

Fahr's Syndrome: A Rare Etiology of Seizure Disorder

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Abstract: Fahr's syndrome is a rare and unremitting neuropsychiatric condition often ranging in symptoms from headache, seizure, chorea, dementia to mania, depression and schizophrenia. CT finding which plays a vital role in diagnosis is suggestive of calcification in the bilateral basal ganglia, cerebral cortex areas, thalamus, dentate nucleus, cerebellum, subcortical white matter, and hippocampus. We are reporting a rare case of a 27 year old gentleman with seizure disorder who was diagnosed with Fahr's syndrome after evaluation.

Keywords: Hypoparathyroidism, Seizure disorder, Hypocalcemia

Key Messages: Fahr's syndrome is a rare clinical condition characterised by calcifications in bilateral basal ganglia, cerebral cortex areas, thalamus, dentate nucleus, cerebellum, subcortical white matter, and hippocampus. The most common cause of this condition is hypoparathyroidism.

1. Introduction

Fahr's syndrome is a rare condition with a prevalence of less than 1 per 1, 000, 000 population. [1] It is an unremitting neuropsychiatric condition often ranging in symptoms from headache, seizure, chorea, dementia to mania, depression and schizophrenia. [2, 3] Hypoparathyroidism is an endocrine disorder where insufficient secretion or effect of parathyroid hormone (PTH) occurs. Clinically patients may present as tingling and numbness, muscle cramps, fatigue. Fahr's syndrome is diagnosed when hypoparathyroidism is combined with basal ganglia calcification. It is a rare clinical condition and hypoparathyroidism being the most common cause. [1, 2, 3]

Fahr's disease and Fahr's syndrome are two closely related conditions both of which are associated with calcification in various areas of brain including the basal ganglia and cortical areas. [4] Fahr's disease is a familial inherited condition and often referred as primary basal calcification whereas Fahr's syndrome occurs secondary to endocrine disorders including thyroid and parathyroid disorders. Clinically patients may present with motor, psychiatric symptoms and cognitive impairment. [3] However, several studies have reported the degree of

calcification is not related to the severity of clinical presentation.

2. Case History

A 27 years old gentleman was admitted with chief complains of severe muscle pain and difficulty in walking for 7 days and headache for 5 days. The patient was a known case of seizure disorder for 10 yrs. There was no history of fever or any other comorbidities. On physical examination Pulse was 113/min, BP =106/74 mmHg, RR=18/min and Temp=98.4degree Fahrenheit. Patient was conscious and oriented to time, place and person. Deep Tendon Reflexes were present bilaterally and normal. In laboratory investigations, his serum Calcium was 3.48 mg/dl which was corrected with i. v. calcium gluconate (10%, 10 ml solution). His phosphorus 7.38 mg/dl, magnesium 1.85 mg/dl, sodium 139 mmol/l, S. parathormone level<1 pg/ml, 25-OH Vitamin D level 20.4 ng/ml. (7-9) His Hb was 10.1 g/dl, TLC was 11850/mm³, platelet count was 468000/mm³. Urine routine and microscopy was normal.

CT brain findings showed confluent areas of calcification in bilateral basal ganglia, bilateral thalamic region, and subcortical areas in frontal region.

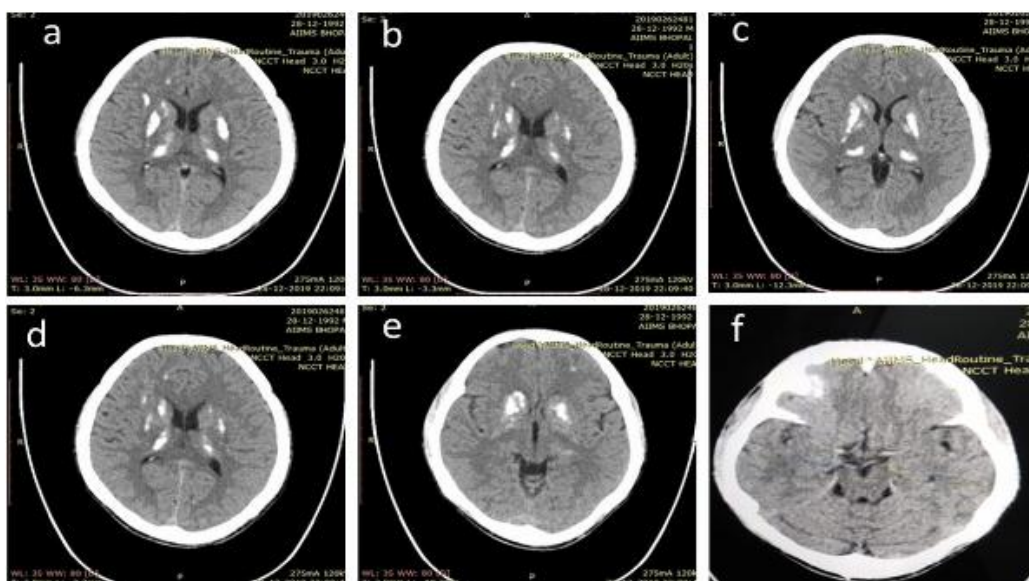


Figure 1 (a) – (f) are showing bilateral calcification on CT in basal ganglia, thalamic region and frontal area in CT head.

