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A rare case of Fahr's disease

Kesar Prajapati

Vishakha Vinod

Sumit Bochiwal

ORIGINAL STUDY

A rare case of Fahr's disease

Kesar Prajapati [a,*], Vishakha Vinod [b], Sumit Bochiwal [c]

[a] Department of Medicine, Baroda Medical College, Vadodara, Gujarat, India
[b] Department of Medicine, SMS Medical College, India
[c] Department of Medicine, Raj University of Health Science (RUHS), India

Abstract

Fahr's syndrome, a rare syndrome, is characterized by symmetrical and bilateral intracranial calcifications. A 23-year-old male patient presented with generalized tonic–clonic convulsion and muscle cramps for 1 month. The patient's blood counts, blood sugar levels, serum sodium, and serum potassium were normal. Computed tomography scan of the brain revealed bilateral symmetrical hyperdensities, suggestive of calcification in globus pallidus, putamen, thalami, caudate and dentate nuclei of the cerebellum, and subcortical white matter of both cerebral hemispheres. The findings were suggestive of Fahr's disease. His serum ionized calcium levels were low with high phosphate levels (with increased parathormone levels), suggesting the association of pseudohypoparathyroidism. He was treated symptomatically and responded well. Fahr's disease should be suspected as a rare cause of convulsion with pseudohypoparathyroidism and hypocalcemia in young patients.

Keywords: Calcification, Fahr, Parathormone

1. Introduction

Fahr's disease, also known as 'idiopathic basal ganglia calcification' or 'bilateral striatopallidodentate calcinosis' is characterized by neurological degeneration leading to convulsions extrapyramidal, psychiatric, or cerebellar symptoms [1]. It is named after its discoverer Karl Theodor Fahr (1930) [2]. The disease may be a part of familial inheritance (autosomal dominant) or nonfamilial (sporadic cases) [3]. It is a rare entity usually manifesting in the age of forties to sixties with twice the prevalence rate in men as compared to women [4–6].

We present here a case of a young man who was diagnosed with Fahr's disease in association with hypoparathyroidism.

2. Case report

A 23-year-old male patient presented to us with a complaint of generalized tonic–clonic seizures for the first time with H/O muscle cramps for 1 month. He was not on any medication previously and had no significant past or family history.

On examination, he was well oriented and vitally stable. Examination revealed tetany and Chvostek's sign positive with B/L short fourth and fifth metacarpals (Fig. 1). He had hard stony nodules subcutaneously over forearms (Fig. 2), dry scaly skin, and hyperkeratosis over both palms. Central nervous system examination was grossly normal with bilateral extensor plantar. The intellectual levels, speech, and motor functions were normal.

The patient's complete blood counts, random blood sugar, serum sodium, and serum potassium levels were normal. His serum ionized calcium levels were low (3.3 mEq/l), phosphate levels were high, and parathormone levels were increased (221 pg/ml). The biochemical profile of the patient is shown in Table 1.

Radiological investigations included radiograph skull, computed tomography scan, and MRI. Computed tomography scan of the brain revealed bilateral symmetrical hyperdensities, suggestive of calcification in globus pallidus, putamen, thalami, caudate and dentate nuclei of the cerebellum, and subcortical white matter of both cerebral hemispheres. SPECT imaging of the brain with 99mTc-HMPAO was not done, although it can be a useful tool

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* Corresponding author at: Baroda Medical College, India. Fax: 7984845100.
E-mail address: kesarprajapati10694@gmail.com (K. Prajapati).

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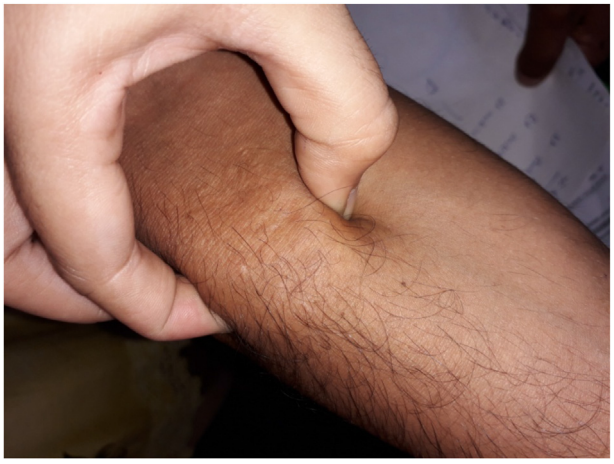

Fig. 1. Subcutaneous calcified nodules.

in showing disruptions of the regional blood flow in conditions of basal ganglia calcifications (Fig. 3). Proband analysis with genetic sequencing of the SCL20A4 gene was done, which showed no abnormality.

