Radiology Case Reports 20 (2025) 1252–1256

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Navigating diagnostic uncertainty in fahr's disease: a case report with neuroimaging correlations ☆,☆☆

Devyansh Nimodia, MBBS[a,*], *Pratapsingh Hanuman Parihar, MD Radiodiagnosis*[a], *Sakshi Dudhe, MBBS*[a], *Ravishankar Patil, MD Radiodiagnosis*[a], *Paritosh N. Bhangale, MBBS*[a], *Rishitha Kotla, MBBS*[b]

[a] *Department of Radiodiagnosis, Datta Meghe Institute of Medical Sciences, Sawangi, Wardha, Maharashtra, India 442001*

[b] *Department of Psychiatry, Datta Meghe Institute of Medical Sciences, Sawangi, Wardha, Maharashtra, India 442001*

ARTICLE INFO

Article history:
Received 17 October 2024
Revised 2 November 2024
Accepted 7 November 2024

Keywords:
Basal ganglia
Calcifications
Fahrs disease
Neuroimaging
Seizures

ABSTRACT

Fahr's disease is a rare neurological disorder which is characterized by the presence of abnormal, symmetrical, and bilateral calcifications within the basal ganglia and other cerebral areas. Seizures are 1 of the symptoms that may aid in its diagnosis. Fahr's disease is diagnosed in adults mostly. In this account, we describe the case of a male in his late 20s who was diagnosed with Fahr's disease. The patient experienced multiple seizures and severe headaches for the past 5 months. His medical history was not significant. Upon his admission to the emergency department, imaging studies (Computed Tomography and Magnetic Resonance Imaging) revealed the presence of bilateral and symmetrical calcifications situated within the bilateral corona radiata, bilateral centrum semiovale, bilateral gangliocapsular region, bilateral thalamus and bilateral dentate nucleus. Laboratory investigations ruled out alternative causes for secondary intracranial calcification. Moreover, the patient had no significant familial history. Considering the clinical, biological, and radiological evaluations, the diagnosis was concluded to align with a sporadic form of Fahr's disease.

Although seizures are less common symptoms associated with Fahr's disease, the identification of bilateral and symmetrical calcifications in the basal ganglia and other regions on radiological imaging in a patient presenting with seizures should warrant consideration of this neurologic disorder, following the exclusion of other potential causes of intracranial calcification.

☆ Competing Interests: The authors declare no competing interest.

☆☆ Acknowledgments: No funding was obtained for this study.

* Corresponding author.
E-mail address: drdevyansh24@gmail.com (D. Nimodia).

https://doi.org/10.1016/j.radcr.2024.11.016

Introduction

Fahr's disease is an uncommon neurological condition which may be either hereditary or occur sporadically. It is characterized by a prevalence rate of less than 1 in 1,000,000. This disorder is predominantly observed in males, with the typical onset manifesting between the third and fifth decades of life [1]. A registry indicates that 67% of individuals diagnosed with Fahr's disease present clinical symptoms, with a higher frequency of occurrence in males compared to females [1].

Calcifications are most frequently identified in the globus pallidus within the basal ganglia; however, they may also be observed in the putamen, caudate nucleus, internal capsule, thalamus, dentate nucleus of the cerebellum, and periventricular white matter [2]. The initial description of this disorder was provided by Karl Theodor Fahr in 1930 [3], and both sporadic and familial instances have been documented [2]. Neurological manifestations encompass headache, vertigo, syncope, movement disorders, seizures, paresis, spasticity, speech impairments, parkinsonism, chorea, and orthostatic hypotension [4]. Notably, a subset of individuals may remain entirely asymptomatic [5]. Seizures represent 1 of the less prevalent clinical presentations of Fahr's disease [6]. Fahr's disease is generally of autosomal dominant or recessive inheritance, but the disease-causing gene is not known [7]. Calcification increases with the progression of Fahr's disease with age [1]. Currently, Fahr's disease is mainly treated with symptomatic treatment [8]. No cure or a standard course of treatment is available for the treatment of Fahr's disease and the prognosis of the disease is hard to predict [9].

