

 Abdulhamit Bora,  Irem Yildirim

Kütahya Health Sciences University, Faculty of Medicine,
Department of Neurology, Kütahya, Türkiye

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Corresponding Author: Irem Yildirim, Kütahya Health Sciences University, Faculty of Medicine, Department of Neurology, Kütahya, Türkiye
Email: iremkaftan@gmail.com

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INTRODUCTION

Fahr's disease is named after the German neurologist Karl Theodor Fahr, who first described the condition in 1930. Also referred to as idiopathic basal ganglia calcification, it is a rare neurodegenerative disorder with an autosomal dominant inheritance pattern. The estimated prevalence is approximately 4.5 cases per 10,000 individuals (1,2).

This condition is also known by other names, including bilateral striopallidodentate calcinosis. It is characterized by abnormal calcium deposits in brain regions involved in movement regulation, such as the basal ganglia, thalamus, dentate nucleus, cerebral cortex, cerebellum, subcortical white matter, and hippocampus (3,4).

It is important to distinguish between Fahr's disease and Fahr's syndrome. Fahr's disease is primarily

An atypical presentation of Fahr's disease

Abstract

Fahr's disease, first described by Karl Theodor Fahr in 1930, is a rare neurodegenerative disorder characterized by bilateral calcification of the basal ganglia and cerebral cortex. Although the average age of onset is between 40 and 50 years, symptoms can occur at any age. A 65-year-old woman presented with gait instability, frequent balance disturbances, and persistent cold feet over the past six months. Neurological examination revealed that she was alert, oriented, and had no significant motor or sensory deficits. No extrapyramidal signs were noted, and her gait was within normal limits. Cranial CT showed multiple calcifications in the bilateral basal ganglia, thalamus, caudate nucleus, and cerebellum. All hematologic, renal, hepatic, and thyroid function tests were within normal limits. This case highlights the asymptomatic nature of Fahr's disease in some individuals and reinforces the importance of long-term follow-up and early intervention if symptoms develop.

Keywords: Fahr disease, asymptomatic, calcification, calcium

idiopathic or genetic, while Fahr's syndrome results from secondary calcifications due to disturbances in calcium metabolism. Common causes of Fahr's syndrome include hypoparathyroidism, pseudohypoparathyroidism, and chronic hypocalcemia, which may be associated with vitamin D deficiency or renal failure (5).

In individuals with Fahr's disease, serum levels of calcium, phosphate, alkaline phosphatase, and parathyroid hormone typically remain within normal ranges. Symptoms most often emerge between the ages of 40 and 50, although they can appear at any age (6).

Fahr's disease is most commonly inherited in an autosomal dominant pattern, but autosomal recessive inheritance and sporadic cases have also been reported. Four key genes have been implicated in the condition: SLC20A2 (40% of cases),

PDGFB (11%), XPR1 (2%), and PDGFRB (2%), while unknown mutations account for approximately 46% of cases (7,8).

Diagnosis is primarily based on the presence of bilateral calcifications in the basal ganglia, progressive neurological deterioration, normal biochemical profiles, and the exclusion of infectious, traumatic, or toxic etiologies. Initial manifestations frequently involve extrapyramidal symptoms, while additional features may include cerebellar dysfunction, speech impairments, cognitive decline, and neuropsychiatric disturbances (9).

This case report presents a patient who exhibited no notable abnormalities upon neurological examination but was incidentally found, through imaging studies, to have lesions characteristic of Fahr disease.

CASE REPORT

A 65-year-old woman presented to the outpatient clinic with complaints of difficulty walking, frequent loss of balance, and cold feet for the past six months. She had a 20-year history of diabetes mellitus (DM), hypertension (HT), and hyperlipidemia (HL), as well as diabetic peripheral neuropathy (PNP) for nine years.

On neurological examination, she was conscious, coherent, and oriented. There were no significant motor deficits or hypoesthesia but reduced vibration sensation was noted in the lower limbs, no extrapyramidal signs or symptoms and cerebellar dysfunction, Romberg test was negative and her gait was within normal limits.

Electromyography (EMG) revealed axonal-type sensorimotor polyneuropathy with prominent sensory involvement in the lower extremities. Based on her medical history and EMG findings, the condition was evaluated as diabetic PNP.

