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Case Report

Seizure-Like Activity in an Adolescent with Fahr Syndrome

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Abstract

Pseudohypoparathyroidism, characterized by parathyroid hormone (PTH)-resistance or PTH-unresponsiveness at target organs, is associated with Fahr syndrome which is a rare neurological condition characterized by an abnormal basal ganglia calcification. We present a pediatric case of a 15-year-old male who exhibited seizure-like activity due to pseudohypoparathyroidism, ultimately revealing basal ganglia calcification consistent with Fahr's syndrome. This case underscores the complexity of integrating endocrine and neurological considerations in diagnosis and management, emphasizing the need for collaborative care across medical specialties.

Keywords: *Pseudohypoparathyroidism; Fahr Syndrome; Basal Ganglia Calcification; Seizure Like Activity; Hypocalcemia*

Abbreviations

PTH: Parathyroid Hormone; iCa: Ionized Calcium; EKG: Electrocardiogram; EEG: Electroencephalogram; IV: Intravenous; CT: Computed Tomography; ACTH: Adrenocorticotropic Hormone; FGF23: Fibroblast Growth Factor 23; APS1: Autoimmune Polyglandular Syndrome Type 1; FD: Fahr Disease

Introduction

The identification of basal ganglia calcifications on imaging studies often occurs incidentally, especially among older individuals without apparent symptoms. This phenomenon, termed Fahr disease, may arise sporadically or within familial contexts. However, when these calcifications coincide with neurological or endocrine disorders, particularly affecting the parathyroid glands, the condition is classified as Fahr syndrome [1]. This distinction holds significant diagnostic and therapeutic implications, as exemplified by the case of a 15-year-old male presenting with seizure-like activity, ultimately diagnosed with pseudo hypoparathyroidism and Fahr syndrome.

In scholarly discussions, the terms Fahr disease and syndrome are frequently interchanged, yet subtle nuances exist: Fahr's disease is associated with primary familial brain calcification, while Fahr's syndrome encompasses secondary etiologies [1,2].

It is imperative to discern Fahr's syndrome from Fahr's disease (FD), where the latter is typified by intracerebral calcifications devoid of abnormalities in phosphocalcic metabolism [3]. This differentiation is pivotal in accurately diagnosing and managing patients presenting with basal ganglia calcifications and related neurological or endocrine symptoms.

Case Presentation

A previously healthy 15-year-old male presented to the emergency department with an abrupt onset of seizure-like activity and facial twitching. Laboratory results are shown in table 1 and revealed hypocalcemia, (serum calcium: 6 mg/dL; ref. range 8.6 - 10.3), hyperphosphatemia (phosphorus: 7 mg/dL; ref. range 2.7 - 4.5), and elevated parathyroid hormone levels (PTH: 419 pg/mL; ref. range 15.0 - 65.0). Additionally, the patient exhibited low levels of 25-hydroxy vitamin D (17 ng/mL; ref. 30 - 100), although alkaline phosphatase levels were within normal limits. While electrocardiogram (EKG) and electroencephalogram (EEG) findings were unremarkable, a CT scan of the brain revealed abnormal mineralization in the basal ganglia, thalami, and subcortical white matter of the frontal lobes as shown in figure 1 and 2. Notably, renal ultrasound findings were normal. The physical examination showed no Trousseau's or Chvostek signs, and the patient remained asymptomatic with no further episodes of seizure-like activity or tremors throughout his hospital stay.

Test	Result	Reference Range
EEG	Normal	
Calcium	5.3 mg/dL	(8.6 - 10.3)
PTH	352 pg/mL	(15.0 - 65.0)
Vitamin D3	18 ng/mL	(30 - 100)
TSH	3.87 u/mL	(0.27 - 4.20)
Phosphorus	8.5 mg/dL	(2.7 - 4.5)
CT brain	Abnormal mineralization in the deep gray nuclei, and in the subcortical white matter of the frontal lobes. This is concerning for Fahr disease	
Bilateral renal ultrasound	Normal ultrasound of the kidneys	

Table 1: *Summary of laboratory and imaging work-up.*

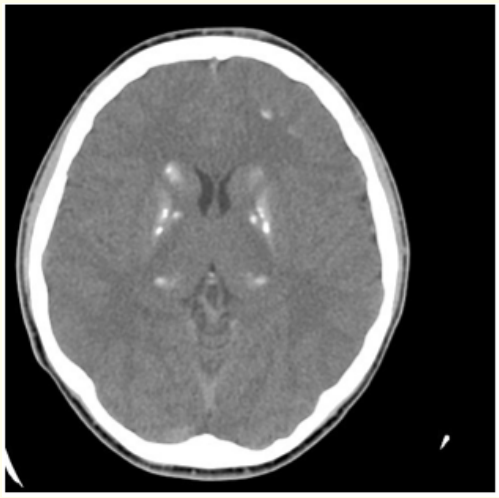

Figure 1: *CT brain.*

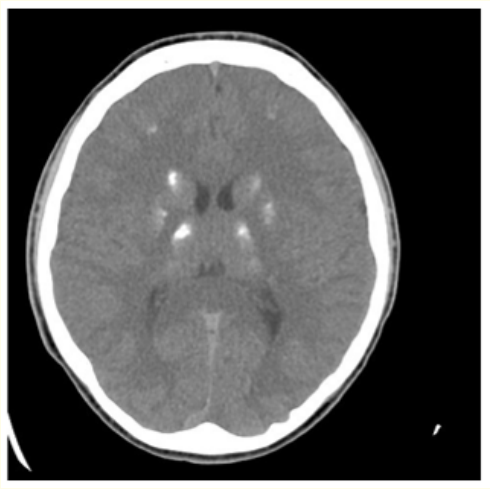

Figure 2: *CT brain axial view.*

Further investigation, including thyroid function tests, ACTH, cortisol, PTH-related peptide, and fibroblast growth factor 23 (FGF23) levels, yielded normal results, suggesting an isolated parathyroid dysfunction.

