

### A Rare Case Presentation of Fahr's Syndrome

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#### Abstract

Fahr's syndrome is a rare, genetically dominant, inherited, neurological disorder characterised by abnormal deposits of calcium in areas of the brain that control movement, including the basal ganglia and the cerebral cortex. Symptoms of the disorder may include deterioration of motor functions, dementia, seizures, headache, blurring of vision, spasticity (stiffness of limbs) and athetosis (involuntary, writhing movements). The most common site of calcification is the globus pallidus. However additional areas of calcification are putamen, caudate nucleus, internal capsule, dentate nucleus, thalamus, cerebellum and cerebral white matter. We are presenting a case of a 30 year old male, who complained of stiffening of upper limbs and blurring of vision followed by giddiness which was associated with slowness of movements. His CT scan revealed a symmetrical large area of calcification over the basal ganglia. Secondary causes of this disease were ruled out to make the clinical diagnosis of Bilateral Striopallidodentate Calcinosis, [BSPDC] which is otherwise called as the Fahr's syndrome.

**Key Words:** Calcium deposits, calcification, Fahr's syndrome, basal ganglia calcification.

#### Introduction

Fahr's disease is a rare, degenerative neurological disease was described for the first time by a German neurologist, Karl Theodor Fahr in 1930. Neuropsychiatric, extra pyramidal and cerebellar symptoms, seizures, Parkinsonian features, dementia and speech disorders may accompany the clinical picture.<sup>[1]</sup> There are also cases without neurological signs, which have been reported. This disease usually appears between the age of 40-60 years.<sup>[1]</sup> Because of the symmetrical involvement of these nuclei, the descriptive terminology, Bilateral Striopallidodentate Calcinosis [BSPDC] has been put forth. This is a very rare disease of unknown prevalence in India.

#### Case Report

A 30 yr old male patient, from Tumakuru was evaluated for complaints of fever with chills and non-productive cough for 3 days. It was also accompanied with perceived stiffening of upper limbs and blurring of vision followed by giddiness (2 to 3 episodes).

Patient did give past history of suffering from 3-4 episodes of upper limb stiffness in the past 2 years. He mentioned that the stiffness was associated with "twisting" type of pain sensation in the hands that

resolved by itself after 25-30 minutes. He also reported sensitivity to cold and gave history of weight gain (20kg increase in 3 months). History of bilateral tremors of the hands that started 1 year back was elicited, it was insidious in onset, non progressive, present only in the fingers of both hands. No aggravating or relieving factors. No other symptoms pertaining to the central nervous system were reported.

Examination showed obese male patient with temperature of 100 degrees Fahrenheit. Blood pressure was recorded to be 140/90. Chvostek's sign was elicited. Trousseau's sign was also elicited. Fundoscopy was normal. Slowness of speech was noticed with Slurring on occasions. Other higher mental functions were intact. No other abnormalities found during systemic examination. Reflexes were normal.

Patient was treated with an antibiotic, antacid and antipyretic for the fever. Patient was also treated with intravenous calcium gluconate, oral calcium carbonate 500mg twice daily, Tab. Thyroxine 50 micrograms once

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daily and vitamin D3 weekly supplements. Patient was advised serum calcium monitoring and monthly follow-up.

On follow-up, ECG done revealed QT prolongation (Figure 1). A CT scan done showed calcification of the bilateral basal ganglia (Figure 2). Further work up revealed the following.

**Table 1.** Investigations

Tests	Values	Reference range
Serum calcium	6.3mg/dL	9-11mg/dL
Ionised calcium	3mg/dL	4.5-5.5 mg/dL
Urine calcium	295mg/24hrs	100-300mg/24hr
Serum albumin	3.5gm/dL	3.5-5.5 g/dL
PTH (Parathyroid Hormone)	0.10pg/ml	10-65pg/ml
TSH (Thyroid stimulating Hormone)	8.24 $\mu$ IU/ml	0.4 – 4 $\mu$ IU/ml
Vitamin D	27ng/ml	20-100ng/ml
Hb%	11gm%	14-16gm%
pH	7.3	7.35-7.45
Serum potassium	3 meq/L	3.5-5.5 mEq/L
LFT	WNL*	
Glucose	WNL*	
Serum phosphate	4.5 mg/dL	3-4.5 mg/dL
Serum magnesium	2.4 mg/dL	1.8-3.6 mg/dL
Alkaline phosphatase	77 U/L	50-160 U/L
Serum creatinine	0.8mg/dL	0.5-2.0 mg/dL