It is crucial to differentiate Fahr's disease from Fahr's syndrome, which is characterized by symmetrical, bilateral calcifications in the basal ganglia, often accompanied by neuropsychiatric manifestations, frequently observed in individuals with parathyroid dysfunctions, notably hypoparathyroidism [10]. We report a clinical case of a patient exhibiting a 5-month history of seizures and cephalalgia, wherein cranial computed tomography disclosed extensive and diffuse calcifications in atypical anatomical regions.

Case presentation

We present a clinical case involving a male patient in his late twenties, employed as a laborer, who demonstrated a 5-month history characterized by the manifestation of seizures and headache. In addition, he reported experiencing episodic cervical discomfort and unusual movements in both upper limbs over the preceding 4 months, along with persistent headaches and dizziness for the past 3 months, all occurring without identifiable precipitating factors such as trauma or substance use.

During the clinical interview, the patient denied any familial history of similar conditions or prior pharmacological treatments. Upon thorough clinical evaluation, the patient appeared to be in satisfactory overall health, with vital signs indicating stability: heart rate recorded at 90 beats per minute, blood pressure measured at 146/70 mmHg, body temperature at a normal 37°C and respiratory rate at 16 bpm (breaths per minute). Furthermore, his blood glucose level was within normal parameters (1.09 g/l), and no additional anomalies were detected, including those observed during the neurological evaluation.

Laboratory investigations encompassing iron, blood glucose, ferritin, parathormone and calcium levels yielded normal results. An electroencephalogram (EEG) revealed no irregularities. The patient was subsequently advised to undergo a noncontrast brain computed tomography (CT) scan for further evaluation.

Axial noncontrast CT imaging of the brain demonstrated extensive, bilateral, symmetrical, irregular, amorphous calcifications located within the bilateral corona radiata (Fig. 1A), bilateral centrum semiovale (Fig. 1B), bilateral gangliocapsular region (Fig. 1C), bilateral thalamus (Fig. 1C), and bilateral dentate nucleus (Fig. 1.D). A distinctive "sun ray" calcification pattern was observed surrounding the bilateral dentate nuclei (Fig. 1D).

Figure 2: Brain magnetic resonance imaging axial sections of brain reveals altered signal alterations as blooming on susceptibility weighted imaging and hyperintensity on T1WI, consistent with calcifications in the same regions as identified in the computed tomography scan, particularly within the bilateral corona radiata (Figs. 2A and D), bilateral gangliocapsular region (Figs. 2B and E), bilateral thalamus (Figs. 2B and E), and bilateral dentate nucleus (Figs. 2C and F).

In light of these findings, a diagnosis of Fahr's disease (FD) was established. Notably, the brain parenchyma appeared devoid of any focal pathological alterations. Considering the clinical and radiological findings, along with the absence of any disorders affecting calcium-phosphorus metabolism or other plausible etiologies, a provisional diagnosis of idiopathic

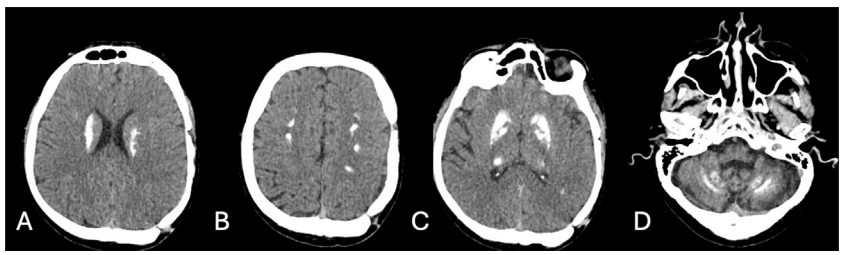

Fig. 1 – Axial noncontrast computed tomography imaging of the brain demonstrated extensive, bilateral, symmetrical, irregular, amorphous calcifications located within the bilateral corona radiata (A), bilateral centrum semiovale (B), bilateral gangliocapsular region (C), bilateral thalamus (C), and bilateral dentate nucleus (D).