Following successful calcium stabilization, initially IV then oral calcium supplements, the patient was discharged home with calcium and calcitriol supplements. His outpatient endocrine follow-up revealed a clinically and hemodynamically stable patient with a normal neurological exam.

Patient's family history was significant for vitamin D deficiency in his mother, hypothyroidism in his maternal aunt, hyperparathyroidism in his maternal first cousin, and renal stones and hypertension in his maternal grandfather.

Discussion

The diagnostic journey in this case was multifaceted, considering the diverse differential diagnoses associated with seizure-like activity in adolescence. Laboratory evaluation revealed hypocalcemia and elevated PTH levels, suggestive of parathyroid dysfunction. The identification of basal ganglia calcifications on neuroimaging further supported the diagnosis of Fahr syndrome in the context of pseudo-hypothyroidism. Differential diagnoses, including vitamin D deficiency, and autoimmune polyglandular syndrome type 1 (APS1), were considered and systematically ruled out through comprehensive laboratory investigations.

Fahr's syndrome, characterized by basal ganglia calcification, is associated with a range of diseases including hyperparathyroidism, hypoparathyroidism, pseudohypoparathyroidism, hypervitaminosis D, tuberculosis, cytomegalovirus infection, toxoplasmosis, and astrocytoma. Due to its multifactorial etiology, it can result in various neurological and psychiatric symptoms such as seizures, dystonia, myoclonus, and Parkinson's disease [4-6].

Pseudohypoparathyroidism, although occurring less frequently as a cause of Fahr syndrome, tends to have a familial origin [3,7]. This condition is characterized by resistance to parathyroid hormone (PTH) despite normal or elevated levels of the hormone. The underlying genetic defects associated with pseudohypoparathyroidism result in impaired signalling pathways, leading to reduced responsiveness to PTH. This familial predisposition underscores the genetic component involved in the pathogenesis of pseudohypoparathyroidism and its association with Fahr's syndrome.

The diagnosis of Fahr's syndrome hinges primarily on cerebral CT scans, widely regarded as the gold standard for detecting intracerebral calcifications [3,4]. These calcifications typically display a bilateral and symmetrical distribution pattern, commonly found in the thalami, dentate, and lenticular nuclei, and in the caudate nuclei, semi-oval center, and white matter [10]. This distinctive distribution pattern observed in imaging studies can serve as a hallmark feature crucial for aiding in the accurate diagnosis of Fahr's syndrome [3].

The management of hypoparathyroidism and Fahr syndrome involves addressing calcium and vitamin D deficiencies while monitoring for complications such as seizures and neuropsychiatric abnormalities. In this case, calcium stabilization was achieved through intravenous calcium supplementation followed by oral calcium and calcitriol therapy [3,11].

Early intervention is considered essential to prevent the development of further calcifications and neurological complications. However, it's important to acknowledge that there is no specific treatment available to halt the advancement of calcifications in the basal ganglia [7]. Long-term management requires regular monitoring of calcium levels and adjustments to supplementation to maintain eucalcemia while minimizing the risk of hypercalcemia. Additionally, regular follow-up with pediatric endocrinology is recommended to ensure optimal management and long-term outcomes.

Fahr's syndrome persists as a rare and significant anatomical, clinical, and radiological condition that arises as a complication of undiagnosed or inadequately treated chronic hypocalcaemia. Because correcting disrupted calcium phosphorus metabolism often results in significant improvement, it is crucial to systematically investigate for parathyroid disorders in patients showing neuropsychological symptoms linked to basal ganglia calcifications [8].

Conclusion

This case highlights the importance of considering metabolic disorders, such as hypoparathyroidism, in the evaluation of basal ganglia calcifications and neurological symptoms, particularly in adolescents presenting with seizure-like episodes. Timely recognition and interdisciplinary management involving endocrinologists and neurologists are essential for optimizing outcomes in patients with Fahr syndrome. Further research is warranted to better understand the underlying mechanisms and therapeutic strategies for this rare but clinically significant condition.

It is imperative to differentiate Fahr's syndrome from Fahr's disease, where the biological evaluation appears normal, necessitating genetic assessment for accurate diagnosis.

The diagnostic criteria for Fahr's syndrome encompass bilateral basal ganglia calcification accompanied by progressive neuropsychiatric and/or extrapyramidal features, absence of autosomal dominant inheritance history, early onset at a young age, and concomitant endocrinopathies.

Conflict of Interest

The authors have no conflicts of interest to disclose.

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