Familial Fahr's disease presenting as stroke like episode - a case report

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Abstract:
We are hereby reporting a case, who presented with hemiparesis and brain imaging showed bilateral basal ganglia calcification. He had an elder sister with very similar clinical illness and imaging findings thereby turning out to be a familial Fahr's disease.

Keyword: Fahr's disease, Basal ganglia calcification

Case report
A 45 year old male patient, a driver by occupation, was admitted with acute onset weakness of right upper and lower limb associated with dysarthria. There was no seizure, bowel or bladder involvement. He was suffering from depressive disorder for the past five years and was on treatment. There was no history of systemic hypertension, diabetes, heart disease or head trauma. He was a smoker and an occasional alcoholic. He was married and has two children. Physical examination showed right hemiparesis with right sided upper motor neuron type of facial nerve palsy. There were no sensory disturbance, no cerebellar signs and no features of raised intracranial tension. His blood pressure was normal. On further workup, complete hemogram, blood sugar, urea, creatinine, electrolytes, urine analysis and liver function tests were normal. ECG was normal. Brain CT imaging showed bilateral symmetric basal ganglion and cerebellar calcification. Since there were neuropsychiatric manifestations and imaging has shown symmetric basal ganglion calcification, a diagnosis of Fahr's disease was considered. To exclude other causes with similar imaging findings, ANA, VDRL and toxoplasma IgM & IgG were sent and found to be negative. His serum calcium was 9 mg/dl, phosphorus - 3.8, alkaline phosphatase - 76 and parathyroid hormone 14ng/ml, lactate – 1.5mmol/L - all within normal limits. On further enquiry into the family history, it was revealed that multiple members of his family had psychiatric complaints in the past, but they were not evaluated in detail. Our patient is the fourth child of third degree consanguinous parents. He has three elder sisters. His father had some mental illness and died 10 years back. His mother died 2 years back due to ischemic heart disease. His immediate elder sister is a schizophrenic and is on antipsychotic medications for the past 20 years.
She had history of weakness of left upper and lower limb 8 months back and her brain imaging done at that time also has shown similar bilateral symmetrical basal ganglion calcification. We did blood investigations in her to exclude other causes of calcification which were all normal. Hence a diagnosis of familial Fahr’s disease was made applying the diagnostic criteria recommended for diagnosing Fahr’s disease. His other two elder sisters were asymptomatic by then and were not willing for further workup and imaging. His children also were asymptomatic. Our patient was treated symptomatically with physiotherapy, antidepressants and supportive care. His weakness improved in a few days and now he is able to pursue his normal activities. The prognosis of the illness and the possibility that it can recur in the family was explained to the patient.

Fig – 1. Bilateral basal ganglia calcification in the male patient

Fig – 2. Bilateral cerebellar calcification in the female patient (she also had bilateral basal ganglia calcification)

Discussion

Familial idiopathic basal ganglia calcification (FIBGC) or Fahr’s disease is a neurodegenerative disorder with characteristic calcium deposit in the basal ganglion and other brain areas visualized on neuroimaging. Within the basal ganglia, the globus pallidus is the most frequent site of calcification, but deposits may be present in the putamen, caudate nucleus, internal capsule, dentate nucleus, thalamus, cerebellum and cerebral white matter. The pathogenesis is not known, but may be secondary to abnormality in transport of iron and other metals along with free radical induced damage to brain parenchyma initiating the process of calcification. Affected individuals are mostly asymptomatic in their childhood and young adulthood. The typical age of presentation is between thirty to fifty years. Occasional cases have also been reported in children.

Persons affected with Fahr’s disease may be asymptomatic and basal ganglia calcification could be an incidental finding. When symptomatic, the common complaints at presentation include clumsiness, gait disturbance, altered speech, swallowing difficulty, involuntary movements, or muscle cramping. In one study, movement disorders were reported as the most common manifestations and among movement disorders, Parkinsonism outnumbered others. Seizures, dementia, cerebellar signs, pyramidal signs, sensory disturbances also can occur. Neuropsychiatric symptoms encompass mild difficulty with concentration and memory to changes in personality and/or
behavior, to psychosis and dementia. Fahr’s disease presenting with stroke like episodes similar to our case is only rarely reported in medical literature.