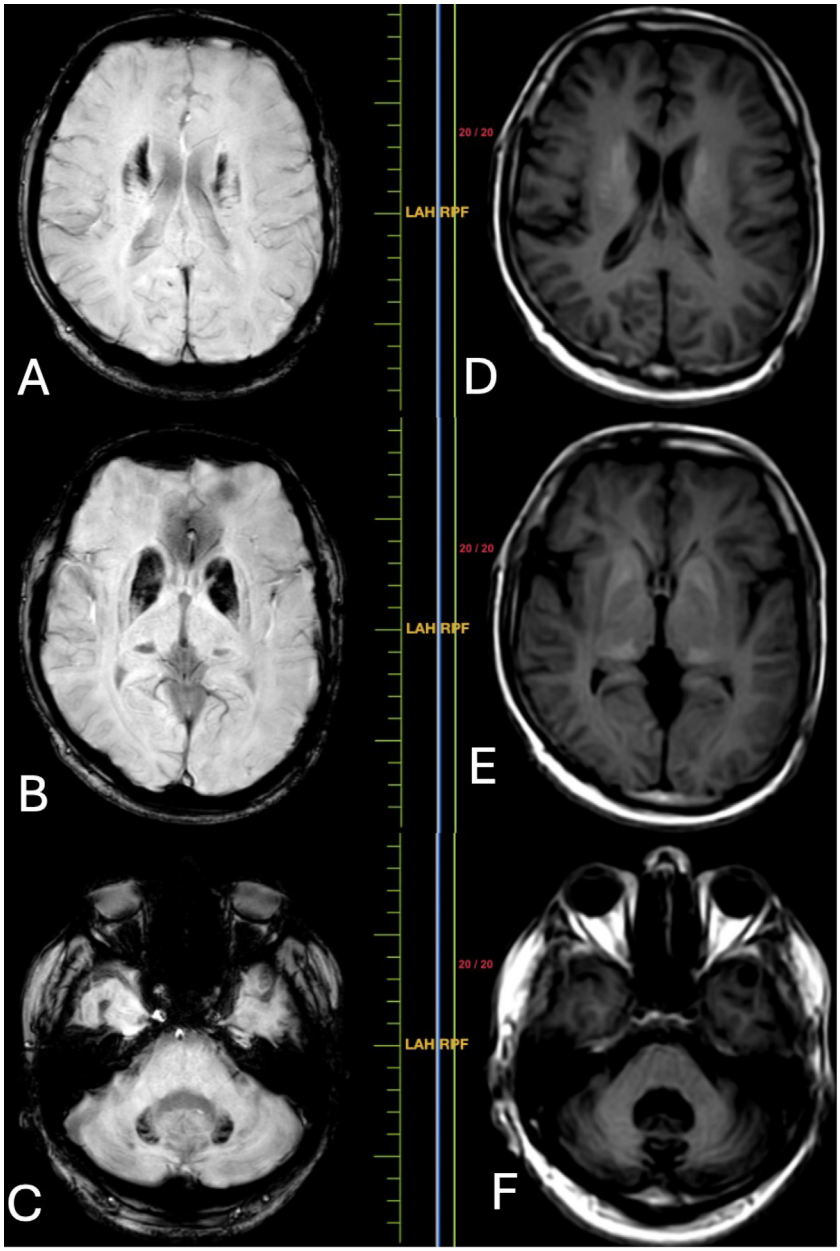

Fig. 2 – Brain magnetic resonance imaging axial sections of brain reveals altered signal alterations as blooming on susceptibility weighted imaging and hyperintensity on T1WI, consistent with calcifications in the same regions as identified in the computed tomography scan, particularly within the bilateral corona radiata (A and D), bilateral gangliocapsular region (B and E), bilateral thalamus (B and E), and bilateral dentate nucleus (C and F).

striopallidodentate calcinosis, commonly referred to as Fahr's disease, was strongly indicated.

