SCIENCE SET
OPEN ACCESS PUBLISHERS

Case Report

Journal of Psychiatry and Neurochemistry Research

Fahr Syndrome and Pseudohypoparathyroidism: A Rare Case Report

Tyagi Ubhadiya[1*], and Mihir Sojitra[1]

B.J. Medical College and Civil Hospital, Ahmedabad, Gujarat, India-380016

[*]Corresponding author: : Tyagi Ubhadiya, B.J. Medical College and Civil Hospital, Ahmedabad, Gujarat, India-380016.

Submitted: 16 October 2024 **Accepted:** 22 October 2024 **Published:** 18 November 2024

Citation: *Tyagi, U., & Sojitra, M. (2024). Fahr Syndrome and Pseudohypoparathyroidism: A Rare Case Report. Journal of Psychiatry and Neurochemistry Research, 2(6), 01-03.*

Introduction

Pseudohypoparathyroidism (PHP) is a rare disorder marked by resistance to parathyroid hormone (PTH), leading to calcium-phosphorus imbalances and distinctive physical features such as brachycephaly, round face, and short stature, collectively known as Albright Hereditary Osteodystrophy (AHO) [1]. An uncommon finding in PHP is basal ganglia calcification, a hallmark of Fahr syndrome [2]. Fahr syndrome, initially documented by Fahr in 1930, manifests with bilateral and symmetrical striatopallidal calcifications. It is associated with a variety of metabolic disorders, particularly dysparathyroidism, including PHP [2, 3, 4]. Here, we present the case of a 22-year-old male with complex neurological symptoms, who was found to have Fahr syndrome with an underlying diagnosis of pseudohypoparathyroidism, highlighting a rare overlap between these conditions.

Case Presentation

A 22-year-old male with a five-year history of epilepsy managed with phenytoin presented to our neurology clinic with weakness, tingling, and rigidity that initially started in his left leg but later extended to involve both hands and legs, with occasional paresthesia in bilateral palms and soles for five months. Additionally, the patient reported abnormal involuntary movements, twitching, and spasms. The patient's personal history revealed a vegetarian diet, decreased sleep, decreased appetite, constipation, and normal bladder function. Upon examination, the patient's vital signs were within normal limits. He exhibited a normal body temperature, a heart rate of 91 beats per minute, and a blood pressure of 130/80 mmHg. Respiratory and cardiovascular examinations were unremarkable. Chvostek's sign and Trousseau's sign were elicited. During the central nervous system (CNS) examination, the patient was found to be alert and oriented. Cranial nerves exhibited normal function with no significant abnormalities detected. However, concerning motor functions, there was bilateral rigidity present in both the upper and lower limbs, along with diminished muscle strength. Abnormal involuntary movements were also noted during fine motor tasks. Sensory systems, including light touch, proprioception, and pinprick were found to be within normal limits. The patient's gait was unsteady, and balance maintenance was challenging. Cerebellar function appeared unremarkable.

Laboratory findings showed normal hemograms, renal function tests, and liver function tests. Serum calcium was found to be low at 4 mg/dL, serum phosphorus was high at 6.21 mg/dL, and the rest of the electrolytes were within normal limits. High serum phosphorus and low serum calcium, along with its characteristic Chvostek's sign, Trousseau's sign, and Qt prolongation on ECG, pointed towards hypoparathyroidism. Further testing showed elevated serum PTH level at 152.6 pg/mL, normal serum Vitamin D level, and high normal serum magnesium level, thus confirming the diagnosis of pseudohypoparathyroidism.

Depending on the history, clinical manifestations, and initial blood investigation, an initial diagnosis of PHP was made. Urinary c-AMP level and genetic testing were not available to further classify the subtype of PHP. For further investigation, non-contrast computed tomography (CT) of the brain was done, which showed multiple supra and infratentorial calcifications, primarily concentrated in the bilateral basal ganglia region and thalami; also, a USG head and neck was performed, but no significant findings were observed. Due to clinical and serological evidence supporting pseudohypoparathyroidism and a CT indicating the possibility of Fahr syndrome, magnetic resonance imaging (MRI) of the brain was conducted, revealing abnormal T1/FLAIR hyperintensity and T2 isointensity without any diffusion restriction in the bilateral caudate, putamen, globus pallidus, and thalami. The imaging findings confirmed the diagnosis of Fahr syndrome in the setting of pseudohypoparathyroidism. During hospitalization, the patient received treatment with oral calcitriol (0.5 ug every 12 hours) and calcium carbonate (600 mg every 8 hours) until stable levels of calcium and phosphorus were attained. The patient was discharged on oral calcium, cholecalciferol supplements, and phenytoin. Emphasis was placed on strict medication adherence for both the patient and relatives. Follow-up after two weeks indicated normal serum calcium (8.4 mg/dL) and serum phosphorus (4.5 mg/dL), with no recurrence of seizures.