**Criteria for diagnosis**
The diagnosis of familial idiopathic basal ganglia calcification (FIBGC) is supported by the following criteria [modified from Moscowitz MA et al 1971, Ellie E et al 1989, Manyam BV 2005]

- Bilateral calcification of the basal ganglia visualized on neuroimaging. Other brain regions may also be affected.
- Progressive neurologic dysfunction, generally including a movement disorder and/or neuropsychiatric manifestations. Age of onset is typically in the fourth or fifth decade, although this dysfunction may present in childhood or later in life.
- Absence of biochemical abnormalities and somatic features suggestive of a mitochondrial or metabolic disease or other systemic disorder
- Absence of an infectious, toxic, or traumatic cause
- Family history consistent with autosomal dominant inheritance

Rarely, symptomatic individuals in families with FIBGC do not show calcification. Thus, in some instances, the diagnosis can be established in the absence of one (but not both) of the first two criteria, providing the remaining criteria are fulfilled. Both of our patients comply with the above mentioned criteria.

**Radiological appearance**
Brain CT is the investigation of choice to identify basal ganglion calcifications. The radiological pattern that is highly suggestive of Fahr’s disease is the symmetry of calcifications – asymmetric or unilateral calcifications can exclude a FD diagnosis. A symmetric disposition should be analyzed further in order to observe a specific pattern: cloudy and/or thin linear pattern located in the basal ganglia (first lesions occur in globus pallidus) can be found in the early part of disease. In later stages, the degree of calcification becomes higher and lead to a massive calcification. Usually this is associated with the “cloudy” and/or thin linear pattern in the peripheral area of the massive calcifications.

**Plain skull radiograph**
The calcifications appear as clusters of punctate densities symmetrically distributed above the sella turcica and lateral to the midline. Subcortical and cerebellar calcifications may appear wavy. Although the sensitivity of CT scan largely surpasses that of plain skull radiographs, the latter are still useful to evaluate abnormalities of bone structures suggestive of other diagnoses. Routine hematological and biochemical tests will be normal. Serum concentrations of calcium, phosphorus and alkaline phosphatase will also be within normal range. Basal calcifications can also occur in other conditions like congenital infections, parathyroid disorders, SLE, celiac disease, brain injury secondary to trauma, toxin and asphyxia and also in certain other neurodegenerative disorders. These disorders can be excluded by proper history, physical examination and appropriate blood investigations. Applying the diagnostic criteria as mentioned above helps in diagnosing Fahr’s disease and differentiating it from other causes of basal ganglion calcification.

**Genetics**
The genetic defect responsible for Fahr's disease has not been identified so far. But genetic analysis in one affected family has shown linkage to chromosome 14q13. It is inherited as autosomal dominant manner, thereby conferring a risk of 50% in the siblings of affected person. Screening of parents and siblings of the proband can be done by physical and neurological examination and brain CT scan after obtaining informed consent. Other family members are tested if one of the parents of the proband is found to be affected. There are ethical issues in screening the asymptomatic adult relatives of the proband as there is no definite treatment available for this disorder. The minimum age at which a negative CT scan can exclude the disease has not been established. It is advised against screening of asymptomatic children less than 18 years of age as it imparts psychological burden over the child rather than offering early preventive treatment.

**Management**

Fahr's disease is an idiopathic neurodegenerative disorder with no definite treatment available until now. The rate of progression and life expectancy varies between affected individuals. A thorough neurological and psychiatric assessment should be carried out to enlist the clinical problems suffered by the patient. Management is mainly symptomatic treatment and supportive care. Anxiolytics, antidepressants may be needed. Appropriate pharmacological therapy should be instituted for involuntary movements and dystonia. Parkinsonian like symptoms may be treated with levodopa, but failure with levodopa has also been reported. There are reports of psychiatric symptoms responding positively to administration of lithium when haloperidol has failed.

**Conclusion**

We report this case as familial Fahr's disease is a rare disease and even rare is the occurrence of stroke like episode in the absence of extrapyramidal involvement. The take home message is that when there is motor weakness associated with neuropsychiatric manifestations, a diagnostic possibility of Fahr's disease should always be considered.

**References**


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