Currently, there exists no definitive therapeutic regimen for Fahr's disease, and management typically focuses on symptomatic relief. Our patient had a history of seizures since 5 years and was not under any pharmacological intervention. The patient was administered anticonvulsant tablet Leviteracetam 500 mg BD which successfully mitigated the patient's seizure activity. The patient was advised follow up after 2 months. The patient had no recurrence of epilepsy noted post-treatment.

Discussion

Fahr's disease is distinguished by its clinical heterogeneity, with certain patients remaining asymptomatic, particularly during middle adulthood, whereas others manifest neuropsychiatric disturbances [10]. This condition is generally transmitted via autosomal dominant or recessive inheritance patterns, although the precise genetic locus implicated has yet to be elucidated [7]. The diagnostic process is predicated upon clinical manifestations, neuroimaging results, and the

exclusion of alternative primary etiologies. Fahr's disease may present sporadically or occur within familial clusters [2].

The clinical manifestations associated with Fahr's disease exhibit considerable variability, with numerous patients remaining devoid of symptoms for extended durations. The onset of symptoms typically transpires in the fourth or fifth decade of life, frequently initiating with cognitive deterioration, psychiatric manifestations, or movement disorders. Seizures, albeit infrequent, are recognized as potential symptoms of Fahr's disease, possibly attributable to dysfunction within cortico-basal connections and inter-hemispheric interactions [11].

Tedrus et al. [12] documented an incidence rate of 0.68% among 3,662 cranial CT examinations, revealing that the disease induces bilateral, asymmetric cerebral calcifications predominantly located in the basal ganglia and cerebellum.

The predominant radiological hallmark of Fahr's disease is the identification of diminutive, bilateral calcifications, typically confined to the Globus pallidus, while also involving the putamen, caudate nucleus, thalamus, dentate nucleus, and cerebral white matter [4].

Lester et al. recorded an atypical case of Fahr's disease characterized by stroke-like manifestations evolving into extrapyramidal syndrome [13]. Ongun et al. [11] reported 2 instances of Fahr's syndrome presenting with seizures, both associated with secondary etiologies.

Kobayashi et al., [14] employing electron microscopy, posited that the pathophysiology of Fahr's disease may encompass initial pericyte injury, resulting in the accumulation of mucopolysaccharides within the cells, succeeded by mineral deposit formation. Hagiwara et al. [15] suggested that anomalies in intracranial oxygen metabolism could be contributory, as elevated cerebrospinal fluid lactate concentrations were observed in a representative case of the ailment.

Fahr's disease is believed to be associated with chromosome 14q [16], predominantly inherited in an autosomal dominant fashion [17], although its exact etiology and progression remain poorly understood. The majority of individuals afflicted with Fahr's disease are adults [18] and typically demonstrate extrapyramidal manifestations [19].

It is crucial to differentiate between Fahr's disease and Fahr syndrome, with the latter arising from secondary etiological factors such as hypoparathyroidism, hyperparathyroidism, cysticercosis, toxoplasmosis, and HIV infection [20]. The prognosis for Fahr's disease remains ambiguous, and symptoms may exacerbate as calcification advances with aging. Computed tomography (CT) scans are frequently employed to diagnose Fahr's disease [19], as they effectively identify bilateral, symmetrical intracranial calcifications, particularly in areas such as the bilateral centrum semiovale, corona radiata, gangliocapsular region, thalamus, and dentate nucleus. Incidental detection of intracranial calcifications occurs in up to 0.3%-1.2% of CT brain scans [21].

In addition to the typical calcified regions observed in Fahr's disease, certain intracranial structures, including the pineal gland, choroid plexus, and dura mater, petroclenoid, interclenoid ligaments, pituitary gland and carotid arteries may also undergo calcification as part of the natural aging process [22]. A variety of pathological conditions, encompassing infections, trauma, metabolic disturbances, and congenital anomalies, can lead to the development of brain calcifications [21].