\*within normal limits

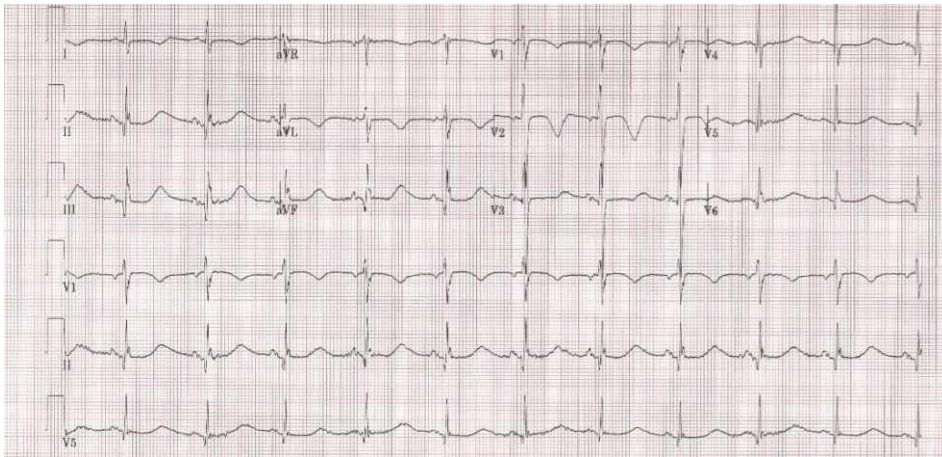
## Discussion

The most common presentations as per the Fahr's Disease Registry are movement disorders, which account for about 55% of the cases. Among these, Parkinsonism was seen in 57% cases, chorea was seen in 19% cases, tremor was seen in 8% cases, dystonia was seen in 8% cases, athetosis was seen in 5% cases and orofacial dyskinesia was seen in 3% cases.<sup>[2]</sup> The other neurological manifestations include a cognitive impairment, cerebellar signs, speech disorders, pyramidal signs, psychiatric features, gait disorders and

sensory changes. The clinical diagnosis of Fahr's disease is based on the combination of clinical features, brain imaging or on an exclusion of other causes of the intracranial calcification. The imaging findings of the symmetric and extensive calcification are usually typical. The disorders of calcium metabolism may occur in association with the intracerebral calcification. It is stipulated that at the molecular level, calcification develops in the vessel wall and in the perivascular space. Due to defective iron transport and free radical production, tissue damage occurs that ultimately leads to calcification. Various clinical conditions coming as differential diagnosis to Fahr's disease are Parkinson's disease, Juvenile parkinsonism, other causes of secondary Parkinsonism like post encephalitic parkinsonism, slow virus infection, drug induced parkinsonism, multi-infarct dementia with parkinsonism, Multisystem degeneration, Huntington's disease and Lewy Body disease. Most common associations include endocrine disorders, mitochondrial myopathies, dermatological abnormalities and infectious diseases. Among endocrine disorders parathyroid disturbances are most commonly associated with Fahr's syndrome. The abnormalities include idiopathic hypoparathyroidism, secondary hypoparathyroidism, pseudohypoparathyroidism and hyperparathyroidism. Other conditions associated with Fahr's syndrome are Kenny Caffey Syndrome Type-1, Mitochondrial myopathies like Kearns-Sayre Syndrome and MELAS (myopathy, encephalopathy, lactic acidosis and stroke), adult onset neurodegenerative conditions like neuroferritinopathy and polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy, dermatological conditions like lipid proctenosis, Intrauterine or perinatal infections like toxoplasmosis, rubella, Cytomegalovirus or Herpes virus infection. Cockayne syndrome, Aicardi-Goutieres Syndrome, Tuberous sclerosis complex, Brucellosis and Coats disease is also associated with Fahr's syndrome.<sup>[3-5]</sup>

Other associated metabolic derangements found with Fahr's syndrome are briefly discussed.

