Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Fahr's disease presenting with ischemic stroke in young adult: a case report of rare disease with unique presentation

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Introduction and importance: Fahr's disease, or bilateral striopallidodentate calcinosis, is a rare autosomal dominant neurological disorder characterized by bilateral symmetrical calcifications in the basal ganglia, thalamus, hippocampus, dentate nucleus, cerebral cortex, and cerebellar subcortical white matter. Typically presenting with cognitive, psychiatric, and extrapyramidal symptoms in middle age, its presentation as an acute ischemic stroke is exceedingly rare. This case report presents this unusual occurrence.

Case presentation: A 32-year-old female presented with sudden onset weakness in her left lower limb, slurred speech, and facial deviation to the right. Over the next 2 days, the weakness extended to her left upper limb. Neurological examination revealed left-sided lower motor neuron lesion of the facial nerve, upper motor neuron signs, mild left-sided motor weakness, and cerebellar signs. Non-contrast computed tomography (CT) and magnetic resonance imaging (MRI) imaging showed extensive symmetrical calcifications in the basal ganglia, thalamus, dentate nucleus, and other deep gray matter structures, along with acute ischemic changes in the right corona radiata and internal capsule. All metabolic and endocrine evaluations were normal.

Discussion: Fahr's disease is associated with abnormal calcium deposition in the brain. The underlying mechanisms for the calcifications remain unclear but may involve disrupted calcium metabolism and alterations in the blood-brain barrier, contributing to a cycle of vascular injury. The coexistence of acute ischemic stroke in this context is rare and may result from microinfarcts due to calcification in small vessels.

Conclusion: This case illustrates that acute ischemic stroke can occur as a manifestation of Fahr's disease. CT scan plays vital role in establishing diagnosis by revealing the symmetrical calcification pattern in the basal ganglia, thalami, and cerebellar dentate nucleus. Establishing the association between Fahr's disease and cerebrovascular disease warrants further studies.

Keywords: Fahr's disease, Fahr's syndrome, bilateral striopallidodentate calcinosis, acute ischemic stroke, cerebrovascular disease, neuroimaging

Introduction

Fahr's disease, also known as bilateral striopallidodentate calcinosis was first described by a German neurologist, Karl Theodor Fahr in 1930. It is a rare, usually autosomal dominant, inherited neurological disorder characterized by the bilateral symmetrical calcification primarily in basal ganglia, thalamus, hippocampus, dentate nucleus, cerebral cortex, and cerebellar subcortical white matter[1].

In the literature, the terms Fahr's disease and Fahr's syndrome are often used interchangeably. However, it has been suggested that Fahr's disease should specifically refer to primary basal ganglia calcifications with no known cause, while Fahr's syndrome should be used for cases where the calcifications have a known underlying cause particularly those affecting the

HIGHLIGHTS

- Fahr's disease is a rare neurological condition marked by symmetrical calcification primarily in the basal ganglia, thalamus, hippocampus, dentate nucleus, cerebral cortex, and cerebellar subcortical white matter.
- Non-contrast computed tomography scans are crucial for diagnosing Fahr's disease, revealing distinctive calcification patterns.
- Acute ischemic stroke can occur as an uncommon manifestation of Fahr's disease.
- Further research is needed to explore the relationship between Fahr's disease and cerebrovascular events, as well as potential treatment options for affected patients.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2025) 87:2444–2448

Received 3 October 2024; Accepted 22 February 2025

Published online 20 March 2025

http://dx.doi.org/10.1097/MS9.0000000000003151

parathyroid gland and resulting in hypoparathyroidism[2,3]. Patients typically present in their 40s and 50s with progressive cognitive deterioration, psychiatric disturbances, and extrapyramidal symptoms[4]. In this article, we present the rare occurrence of acute ischemic stroke as the initial presentation in a young female with Fahr's disease.

Case presentation

A 32 year-old female presented with weakness in her left lower limb 6 days prior. She also developed slurred speech and facial deviation to the right at the same time. The weakness in left lower limb progressively extended to involve her left upper limb over the period of 2 days. There was no history of abnormal sensations, such as numbness or tingling, and no history of fever, headache, abnormal body movements, or loss of consciousness. There was no history of other cranial nerve involvement. There was no history of recent trauma or prior similar neurological symptoms. She had no history of comorbidities, recent infections, vaccinations, or travel.

On examination, the patient was alert and oriented to time, place, and person. The Glasgow Coma Scale was E4V5M6. Cranial nerve examination revealed facial asymmetry, with deviation of the mouth to the right and weakness of the left facial muscles, consistent with a lower motor neuron lesion. The remaining cranial nerves were intact. Motor examination showed slightly decreased muscle strength (Grade 4/5) in the left upper and lower limbs, with no evidence of muscle atrophy or fasciculations. The right upper and lower limbs had normal muscle strength (Grade 5/5). Muscle tone was normal in the bilateral upper and lower limbs. Deep tendon reflexes were 2+ on both sides. Babinski's sign was present on the left, indicating an upper motor neuron lesion, and negative on the right. Pronator drift was positive on the left side. Sensory examination was normal. On the heel-shin test the patient could not trace the shin in a straight line and moved the heel from side to side. Patient was unable to walk in tandem. Romberg's test was negative. There were no meningeal signs such as neck stiffness or photophobia.