If symmetrical calcifications are identified within the basal ganglia, cerebellum, thalamus, and subcortical white matter, and other potential pathologies have been excluded, Fahr's disease warrants consideration. Confirmatory diagnosis necessitates thorough family history evaluation and longitudinal follow-up [6].

In this particular instance, the patient's demographic information, symptomatic presentation, and significant calcification observed in computed tomography scans substantiate the diagnosis of Fahr's disease.

Despite the absence of analogous cases within the familial lineage, it is plausible that asymptomatic variants may be present. The laboratory evaluations of the patient revealed normal calcium and phosphate concentrations, thereby excluding the likelihood of parathyroid dysfunction.

The patient has experienced a history of seizures over the preceding 5 years and has been undergoing pharmacological intervention, with recent alterations in behavior noted by family members. The observed behavioral modifications, depressive symptomatology, age of the patient, and computed tomography findings-coupled with the lack of a positive familial history-indicate a sporadic manifestation of Fahr's disease. Currently, there exists no definitive therapeutic regimen for Fahr's disease, and management typically focuses on symptomatic relief [23]. Although a variety of clinical trials have been undertaken, substantial advancements have yet to be realized. In this scenario, the administration of anticonvulsants successfully mitigated the patient's seizure activity, with no recurrence of epilepsy noted post-treatment.

Conclusions

In conclusion, Fahr's disease represents a rare neurodegenerative disorder that remains inadequately elucidated. The diagnostic process is contingent upon a synthesis of clinical, biological, and radiological data; however, regrettably, no targeted intervention is available to impede its progression. Nevertheless, symptomatic management may prove beneficial in alleviating specific symptoms during the initial phases of the disease. This case merits documentation due to the infrequency and clinical heterogeneity associated with the condition, which frequently results in diagnostic delays. Seizures, particularly generalized seizures, constitute some of the rarest manifestations of Fahr's disease, as exemplified by the patient in this report. Upon encountering convulsive seizures accompanied by bilateral and symmetrical calcifications of the basal ganglia, and in the absence of a more conclusive diagnosis, Fahr's disease should invariably be contemplated.

Ethics approval and consent to participate

Written consent taken.

Consent for publication

Written consent taken.

Availability of data and material

N/A.

Authors' contributions

DN and PHP was involved in providing clinical details of the patient. RP discussion on the pathology. SD accumulated the results of the patient's radiological investigations. PNB and RK was involved in collecting images and formatting data. All authors have read and approved the manuscript.

Patient consent

Informed and written consent was obtained from the patient.

REFERENCES

[1] Manyam BV, Walters AS, Narla KR. Bilateral striopallido dentate calcinosis: clinical characteristics of patients seen in a registry. Mov Disord 2001;16:258–64. doi:10.1002/mds.1049.

[2] Chevalier D, Marie I, Tillon J, Lévesque H. A cause of cerebral calcifications not to be ignored: Fahr syndrome. Rev Med Interne 2005;26:668–77. doi:10.1016/j.revmed.2005.03.013.

[3] Fahr TH. Idiopathische verkalkung der hirngefasse. Zentralbl Allg Pathol 1930;50:129–33.

[4] Manyam BV. What is and what is not 'Fahr's disease. Parkinsonism Relat Disord 2005;11:73–80. doi:10.1016/j.parkreldis.2004.12.001.

[5] Modrego PJ, Mojonero J, Serrano M, Fayed N. Fahr's syndrome presenting with pure and progressive presenile dementia. Neurol Sci 2005;26:367–9. doi:10.1007/s10072-005-0493-7.

[6] Ayoub B, Chakib C, Khalil M, Hicham B. Fahr´s disease presenting with epileptic seizures: a case report. PAMJ Clin Med 2020;15:3. doi:10.11604/pamj-cm.2020.3.55.23810.

[7] Oliveira JR, Spiteri E, Sobrido MJ, et al. Genetic heterogeneity in familial idiopathic basal ganglia calcification (Fahr disease). Neurology 2004;63:2165–7. doi:10.1212/01.wnl.0000145601.88274.88.