Hypocalcemia, is low calcium levels in the blood serum. Although there are many causes of hypocalcemia, impaired PTH production and impaired Vitamin D production are the most common causes. Diagnosis of hypocalcemia should generally be confirmed with a



**Figure 1.** Electrocardiogram revealed a QT prolongation pattern.



**Figure 2.** CT scan of the brain revealed bilateral basal ganglia calcification.

corrected calcium or ionised calcium level. The reference range for serum calcium is 8.5-10.2 mg/dl. Level of 4.6-5.3 mg/dl is normal reference range for ionised calcium. Neurologic symptoms of hypocalcemia include irritability, impaired intellectual capacity, depression and personality changes, seizures and uncontrolled movements.

Hypoparathyroidism is decreased function of the parathyroid glands with underproduction of parathyroid hormone. This can lead to low levels of calcium in the blood, which interferes with normal muscle contraction and nerve conduction.

Hypothyroidism is a common disorder of the endocrine system in which the thyroid gland does not produce enough thyroid hormone. It can cause a number of symptoms, such as poor ability to tolerate cold, a feeling of tiredness, constipation, depression and weight gain amongst others.<sup>[6]</sup>

Thyroid dysfunction is frequently associated with disturbances of calcium and phosphorous homeostasis and are important cause of secondary osteoporosis<sup>[1]</sup>. In hypothyroidism there is a depressed turnover due to impaired mobilisation of calcium into the bone. There is increased production of thyroid calcitonin that can promote the tubular reabsorption of phosphate and also favour the tubular excretion of calcium.<sup>[7-9]</sup>

Thyroid hormone determines the mineral pool in the blood by influencing mobilisation in blood and their clearance through urinary excretion due to its effect on

Glomerular filtration rate (GFR) or renal plasma flow.<sup>[7-9]</sup> Low levels of calcium in hypothyroid cases reflect poor metabolism of calcium. Low levels of magnesium reflect influence of thyroid hormone on GFR and thereby clearance of these minerals by filtration. A significant decrease in serum calcium is demonstrated and is mainly due to the low levels of parathyroid hormone and low levels of calcitonin in hypothyroidism.<sup>[7]</sup>

Magnesium level is reduced due to influence on GFR and decreased clearance. In hypothyroidism there is an increased renal blood flow leading to high clearance of magnesium from the kidneys.<sup>[7-9]</sup>

Insufficient parathyroid hormone (PTH) activity disturbs body calcium homeostasis with inadequate mobilisation of calcium from bone matrix, reabsorption from the kidney and decreased synthesis of 1-hydroxyvitamin D, resulting in hypocalcemia and hypophosphatemia. The electrolyte alterations affect the neuromuscular system and usually result in spasms, cramps and twitching.

Primary hypoparathyroidism can occur due to an activating mutation of calcium sensing receptor (CaSR). Most patients remain asymptomatic and therefore not diagnosed until adulthood. Keeping primary hypoparathyroidism in mind we need to differentiate from a few other similar conditions. The differential diagnosis of hypoparathyroidism includes post-surgical ablation of parathyroid glands and

abnormal parathyroid gland development.

Fahr's disease is a rare inherited or sporadic neurological disorder with a prevalence of <1/1,000,000.<sup>[10]</sup>

Computed tomography scan remains the most effective screening tool in Fahr's disease. Molecular genetics of this disease have not been studied extensively so no prenatal or genetic tests are available for genetic counselling. The treatment include symptomatic support. Atypical antipsychotics are preferred for the psychiatric symptoms because of the coexistence of the extra pyramidal syndrome in these group of patients.

## Conclusion

The goals of research are to locate and understand the actions of the genes which are involved in this disorder. We believe there may be some immunological basis associated with calcifications of Fahr's syndrome which needs further studies.

**Financial support and sponsorship:** Nil

**Conflicts of interest:** Nil

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