A complete blood count, renal function test, serum electrolytes, liver function tests, lipid profile, thyroid function tests, prothrombin time, erythrocyte sedimentation rate, viral serology markers, and routine urine were within normal limits. Abnormality of calcium metabolism was ruled out, as serum calcium, phosphorus, parathyroid hormone, and vitamin D levels were all normal. (Total calcium: 2.4 mmol/L, phosphorus: 0.7 mmol/L, parathyroid hormone: 64.5 pg/ml vitamin D: 36.6 ng/ml) Echocardiography and electrocardiogram (ECG) were also normal.

Non-contrast computed tomography (NCCT) imaging of head revealed extensive symmetrical amorphous (+840 Hounsfield unit) calcification involving both supra and infratentorial compartments with preferably sitting in deep gray matter of bilateral basal ganglia, thalamus, dentate nucleus, midbrain, and pons. Symmetrical T1 high T2/FLAIR heterogeneous low signal intensity was noted in bilateral caudate nucleus, thalamus, bilateral dentate nucleus of cerebellum, and pons (Fig. 1A and B). These areas showed blooming on Gradient Echo sequences (Fig. 2). Small foci of restricted diffusion were noted in the right corona radiata on diffusion-weighted imaging (DWI) (Fig. 3). Magnetic resonance venography scan was normal.

With normal metabolic and endocrine function and classical calcification patterns in the NCCT head, Fahr's disease was diagnosed with coexisting ischemic stroke. As she presented to the hospital more than 24 hours after the onset symptoms, she was treated with dual antiplatelet therapy consisting of aspirin (300 mg) plus clopidogrel (300 mg) and atorvastatin (40 mg). Physiotherapy was initiated to address her weakness and ataxia. On follow-up after 2 weeks, she could perform her usual daily activities independently.

Discussion

Fahr's disease is a degenerative neurological disorder of rare occurrence characterized by abnormal idiopathic bilateral calcium deposition and associated cell loss in the areas of brain that control movement, that includes basal ganglia and cerebral cortex. It has an autosomal dominant, familial, and sporadic pattern of manifestation[1,5–7]. The calcified deposits composed of calcium carbonate and calcium phosphate can occur in other

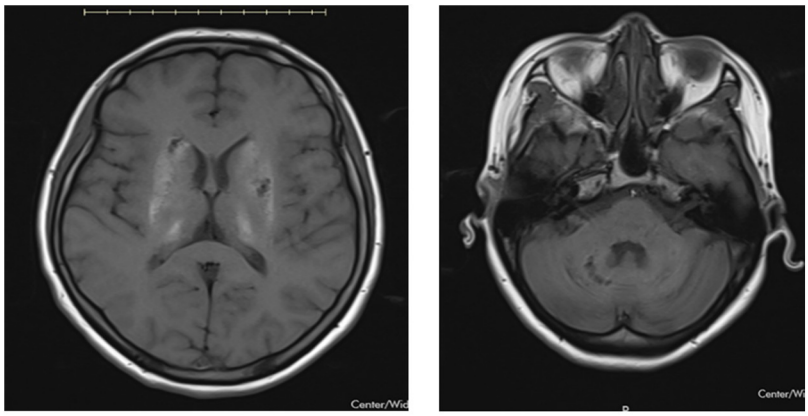

Figure 1. (A) T1 W images showing high signal intensity in bilateral caudate head, lentiform nucleus, and thalamus. (B) T1W images showing high signal intensity in bilateral dentate nucleus.

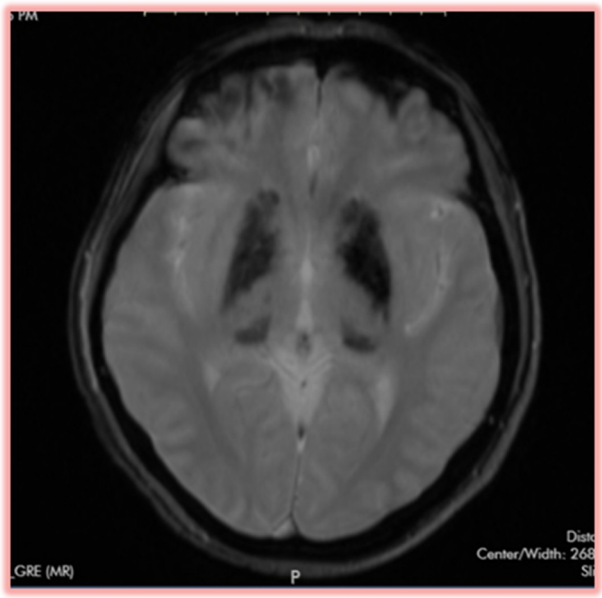

Figure 2. GRE showing low signal intensity (blooming artifacts) in bilateral basal ganglia and thalamus.

areas such as thalamus, hippocampus, dentate nucleus, centrum semiovale, and cerebellar subcortical white matter apart from basal ganglia and cerebral cortex[1,7]. Abnormal calcium deposition in the brain is thought to result from disrupted calcium metabolism or blood-brain barrier changes. It gives rise to the vicious cycle of calcification that begins in the vessel walls, progresses to neurons, and perpetuates further injury by compressing blood vessels and reducing blood flow[8]. The extensive calcium and phosphate depositions in the vessels could be a potential cause of stroke in Fahr's disease.

