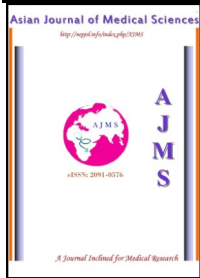


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Fahr's Disease: Report of Two Cases

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Abstract

Two cases of Fahr's disease (one female and one male) are reported here. One is young and symptomatic with neuropsychiatric disturbances. The second case is old and asymptomatic, detected incidentally on CT scan when he presented with cerebrovascular accident. Both of them had intracranial calcifications in bilateral basal ganglia and cerebral hemispheres. CT scan helped in establishing the diagnosis.

Key Words: Fahr's disease; Fahr's syndrome; Bilateral striopallido dentate calcifications

1. Introduction

Fahr's disease (FD) or Fahr's syndrome is characterized by bilaterally symmetrical calcifications in basal ganglia, dentate nucleus and subthalamus. It was first described by Fahr in 1930. Clinically these patients may be symptomatic or asymptomatic. Symptomatic patients show developmental and motor disability, tetany, parasthesia, cataract, epileptic syncope and intracranial calcification. Etiology is not clear. FD should be diagnosed based on clinical aspects, neuroimaging findings and the exclusion of other primary causes.

We are reporting two cases of Fahr's disease diagnosed on our CT scan with two different clinical presentations.

Case 1:

Twenty years old girl, born of non consanguineous marriage as a 4th child to healthy parents, presented to psychiatry department of our hospital with chief complaints of abnormal body movements since one week. The mother said that the patient had sudden onset generalised tonic clonic seizures lasting for 5 minutes with incontinence of urine. She started having episodes of dystonia, tics and speech alterations following the seizure. Her cognitive functions were subnormal. She was completely normal till one week back. She had no fever or head ache before the start of illness. There was nothing contributory in family history.

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General examination was normal. Neuropsychological evaluation showed an overall intelligence below the average expected for her age and educational level. Hamilton anxiety rating scale score was 30. Her skills related to the understanding of language and nominations were normal. No focal neurological deficits noted. Detailed examination revealed dystonia and choreoathetoid movements of upper limbs involving the hand. She had slurring of speech and an increased emotional lability. Her IQ was found to be 70. Slit lamp and fundus examination of eyes showed no Kayser-Fleischer rings. All the other systems were normal on examination.

Laboratory tests including erythrocyte sedimentation rate, C-reactive protein, ANF, VDRL, ceruloplasmin, serum copper, CPK, lactate, calcium ion, phosphorus, magnesium, urinary calcium, hepatic and renal function tests, protein electrophoresis, TSH, free T4, and parathormone were all normal. EEG and sleep deprived EEG results were evaluated as normal. CT scan of the head revealed symmetrical calcifications involving the globus pallidum, putamen, caudate, internal capsule, thalamus, subthalamus, subcortical white matter and dentate nuclei of cerebellum on both sides (Fig. 1a, 1b).

Her dystonia and chorea responded partially to the treatment with antiepileptic (carbamazepine) and antipsychotics (haloperidol). The possible differential diagnoses including Parkinson's disease, Huntington's chorea, Wilson's disease, low-grade astrocytoma,

Binswinger disease, etc were ruled out by laboratory and clinical examination. Final diagnosis of Fahr's disease was made.

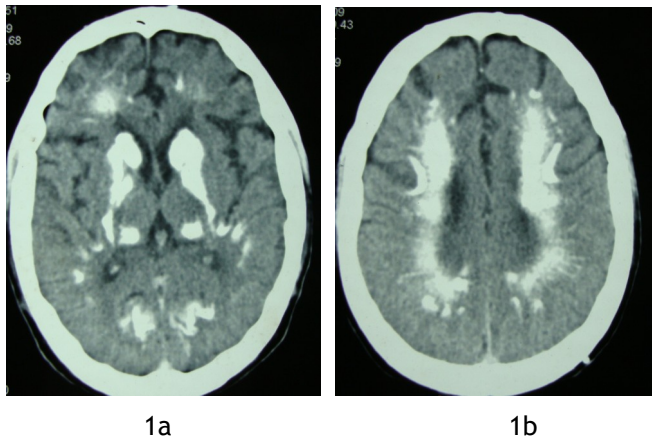


Fig 1a. Axial image of brain at the level of lateral ventricles shows diffuse dense calcifications involving basal ganglia, caudate nucleus, thalamus and cerebral white matter symmetrically on both sides. Fig 1b. Axial image of brain at superior to ventricles shows dense symmetric calcifications in corona radiata and centrum semiovale.