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Routine ECG was done which showed QT prolongation, sinus tachycardia with low voltage QRS complexes.^[5]

Further 2D echo in view of ECG changes was done showed mild pericardial effusion, grade 1 diastolic dysfunction, EF=50 to 55%. USG neck and abdomen were within normal limits.

Based on the serological, radiological investigation the diagnosis of Fahr's syndrome in a case of seizure disorder was made. The patient was given corrections for hypocalcemia. Anti-epileptic drugs and Vitamin D3 were also given. His symptoms improved in the next 2 months.

3. Discussion

Fahr's syndrome is one those rare entities about which a lot remains to be explored. German neurologist Karl Theodor Fahr in 1930 was first one to describe this syndrome.^[6] Bomberger was the first to observe histologic findings in the form of symmetrical brain calcifications.^[2] Eaton et al in 1939 discovered the close relation between the basal ganglia calcification and hypoparathyroidism.^[2]

Basal ganglia calcification is a neurological disorder, in which there are calcium deposits abnormally present in the areas of the brain that control motor activity, leading to neuropsychiatric symptoms.^[3] Bilateral basal ganglia calcification is however seen both Fahr disease and Fahr's syndrome.^[4, 7] Confusion has been there in literature regarding the Fahr disease and Fahr's syndrome. Literature has clearly pointed out that Fahr's syndrome is not exactly Fahr's disease, although clinical symptoms are similar in both. The differences basically are in etiology, prognosis, and treatment.^[4]

Fahr disease is a familial idiopathic basal ganglia calcification, a rare hereditary neurodegenerative disease.^[8, 9] Important points to notice regarding the disease is that it has an autosomal dominant or recessive mode of inheritance with age of onset mainly in 40-60 years. It has large, progressive, bilateral symmetrical calcification of the basal ganglia and exclusive of infection, trauma, or poisoning. It is also exclusive of mitochondrial or metabolic diseases or other systemic diseases. Genetic studies have revealed mutations in SLC20A2, PDGFRB, PDGFB, and XPR1 genes, along with novel mutations in the myogenic regulating glycosylase gene.^[8, 9]

Fahr's syndrome is the secondary form where calcification occur secondary to a known cause like hypoparathyroidism, infectious diseases like brucellosis, toxoplasmosis.^[4, 8]

With the improvement in the means of diagnosis, cases of Fahr's syndrome caused by hypoparathyroidism have gradually increased in recent years. Most patients have neuropsychiatric symptoms or motor disorder, including seizure, early onset dementia, chorea etc.^[1] Furthermore, some rare complications have also been reported, such as cerebral haemorrhage and thoracic ossification of the posterior longitudinal ligament. In addition to

hypoparathyroidism, Fahr's syndrome has also been observed in neuroferritinopathy, Kenny-Caffey syndrome type 1, intrauterine or perinatal infection (e.g., toxoplasma gondii, rubella), tuberous sclerosis complex, brucella infection, etc.^[10]

Abnormal deposition of calcium is usually present in the areas of the brain responsible voluntary activities including the basal ganglia, thalamus, dentate nucleus, cerebral cortex and cerebellum. The Cardiac manifestation in Fahr's syndrome may be attributed to hypocalcaemia which in turn may be attributed to primary hypoparathyroidism. Late stages of uncorrected hypocalcaemia may also present with hypocalcaemic cardiomyopathy.^[5] In our case patients ECG showed the QT prolongation, low voltage QRS complexes with sinus tachycardia. Further an echocardiographic study was done which suggests mild pericardial effusion and grade 1 diastolic dysfunction.

Currently there is no definitive treatment for Fahr's syndrome. Treatment addresses symptoms on an individual basis. If underlying metabolic disturbances are found, correcting the underlying abnormalities may improve the presenting symptoms. For the patients presenting with seizure activity, as in our case antiepileptic drugs such as levetiracetam, valproate and carbamazepine are appropriate. In a young female patient of childbearing age, the use of teratogenic medications including valproic acid and carbamazepine should be avoided.^[1, 11]

The possibility of hypoparathyroidism should be considered in patients with chronic hypocalcemia, recurrent tetany, and even neuropsychiatric symptoms. Hypoparathyroidism is a common cause of basal ganglia calcification.^[8, 12] Therefore, it is recommended that blood calcium, phosphorus, and PTH levels should be measured in all individuals with basal ganglia calcification to exclude hypoparathyroidism.

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