In the event of calcifications in the basal ganglia, causes like infections (TORCH, tuberculosis, neurocysticercosis, brucellosis, and HIV), metabolic disturbances (hypervitaminosis D, diabetes mellitus type I, and hypoparathyroidism), congenital (infancy presentation with ophthalmological abnormality may occur in Rubella, and mitochondrial diseases), connective tissue diseases, and vascular (calcified angiomas) must be ruled out [1,7–9].

Specifically, if the patient presents with latent tetany and myopathic changes along with changes in somatosensory, visual, and brain stem auditory responses, causes of parathyroid dysfunction must be

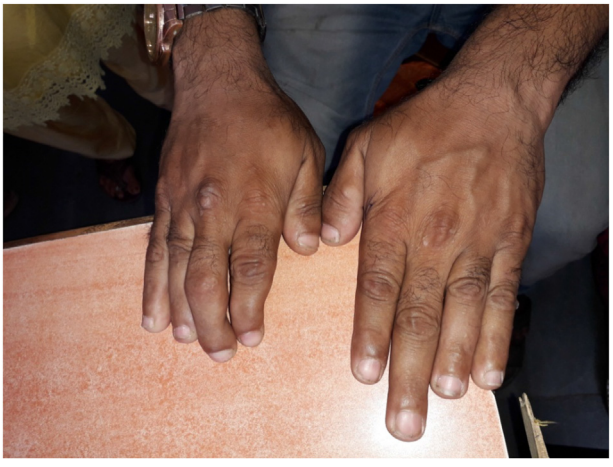

Fig. 2. Bilateral short fourth and fifth metacarpals.

Table 1. Investigations for the patient.

Biochemical parameters	Values	Normal range
Hemoglobin	14.1 g/dl	12–17 g/dl
Total leukocyte count	6500/cumm	4000–11000/cumm
Differential leukocyte counts		
Neutrophils	59%	40–70%
Lymphocytes	32%	20–40%
Monocytes	6%	2–8%
Eosinophils	2%	1–6%
Basophils	1%	0–1%
Platelet counts	2.1 lacs/cumm	1.5–4 lacs/cumm
RBS	143 mg/dl	80–200 mg/dl
Serum sodium	140 mEq/l	135–150 mEq/l
Serum potassium	3.9 mEq/l	3.5–5.5 mEq/l
Ionized calcium	3.3 mEq/l (decreased)	4.5–5.5 mEq/l
Phosphate	6.8 mg/dl (increased)	2.5–4.5 mg/dl
PTH	221 pg/ml (increased)	14–65 pg/ml

PTH, parathyroid hormone; RBS, random blood sugar.

sought. Hypoparathyroidism may occur secondary to iatrogenic, surgical removal, radiotherapy of the neck, or idiopathic causes. There may be cases of inherited hypoparathyroidism where symptoms may present from early childhood. Autoimmune hypoparathyroidism (polyglandular syndrome) may present in adolescence in association with adrenal insufficiency, thyroid disease, and diabetes mellitus [1,7–9].

Other associative diseases of Fahr's disease include corticobasal degeneration, mitochondrial encephalopathy, central nervous system lupus, motor neuron disease, Alzheimer's disease, or frontal lobe dementia, which must be ruled out after confirming the diagnosis of Fahr's disease [1,7–9].

The patient was managed symptomatically by anticonvulsants, calcium, and vitamin D3 supplements.

The patient achieved normal calcium levels with resolution of symptoms. He has been continued till present with oral supplementation of calcium and vitamin D3 for maintenance of serum calcium now.

3. Discussion

The diversity in the age of presentation of Fahr's disease has made it an interesting entity allowing for further research into the mechanism of its occurrence. Against the usual presentation at later age (>40 years) [4], similar to our case, certain cases have been reported at a younger age [5,6].

As this disease is a rare entity with no reported prevalence and calcification of the basal ganglia is an imprecise radiological finding (also observed in 1% normal cases), the diagnosis of this disease can go unaccounted for a long time [1].