Discussion

This case provides important insight into the rare overlap between pseudohypoparathyroidism (PHP) and Fahr syndrome, presenting uniquely with adult-onset neurological symptoms despite PHP typically manifesting in childhood. Although adult-onset neurological manifestations of PHP are uncommon, this case broadens the clinical understanding of these disorders and highlights the significance of early diagnosis, timely intervention, and multidisciplinary care to prevent long-term complications. Pseudohypoparathyroidism (PHP) encompasses a spectrum of disorders, each with distinct genetic and clinical features. Pseudohypoparathyroidism (PHP) is a rare disorder marked by end-organ resistance to parathyroid hormone (PTH), often linked to GNAS mutations [5]. The typical laboratory results show hypocalcemia, hyperphosphatemia, and elevated serum PTH levels, despite normal serum magnesium and vitamin D levels [6]. Due to its varied presentations, PHP is further categorized into types 1a, 1b, 1c, type 2, and pseudo pseudohypoparathyroidism (PPHP). " [7] [Figure 1]. Type 1 shows impaired cAMP production, indicating an early signaling defect, while Type 2 has a normal cAMP response, suggesting a downstream pathway defect [8]. PHP1a and PHP1c are associated with Albright Hereditary Osteodystrophy (AHO), characterized by brachydactyly, short stature, obesity, and subcutaneous ossifications, while PHP1c presents with isolated PTH resistance without AHO features [5, 9]. PPHP shares AHO traits but lacks hormone resistance, stemming from paternal GNAS mutations [7]. These subtypes often involve associated endocrinopathies such as hypothyroidism, growth hormone deficiency, and hypogonadism [9].

Types	Hormone resistance	AHO	Response to PTH
PHPIa	PTH, TSH, GnRH, GHRH	Present	Blunted cAMP and urine PO_4^{3-} excretion
PHPIb	PTH (±TSH)	Absent	Blunted cAMP and urine PO_4^{3-} excretion
PHPIc	PTH, TSH, GnRH	Present	Blunted cAMP and urine PO_4^{3-} excretion
PPHP	None	Present	Normal response
PHPII	None	Absent	Normal cAMP response, blunted urine PO_4^{3-} excretion

AHO, Albright's hereditary osteodystrophy; GnRH, gonadotropin-releasing hormone; GHRH, growth hormone-releasing hormone; PHPII, pseudohypoparathyroidism type II; PHPIa, PHP type Ia; PHPIb, PHP type Ib; PHPIc, PHP type Ic; PPHP, pseudoPHP; PTH, parathyroid hormone; TSH, thyrotrophin-secreting hormone.

Figure 1: Categorization of Pseudohypoparathyroidism

PHP involves disruption of Gsα/cAMP/PKA signaling, affecting multiple hormone pathways regulated by Gsα-coupled receptors [1]. Diagnosis relies on biochemical tests and GNAS genetic testing to confirm the subtype [10]. Treatment includes vitamin D analogs and calcium supplements, with specialized care for AHO features and endocrinopathies. Genetic counseling and long-term follow-up are essential to improving outcomes and quality of life [1-11]. Fahr disease is characterized by abnormal idiopathic brain calcifications, particularly in the basal ganglia, dentate nuclei, and other areas [12-14]. It can occur as a primary genetic disorder [12-16] or as a secondary condition frequently linked to calcium-phosphorus metabolism disorders like pseudohypoparathyroidism, infections, or toxic exposures [3-18]. The exact pathophysiology behind the mineral deposition is unknown [17, 19]. Presentation is often asymptomatic but can present with movement disorders, psychiatric symptoms, and other CNS symptoms, for example, seizures, headaches, etc. This wide range of presentations further complicates diagnosis and management [12, 19]. A non-contrast CT scan is the primary diagnostic tool, with MRI offering additional detailed insights. [13-19].

The treatment strategy implemented in this case aligns with current clinical guidelines. The patient was initially treated with intravenous calcium carbonate to address acute hypocalcemia, followed by oral calcium and cholecalciferol supplementation to stabilize calcium levels and prevent future episodes [6-13]. Long-term monitoring of calcium and phosphate levels is critical to prevent complications like nephrocalcinosis. Seizures were managed with antiepileptics [12-19]. The patient's movement disorders and muscle rigidity were addressed through supportive care. Neuropsychiatric symptoms, if present, are managed by antidepressants, antipsychotics, or procognitive drugs [12-19]. This reflects the multidisciplinary approach needed to manage Fahr syndrome's neurological manifestations.