[8] Saleem S, Aslam HM, Anwar M, et al. Fahr's syndrome: Literature review of current evidence. Orphanet J Rare Dis 2013;8:1562013. doi:10.1186/1750-1172-8-156.

[9] Abubakar SA, Saidu S. Idiopathic bilateral strio-pallido-dentate calcinosis (Fahr's disease): a case report and review of the literature. Ann Afr Med 2012;11:234–7. doi:10.4103/1596-3519.102855.

[10] Cavalcanti-Mendes Gde A, Carvalho GT, Christo PP, Malloy-Diniz LF, Sousa AA. An unusual case of Fahr's disease. Arquivos de Neuro-psiquiatria 2009;67:516–18. doi:10.1590/s0004-282x2009000300029.

[11] Ongun N, Degirmenci E, Erdogan C. Fahrś syndrome presenting with epileptic seizure: Two case reports. North Clin Istanb 2016;3:71–4. doi:10.14744/nci.2015.47966.

[12] Tedrus GMAS, Fonseca LC, Nogueira EJ. Basal ganglia calcification on computed tomography: clinical characteristics in 25 patients. Arq Neuropsiquiatr 2006;64:645–9. doi:10.1590/s0004-282x2006000100021.

[13] Lester J, Zúñiga C, Díaz S, Rugilo C, Micheli F. Diffuse intracranial calcinosis: Fahr disease. Arch Neurol 2006;63:1806–7. doi:10.1001/archneur.63.12.1806.

[14] Kobayashi S, Yamadori I, Ohmori M. Idiopathic nonatherosclerotic cerebral calcification (Fahr' disease): an electron microscopic study. Acta Neuropathol 1987;73:62–6. doi:10.1007/BF00695503.

[15] Hagiwara N, Ooboshi H, Ishibashi M, et al. Elevated cerebrospinal fluid lactate levels and the pathomechanism of calcification in Fahr' disease. Eur J Neurol 2006;13:539–43. doi:10.1111/j.1468-1331.2006.01345.x.

[16] Kawaguchi Y, Okamoto T, Taniwaki M, et al. CAG expansions in a novel gene for Machado-Joseph disease at chromosome 14q32.1. Nat Genet 1994;8:221–8. doi:10.1038/ng1194-221.

[17] Moskowitz MA, Winickoff RN, Heinz ER. Familial calcification of the basal ganglions: a metabolic and genetic study. N Engl J Med 1971;285:72–7. doi:10.1056/NEJM197107082850202.

[18] Cummings JL, Gosenfeld LF, Houlihan JP, McCaffrey T. Neuropsychiatric disturbances associated with idiopathic calcification of the basal ganglia. Biol Psychiatry 1983;18:591–601.

[19] Avrahami E, Cohn DF, Feibel M, Tadmor R. MRI demonstration and CT correlation of the brain in patients with idiopathic intracerebral calcification. J Neurol 1994;241:381–4. doi:10.1007/BF02033355.

[20] Harrington MG, Macpherson P, McIntosh WB, Allam BF, Bone I. The significance of the incidental finding of basal ganglia calcification on computed tomography. J Neurol Neurosurg Psychiatry 1981;44:1168–70. doi:10.1136/jnnp.44.12.1168.

[21] Fenelon G, Gray F, Paillard F, Thibierge M, Mahieux F. A prospective study of patients with CT detected pallidal calcifications. J Neurol Neurosurg Psychiatry 1993;56:622–5. doi:10.1136/jnnp.56.6.622.

[22] Gligorievski A. CT diagnosis of Fahr disease, a case report. Clin Case Rep Rev 2018;26:1–3.

[23] Loeb JA, Sohrab SA, Huq M, Fuerst DR. Brain calcifications induce neurological dysfunction that can be reversed by a bone drug. J Neurol Sci 2006;243:77–81. doi:10.1016/j.jns.2005.11.033.