Case 2:

Fifty nine year old male, a school head master, arrived at the emergency department of our hospital with sudden onset of altered consciousness and vomiting since that morning. The onset was acute in the early morning with no aura. He had weakness of his right side of the body. He was a known diabetic and hypertensive, on regular medical treatment. Diagnosis of acute cerebrovascular accident was made. Non contrast CT scan showed acute intraparenchymal haemorrhage involving the left internal capsule genu and corona radiata with intraventricular extension. Surprisingly there were extensive dense bilateral symmetric calcifications seen involving the corpus striatum, centrum semiovale, thalami and cerebellar hemispheres in dentate nuclei (Fig-2).

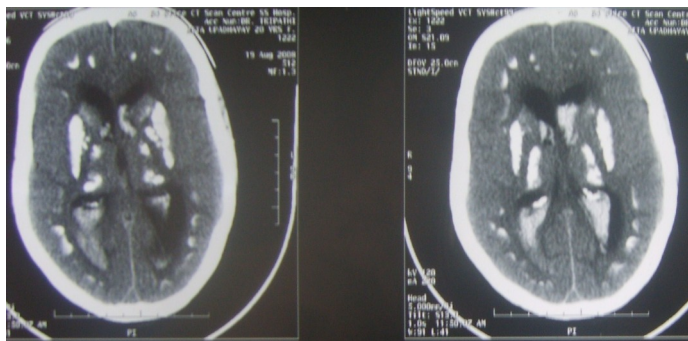


Figure-2: Axial images at the level of ventricles show acute parenchymal haemorrhage involving left internal capsule with intraventricular extension. Bilateral symmetric calcifications are seen as incidental findings in basal ganglia, caudate head, thalami and centrum semiovale.

Neurological examination revealed right sided hemiplegia, expressive dysphasia, dysarthria and a wide base gait but no Parkinsonian features.

The patient never had hospitalisations before for any complaints. He had normal social and personal relations. No abnormal psychiatric behaviours or mental disorders in his parents. His laboratory examinations including parathyroid hormone levels were found normal. This case of Fahr's disease had been asymptomatic throughout the patient's life.

2. Discussion

FD is supposed to be a rare disease with unknown prevalence. Typically the age at onset of clinical symptoms is 30 to 60 years. Early-onset types show a more progressive deteriorating course with features mimicking schizophrenia and resulting in presenile dementia.¹ The clinical evolution is that of a degenerative disorder, rather than a developmental disorder.²

FD should be differentiated from Fahr's syndrome. The latter is defined as symmetric and bilateral calcifications of the basal ganglia associated with neuropsychiatric manifestations that preferentially occur in patients with parathyroid disorders, especially hypoparathyroidism.³ As these calcifications tend to show a predilection for the dentate nuclei and basal ganglia, a descriptive term 'Bilateral Striopallido Dentate Calcinosis (BSPDC)' appears most appropriate.⁴

Inheritance: It may occur in a sporadic or familial manner. It is believed to have autosomal dominant inheritance, but a few cases have been reported to have autosomal recessive inheritance in literature.⁵ Recent mapping to chromosome 14q of a susceptible locus for FD has been reported.²

Etiopathogenesis: The physiopathological mechanism of FD is not completely understood. Using electron microscopy, Kobayashi et al⁶ proposed, as a physiopathological mechanism, initial damage to pericytes, promoting the accumulation of mucopolysaccharides in their cytoplasm, followed by mineral deposits. Others suggested abnormalities in intracranial oxygen metabolism after the observation of elevated cerebrospinal fluid lactate levels in a few case of the disease.⁷ Calcium and other mineral deposits were found in the walls of capillaries, arterioles, and small veins and in perivascular spaces. Pathological studies show that calcium is the major element present.

Clinical Features: It may present with neuropsychiatric, extrapyramidal and cerebellar (neurological) symptoms.⁸ The most frequent neuropsychiatric syndromes associated with FD are schizophrenia-like psychosis, mood and personality disorders and cognitive disorders, notably executive dysfunctions. These conditions have been suggested to be caused by cortico-subcortical disconnection mediated by the basal ganglia, especially involving the frontostriatal and limbic circuits.⁷

The main neurological manifestations of FD include motor disorders such as parkinsonism, dystonia, tics, speech alterations, epilepsy (with new onset generalised tonic clonic seizures) and motor deficits, which are probably due to involvement of the frontostriatal motor system.⁷