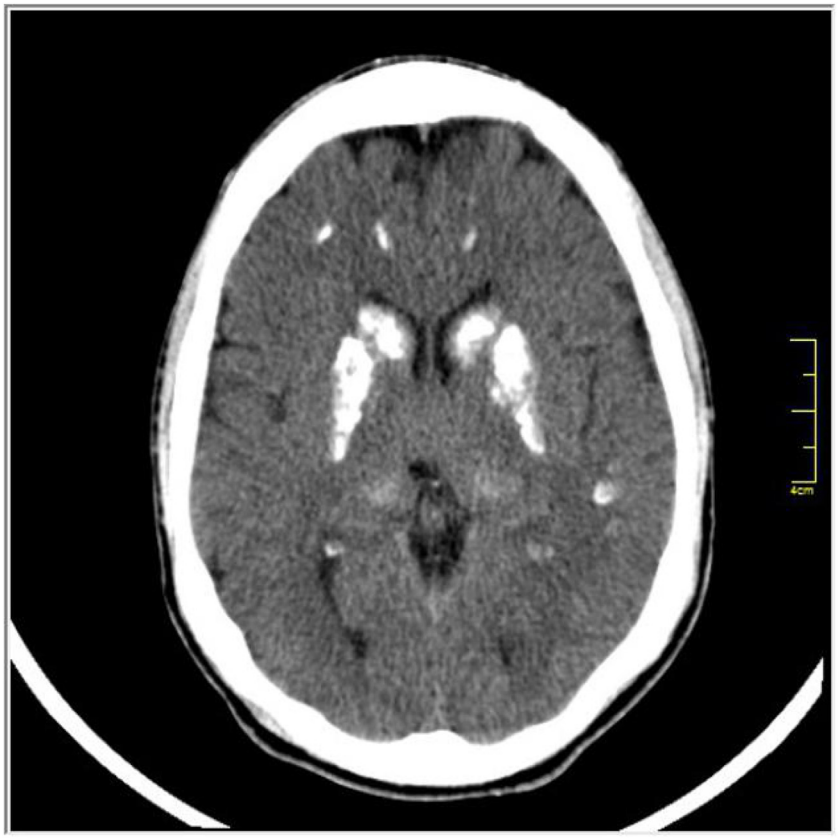

Fig. 3. Computed tomography brain findings in Fahr's syndrome, showing bilateral basal ganglia calcification.

Literature search has shown that certain genetic mutations in the genes like the idiopathic basal ganglia calcification gene, SLC20A2, and PGDFRB gene (that regulates the phosphate transporter) may underlie the defective calcification in certain parts of the brain like putamen, globus pallidus, caudate nucleus, thalamus, cerebellum, and junctional aspect of white matter and cortex [7]. The mutations may be autosomal dominant or recessive, which may guide the early or late age of presentation. The sporadic cases demand further search on the environmental factors that may make an individual prone to an early and different presentation [7].

The area of the brain affected by the calcification may decide the type of symptoms. Common symptoms include movement disorders like tremors, slowness of movements, rigidity, and ataxia; psychiatric manifestations like mood disorders an psychosis; and neurological disorders like convulsions, dementia, and cognitive and behavioral abnormalities. Dementia without extrapyramidal symptoms is also found, which is a rare finding [8].

Among the other symptoms are oral manifestations like oligodontia and advanced periodontitis as reported by Aditya et al. [5] The patient in their study [5] was a 23-year-old female, who along with oral symptoms, presented with stunted growth, calcifications in the brain, osteoporosis, seizures, and disorientation, findings very similar to the present study (except for oral manifestations).

The metabolic derangements in the brain functionality due to a pathological calcification in the basal ganglia or other parts of the brain have been seen in patients with Fahr's disease [3]. Fluoro-L-dopa MRI uptake study witnessed reduced blood flow and glucose metabolization causing decreased functioning of the brain centers [9].

Fahr's disease has shown to have a frequent association with pseudohypoparathyroidism whereby the calcification in the brain causes a fall in the serum calcium levels, thereby stimulating the secretion of parathyroid hormone (PTH). Owing to genetic mutations, there is resistance to the action of PTH, resulting in low serum calcium levels and high phosphate levels despite the increase in PTH. Pseudohypoparathyroidism, as observed in the present study and a few previous case reports [3–5], is the primary differential to be sorted as there may be various other causes for hypoparathyroidism.

The association link between brain calcification and hypocalcemia remains an enigma. Possible explanations include augmented calcium–phosphorus

complexes secondary to disrupted blood−brain barriers allowing influx, interference of psychiatric conditions with calcium signaling regulation, and resistance to parathormone (pseudohypoparathyroidism) [10].

The treatment remains symptomatic without any standardization for the control of the disease [10]. The present patient was managed with anticonvulsants, calcium, and vitamin D3, to which he responded well with the achievement of normal calcium levels. PTH substitution is not recommended unless the patient develops hypercalciuria and kidney complications [3].

Fahr's disease should be suspected as a rare cause of convulsion with pseudohypoparathyroidism and hypocalcemia in young patients. Imaging and biochemical investigations form the key to accurately diagnosing the condition after ruling out the causes of basal ganglia calcification and hypoparathyroidism. As there is no definitive cure for the disease, early diagnosis and normalization of serum calcium levels remain the key to delaying further calcification in the brain.

Conflicts of interest

There are no conflicts of interest.

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