Mini-Mental State Examination (MMSE) scores were as follows: Orientation: 9/10, Immediate Memory: 3/3, Attention and Calculation: 5/5, Recall: 2/3, Language: 6/9. The total score was 25/30, which was not indicative of progressive dementia. During follow-up the patient underwent psychiatric evaluation, which revealed no evidence of psychosis.

Escitalopram 5 mg once daily was initiated for anxiety management. At the six month follow-up neurological examination findings remained unchanged.

Axial cranial computed tomography (CT) scans showed multiple calcified areas in the bilateral basal ganglia, thalamus, caudate nucleus, and cerebellum (Figure 1, Figure 2). Cranial magnetic resonance imaging (MRI) revealed diffuse calcifications with low signal intensity in T2-weighted sequences and high signal intensity in T1-weighted sequences, particularly in the bilateral cerebellar hemispheres at the level of the dentate nuclei (Figure 3, Figure 4).

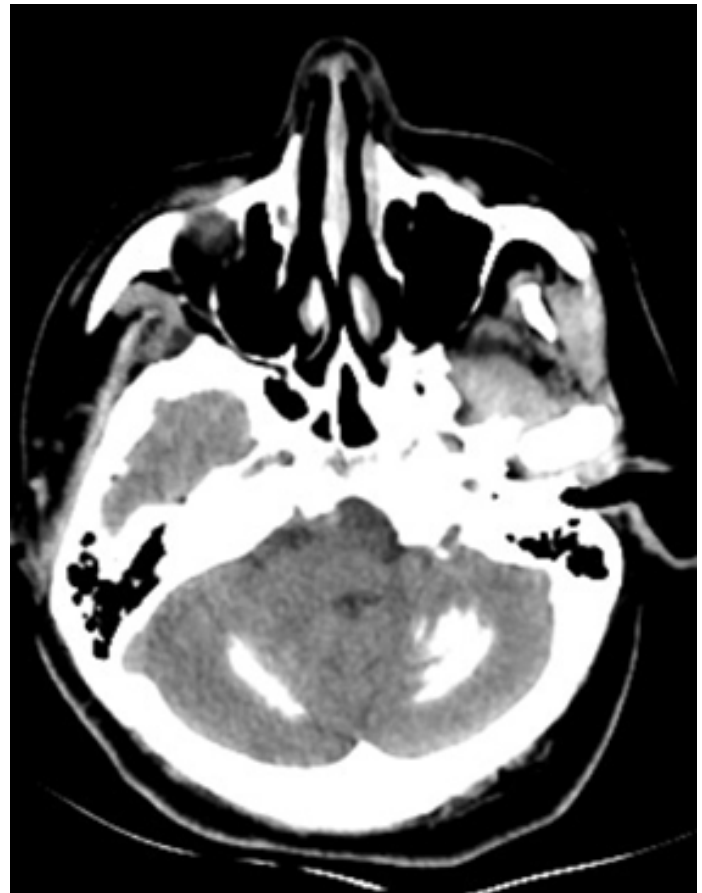


Figure 1. Cranial CT section, cerebellar calcification

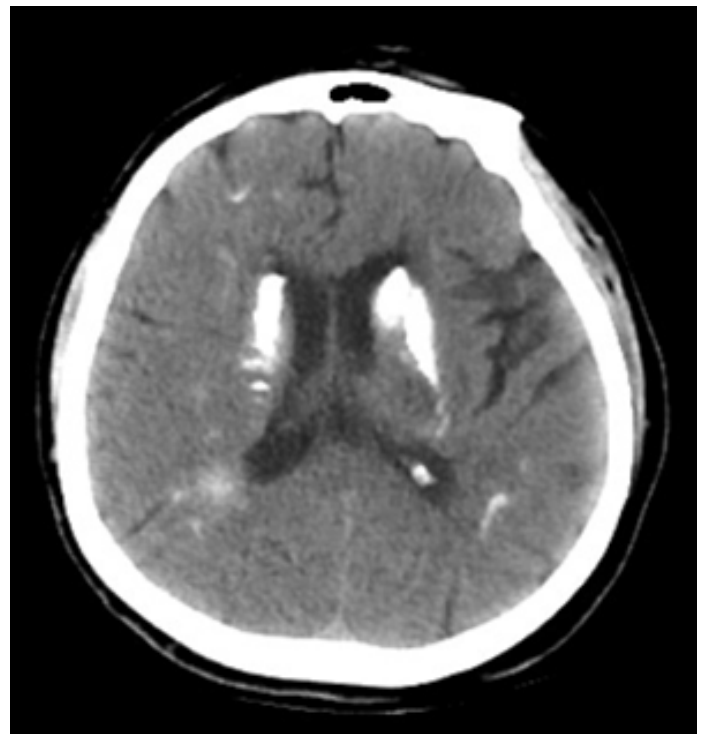


Figure 2. Cranial CT axial section, bilateral lentiform nucleus calcification

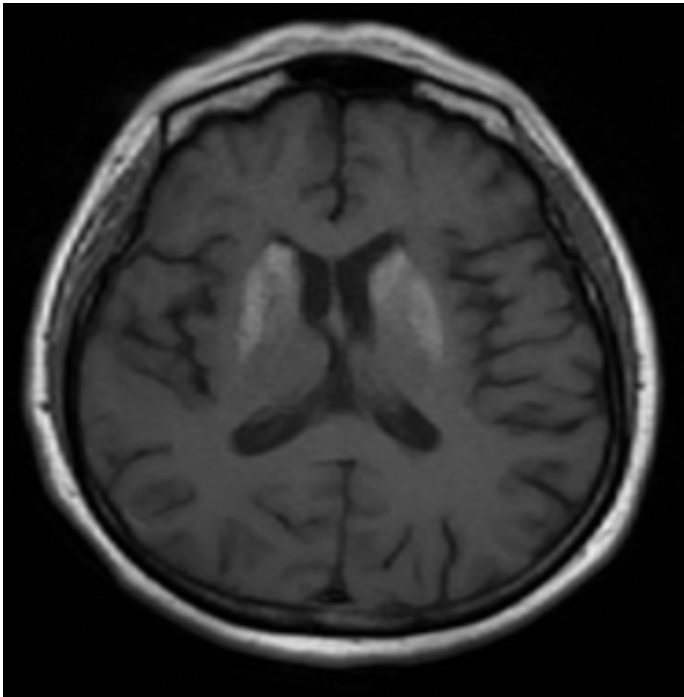


Figure 3. Brain MRI T1 section, bilateral symmetric globus pallidus hyperintensities

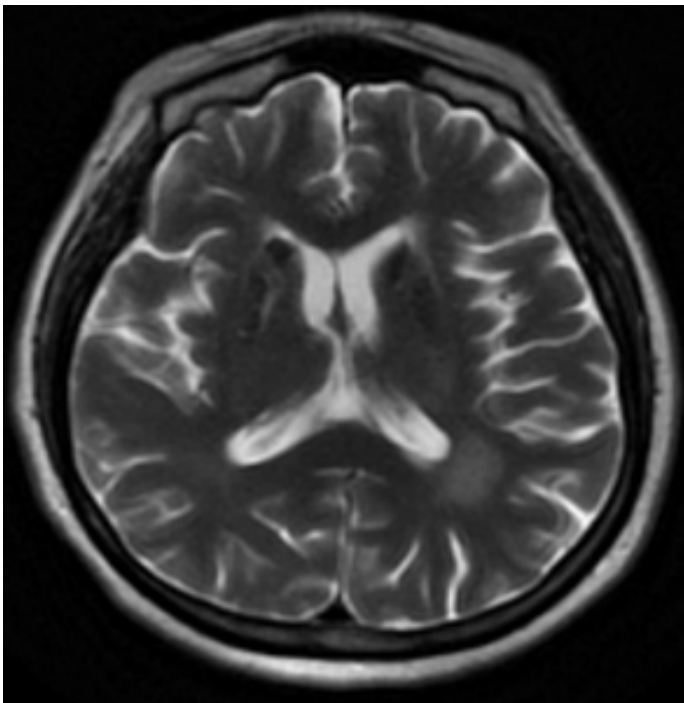


Figure 4. Brain MRI T2 section, bilateral symmetric globus pallidus hypointensities

Laboratory tests were performed to exclude secondary causes of brain calcifications:

- **Serum calcium:** 9.1mg/dL (Normal)
- **Phosphorus:** 3mg/dL (Normal)

- **Parathyroid hormone (PTH):** 26.7pg/mL (Normal)
- **Vitamin D:** 26.76ng/mL (Low-Normal)

Additional laboratory evaluations, including complete blood count, urine analysis, liver and renal function tests, thyroid function tests, parathormone, calcium, phosphorus, vitamin D, and vitamin B12 levels, were all within normal limits.