Neuroimaging: The discrepancy between the clinical presentation and imaging findings has been reported. There have been clinically asymptomatic patients with positive brain imaging findings. Even in those with clinical symptoms, the imaging correlation is still poor.¹

Recognition of the intracranial calcifications in Fahr's syndrome has been made easier by CT. Calcifications consist of hydroxyapatite of a nature similar to that found in bones. Other elements include zinc, iron and magnesium.⁹ The most common radiologic feature of FD is the presence of bilateral intracranial calcifications which are usually seen in the globus pallidus, but may also affect the putamen, caudate nucleus, thalamus, dentate nucleus and white matter of the cerebral hemispheres.⁷

The appearance of calcifications on magnetic resonance imaging (MRI) is non-specific.¹⁰ It has been suggested that the unusual hyperintense T2-weighted images seen on MRI may reflect a slowly progressive metabolic or inflammatory process in the brain, which subsequently calcifies.⁴ When calcific deposits seen in CT present as hyperintensities in T1-weighted images this might be due to the paramagnetic effect of the different mineral ions present in SPD deposits and mainly to manganese¹⁰ or due to proteins and mucopolysaccharides binding the mineral ions.⁹

X ray of skull may not reveal calcifications always. Topographic image studies are promising to predict neurological deficits. Studies using 99mTc-hexamethylpropylenamine oxime (99mTc-HMPAO), single proton emission computed tomography (SPECT) revealed markedly decreased perfusion to the basal ganglia

bilaterally with decreased perfusion to the cerebral cortices in BSPDC. Positron emission tomography scan using fluorodopa did not show any significant difference between BSPDC patients and control subjects.⁴ But Benke et al¹¹ performed a PET scan on a patient with neuropsychiatric symptoms related to FD which demonstrated glucose hypometabolism in the basal ganglia and frontal lobes.

Electroencephalogram, nerve conduction studies and pattern shift visual-evoked potentials studies are generally normal. Brainstem auditory-evoked potentials may vary from normal to minor abnormalities.⁴ EEG and sleep deprived EEG results are usually normal.⁸

There is no prenatal or genetic test available for genetic counselling. CT scan remains the most effective screening tool for adult relatives. However, false negative results may still occur. The minimum age at which a negative CT scan can exclude the disease is not established yet.¹

Differential Diagnosis: It should be emphasized that there are other conditions that can also produce intracerebral calcifications. These conditions include endocrinopathies (hypothyroidism, hypogonadotropic hypogonadism), systemic diseases (systemic scleroderma, systemic lupus erythematosus), infections (toxoplasmosis, neurocysticercosis, German measles, neurobrucellosis, HIV), primary or secondary calcified brain tumors, and various diseases such as tuberous sclerosis, mitochondrial encephalopathy, myotonic muscle dystrophy, measles and smallpox encephalitis, post-anoxia disorders, phacomatosis, Cockayne syndrome, neonatal anoxia, idiopathic hemochromatosis, heavy metal and carbon monoxide intoxication, treatment with methotrexate, and radiotherapy.⁷ These diseases cause bilateral and non-symmetric cerebral calcifications mainly located in the basal ganglia and cerebellum. Huntington's chorea, Wilson's disease, oligodendroglioma, low-grade astrocytoma and Binswinger disease should be considered in young patients who present predominantly with movement disorders.⁵

All the above-mentioned differential diagnoses should be effectively ruled-out in all cases. Therefore, Fahr's disease or BSPDC is a diagnosis of exclusion. Etiology is not directly correlated with image calcification pattern, except for some differences noticed in calcifications site in dystrophic senile ones. The only difference noted in the calcifications pattern was their absence in

subcortical region and basal nucleus and their presence in semioval center, in patient with senile calcifications.⁹

Treatment and prognosis: There is neither a cure for Fahr Disease, nor a standard course of treatment. The prognosis is variable and hard to predict.² Although treatment of underlying etiologies (such as hypoparathyroidism or mitochondrial encephalopathy) has led to neuropsychiatric improvement, there are no specific treatments to limit calcification progression.¹² Antipsychotics and antiepileptics help control the symptoms. No treatment recommendation is made for asymptomatic patients.

3. Conclusion

FD should be included in the differential diagnosis of patients who present with psychiatric symptoms associated with motor disorders when calcifications are found mainly in the basal ganglia. Making a clinical diagnosis of Fahr's disease relies on the combination of clinical features, brain imaging, and exclusion of other causes of intracranial calcifications. To remember, FD may be asymptomatic (like our second case) or symptomatic with neuropsychiatric manifestations (like our first case).

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