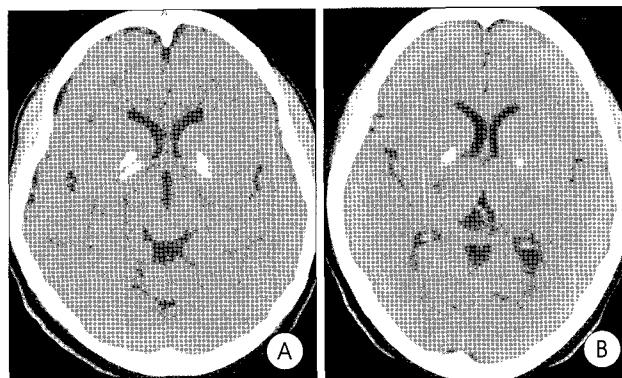


Fig. 1. Brain computed tomography scans of the patient (A) and her mother (B) show bilateral calcifications in the basal ganglia.

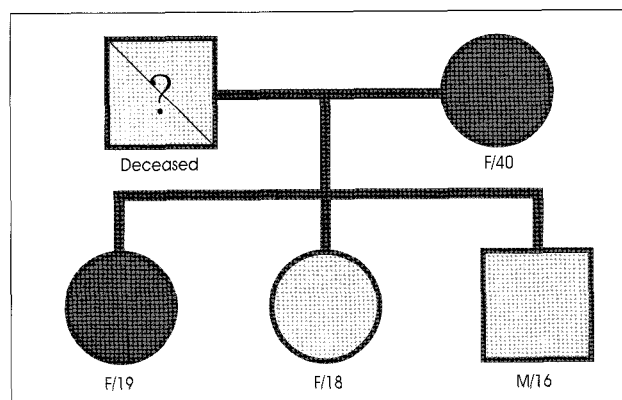


Fig. 2. A pedigree of familial idiopathic basal ganglia calcification (square : male, circle : female, dark gray : with FIBGC, pale gray : without FIBGC).

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(CT) scan of the brain revealed bilateral calcifications in the basal ganglia (Fig. 1A).

Upon further investigation, it was discovered that the patient's mother also had similar clinical features: mask-like facial features, slowed intellectual functioning, and bilateral calcifications in the basal ganglia on CT (Fig. 1B). The mother also had a gait disturbance and mild dystonia. The patient's father had died of stomach cancer and had experienced no psychomotor dysfunctions during his lifetime. Neither the patient's brother nor sister experienced psychomotor dysfunctions, and their CT scans were within normal limits. The patient's pedigree was subsequently constructed (Fig. 2), and is strongly suggestive of an autosomal dominant inheritance.

Discussion

FIBGC is a rare, degenerative neurological disorder with characteristic calcium deposits in the basal ganglia and other areas of the brain, as visualized on neuroimaging. There is no apparent explanation for the calcification that appears in these brain regions. This condition is often referred to as Fahr's disease, cerebrovascular ferocalcinosis, or stridopallidodentate calcinosis. Most patients are asymptomatic during childhood and young adulthood. Disease prevalence often peaks between the third and fifth decades of life, with a gradual progression of neuropsychiatric and movement disturbances. The first manifestations include clumsiness, fatigue, unsteady gait, dysarthria, dysphagia, athetosis, and/or muscle cramping. Various types of seizures occur frequently. Neuropsychiatric symptoms, often the first or most prominent manifestations, range from mild difficulties with concentration and memory to changes in personality or behavior, followed by psychosis and dementia. Ellie et al. suggested the following diagnostic criteria²⁾: First, bilateral calcification of the basal ganglia is visualized on neuroimaging. Second, progressive neurological dysfunction, generally including a movement disorder and/or neuropsychiatric disturbance, is noted. Third, the age of onset is typically in the fourth or fifth decade of life, although this dysfunction may appear as early as childhood. Fourth, there are no biochemical abnormalities or somatic features suggestive of a mitochondrial or metabolic disease or other systemic disorder. Fifth, there are no infectious, toxic, or traumatic causes. Sixth, there is family history consistent with autosomal dominant inheritance. In our case, both patients presented with dystonia and demonstrated bilateral calcification of the basal ganglia on CT. The daughter developed symptoms in the second decade and the mother in the sixth decade. Neither patient had any biochemical abnormalities.

Brain CT scans, which easily detect calcium, are more sensitive than magnetic resonance imaging (MRI) for localizing

and assessing the extent of cerebral calcifications⁶⁾. The calcifications in FIBGC are difficult to distinguish from those secondary to hypoparathyroidism⁹⁾ or other causes. The lenticular nucleus, particularly the internal globus pallidus, is most frequently affected^{6,7)}. Calcifications in the putamen, thalami, caudate, and dentate nuclei are common. The cerebellar gyri, brainstem, centrum semiovale, and subcortical white matter may also be affected. Diffuse atrophic changes with dilatation of the subarachnoid space and/or ventricular system may coexist with calcifications. Brain CT scans of the patient and her mother showed bilateral calcifications in the globus pallidus; no other brain areas were affected. Calcification appears to be progressive, as the calcifications are generally more extensive in older individuals. There is also documented evidence in FIBGC patients followed longitudinally of an increase in calcification over time⁷⁾. However, this pattern does not always hold true.

The gene or genes responsible for FIBGC are unknown. Linkage to chromosome 14q has been established in one family³⁾. Linkage testing is available on a research basis only. FIBGC is inherited in an autosomal dominant manner^{1,2,4,8)}. The proportion of cases caused by de novo gene mutations is unknown. Offspring of an affected individual have a 50% risk of being affected; however, prenatal testing is not currently available. Unfortunately, we were not able to perform a gene study due to difficulties in commercial use.

The selective removal of calcium deposits from the brain without affecting calcium in the bones and other tissues appears to be an impossible task. Treatment with central nervous system-specific calcium channel blocking agents, like nimodipine, has been unsuccessful. In one patient, disodium etidronate showed symptomatic benefits but did not reduce calcification⁵⁾. We prescribed disodium etidronate (Dinol, Chodang pharmaceuticals, Seoul, Korea) in both patients for a period of two months, but at follow-up, their symptoms had not improved.

Conclusion

Even though asymptomatic basal ganglia calcification is more frequent, it is able to cause psychomotor symptoms and be inherited as autosomal dominant pattern. We present the results of a clinical study of two patients in a family affected with FIBGC for the purpose of emphasizing that we must pay attention to the possibility of FIBGC if a patient shows basal ganglia calcification on brain CT, and psychomotor symptoms.

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