In this case, although no underlying secondary cause was identified, the diagnosis of Fahr's disease was established based on the characteristic radiologic findings.

DISCUSSION

Fahr's syndrome is a rare neurodegenerative disorder characterized by symmetrical calcifications, primarily in the basal ganglia, cerebellar dentate nucleus, and centrum semiovale. The clinical presentation is variable and may include neurological and psychiatric symptoms such as parkinsonism, dystonia, tremor, chorea, ataxia, dementia, and mood disorders. Asymptomatic cases have also been reported in the literature (10).

Also referred to as primary familial brain calcification, Fahr's disease is defined by bilateral calcifications in specific brain regions, including the basal ganglia, cerebellum, and cerebral cortex. Although it typically presents with a range of neurological and psychiatric manifestations, the present case is notable for the absence of significant clinical symptoms, with the diagnosis made primarily based on neuroimaging findings.

The incidental detection of characteristic calcifications through MRI underscores the importance of recognizing asymptomatic cases. A study by Harati et al. reported that two initially asymptomatic patients later developed symptoms during long-term follow-up, highlighting the need for regular monitoring of asymptomatic individuals (11).

Although asymptomatic presentations of Fahr's disease are relatively uncommon, they have been documented. In one study involving 99 cases, approximately 33% of patients were asymptomatic, while the remainder exhibited various neurological and psychiatric symptoms. This finding emphasizes that, although radiological evidence of calcification is a hallmark of the disease, clinical signs may be absent or delayed (12). In our case, no additional findings were noted apart from the six-month follow up. A review of the patient's previous neurology outpatient visits over the years revealed no signs of dementia or psychiatric condition; complaints and investigations were related to diabetic PNP.

The asymptomatic nature of Fahr's syndrome complicates a comprehensive understanding of its pathophysiology. The presence of calcifications without accompanying clinical symptoms suggests that factors such as the localization and size of calcifications, as well as individual brain reserve, may influence symptom development. Therefore, it is essential to assess the clinical significance of calcifications identified in asymptomatic individuals.

Several hypotheses have been proposed to explain the mechanisms underlying asymptomatic presentations in Fahr's syndrome:

1. Location and Extent of Calcification

The specific sites and severity of calcifications may influence symptom manifestation. Minimal deposits in non-critical brain regions may not disrupt neurological function, allowing individuals to remain symptom-free (5). Our case demonstrated prominent Fahr-related calcifications, yet remained clinically asymptomatic, which underscores the potential for significant radiological burden to exist without corresponding neurological impairment.

2. Individual Neural Flexibility

Variations in neural plasticity and brain reserve across individuals could account for different clinical presentations. Some individuals may adapt more effectively to structural changes, compensating for dysfunction caused by calcifications (13).

3. Genetic Heterogeneity

Mutations in various genes, such as SLC20A2, PDGFB, and PDGFRB, have been associated with Fahr disease. The specific genetic mutation may influence the clinical phenotype, with some mutations linked to a more benign course. In our case genetic testing could not be completed due to financial limitations.

4. Age-Related Penetrance

The age at which calcifications develop or progress may contribute to symptom variability. Younger individuals with early-stage calcifications may remain asymptomatic, while older individuals with more extensive calcifications may develop clinical features. Although our patient was older than the typical age for the Fahr's disease, no clear neurological examination findings were observed, cognitive function remained stable. In this regard, clinical presentation may be considered somewhat atypical compared to the usual disease course.

CONCLUSION

In summary, the existence of asymptomatic cases in Fahr's syndrome illustrates the heterogeneous nature of the disorder and underscores the need for personalized approaches to clinical management. Recognizing and monitoring these cases is essential for early detection of potential symptom development and for guiding appropriate interventions.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Patient Informed Consent

Informed consent was obtained from the patient.

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