Conclusion

This case highlights the rare overlap between pseudohypoparathyroidism (PHP) and Fahr syndrome, emphasizing the importance of recognizing metabolic causes behind complex neurological symptoms. While PHP usually presents in childhood, adult-onset cases pose challenges in diagnosis and management. Timely correction of calcium-phosphate imbalances, including electrolyte-induced seizures unresponsive to antiepileptic drugs, is essential to prevent complications such as brain calcifications, movement disorders, and Fahr syndrome. Managing these conditions requires a multidisciplinary approach involving neurology, endocrinology, and genetics. Further research should focus on understanding the pathophysiology of brain calcifications, exploring adult-onset PHP for earlier diagnosis, and developing evidence-based protocols for better long-term care.

Reference

1. Linglart, A., Levine, M. A., & Jüppner, H. (2018). Pseudohypoparathyroidism. Endocrinology and Metabolism Clinics of North America, 47(4), 865–888.
2. Swami, A., & Kar, G. (2011). Intracranial hemorrhage revealing pseudohypoparathyroidism as a cause of Fahr Syndrome. Case Reports in Neurological Medicine, 28, 407567.
3. Debbabi, W., Khelifi, D., Kharrat, I., & Samet, S. (2022). Fahr Syndrome discovered in adulthood revealing a rare GNAS mutation in pseudohypoparathyroidism type 1a in a Tunisian family. Clinical Case Reports, 10(5), e05849.
4. Donzuso, G., Mostile, G., Nicoletti, A., & Zappia, M. (2019). Basal ganglia calcifications (Fahr's Syndrome): Related conditions and clinical features. Neurological Sciences, 40(11), 2251–2263.
5. Wan, Y., Zuo, Y., Zhang, N., Wang, K., Zhang, R., & Chen, Z. (2023). GNAS locus: Bone-related diseases and mouse models. Frontiers in Endocrinology, 14, 1255864.
6. Mantovani, G., Bastepe, M., Monk, D., de Sanctis, L., Thiele, S., & Usardi, A., et al. (2018). Diagnosis and management of pseudohypoparathyroidism and related disorders: First international consensus statement. Nature Reviews Endocrinology, 14(8), 476–500.
7. Imam, A. A. (2023). Pseudohypoparathyroidism versus signaling disorder: A case report. SAGE Open Medical Case Reports, 11, 2050313X231205776.
8. Silva, J. D. R., Rocha, G. F. M. A., & Oliveira, M. J. M. (2021). An intricate case of sporadic pseudohypoparathyroidism type 1B with a review of literature. Archives of Endocrinology and Metabolism, 65(1), 112–116.
9. Mantovani, G., Bastepe, M., Monk, D., de Sanctis, L., Thiele, S., & Ahmed, S. F., et al. (2021). Recommendations for diagnosis and treatment of pseudohypoparathyroidism. Hormone Research in Paediatrics, 93(3), 182–196.
10. Huang, S. (2022). Clinical and genetic analysis of pseudohypoparathyroidism. BMC Endocrine Disorders, 22(1), 98.
11. Germain-Lee, E. L. (2019). Management of pseudohypoparathyroidism. Current Opinion in Pediatrics, 31(4), 537–549.
12. Amisha, F., & Munakomi, S. (2023). Fahr Syndrome. In StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–.
13. Berrabeh, S., Messaoudi, N., Elmehraoui, O., Assarrar, I., Karabila, I., & Jamal, A., et al. (2023). Hypoparathyroidism and Fahr's Syndrome: A case series. Cureus, 15(6), e40502.
14. Mohammedin, A. S., Alkharashi, A. F., Alabdulqader, A. A., Abualola, H. A., & Serih, M. A. (2021). Fahr's Syndrome presenting with hypocalcemia and psychotic features. Cureus, 13(9), e18091.
15. Pahadiya, H. R., Mathur, A., Khan, M. A., Seth, A., & Mathur, A. (2023). Intracranial calcinosis: Fahr's Syndrome. Indian Journal of Endocrinology and Metabolism, 27(2), 187–188.
16. Brunetti, V., Ferilli, M. A. N., & Luigetti, M. (2019). Fahr's Syndrome in a sporadic case. Neurology India, 67(6), 1573–1574.
17. Sallì, M., D'Arienzo, A., Bonanno, M., Morello, S., Sanfilippo, A., & Mauro, G. L., et al. (2016). Femoral neck fracture in Fahr's Syndrome: A case report. Clinical Cases in Mineral and Bone Metabolism, 13(3), 265–267.
18. Qassimi, F., Boujraf, S., Lamgari, G., Boukniter, A., Bout, A., & Aarab, C., et al. (2023). Catatonia revealing a Fahr Syndrome. Journal of Neurosciences in Rural Practice, 14(2), 386–388.
19. Jaworski, K., Styczyńska, M., Mandecka, M., Walecki, J., & Kosior, D. A. (2017). Fahr Syndrome - an important piece of a puzzle in the differential diagnosis of many diseases. Polish Journal of Radiology, 82, 490–493.