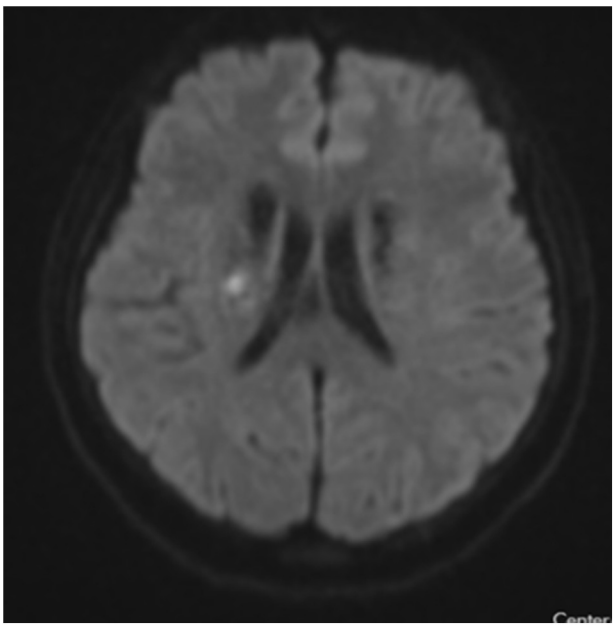

Figure 3. DWI showing high signal intensity in right corona radiata- diffusion restriction (lacunar infarct).

The age of onset can be variable with most common age group being 40–60 years with male to female ratio being 2:1[9–11]. The clinical presentation of Fahr's disease varies from asymptomatic one to mild symptoms like headache, and vertigo to movement disorders like parkinsonism and hyperkinetic movement disorder (chorea, tremor, dystonia, athetosis, and orofacial dyskinesia) and psychiatric disorders such as psychosis and depression, cognitive impairment, dementia, cerebellar impairment and speech disorder[6,7,12–16]. The variability of symptoms is due to division of basal ganglia into dorsal and ventral systems. The dorsal striatum plays a role in motor and cognitive function and ventral striatum plays role in motivational function[12].

Patients who become symptomatic early in adulthood mostly develop psychiatric or cognitive disorders, like psychosis, whereas patients who become symptomatic later in life develop mainly movement disorders in combination with other clinical features[13]. The differential diagnosis for pathological intracranial calcification includes several conditions, such as idiopathic and secondary hypoparathyroidism, hyperparathyroidism, changes following thyroidectomy, birth asphyxia, calcified infarct, and infections like cysticercosis, toxoplasmosis and HIV infection[14].

Co-occurrence of acute ischemic stroke and Fahr's disease is a rare finding. Transient ischemic attack- like episodes or acute ischemic episodes have been described before[14–18]. It has been postulated that, underlying pathogenic process of Fahr's disease resulting in extensive calcium and mineral deposits in affected vessels (capillaries and arterioles) leads to micro infarcts and young-onset cerebrovascular disease. This mechanism is different from common causes affecting small vessels such as arteriosclerosis, cerebral amyloid angiopathy, and immunologically mediated small vessel diseases[14,17,19]. Genetic factors may play a role as mutations in the genes like myogenesis regulating glycosidases gene have been identified in the Fahr's disease patient with stroke[18].

With heterogenous clinical presentation, the diagnosis is based on neuroimaging such NCCT scan or magnetic resonance imaging (MRI) in absence of another explanation for calcification[7]. On NCCT the calcifications present as high-density areas whereas in MRI high-intensity areas are found[20]. Typically, calcifications linked to endocrine, toxic, metabolic, or degenerative disorders are widespread and symmetrical. In contrast, calcifications resulting from infections, vascular issues, or tumors often appear scattered and asymmetric in their distribution and size[14].

Selective removal of deposited calcium from brain without affecting calcium in other parts of body such as bone or tissues is not possible currently[7]. Fahr's disease is managed conservatively with symptomatic relief and supportive care as specific treatments are not available. Family history screening and genetic counseling are important for the early detection and management of the disease, especially in the families with known history[21]. Management of ischemic stroke in Fahr's syndrome patients involves standard stroke treatment protocols, including medical interventions and rehabilitation[14]. Antipsychotics for the psychiatric symptoms prove helpful but with risk of malignant neuroleptic syndrome[22]. Management of parkinsonian symptoms along with physical

and occupational therapy helps to maintain mobility and independence[5].

This case highlights the rare presentation of Fahr's disease with acute ischemic stroke in a young adult, providing valuable insights into its neurovascular implications. However, the study is limited by the lack of genetic analysis to confirm familial patterns and the absence of long-term follow-up to assess neurological outcomes. Future research should focus on elucidating the genetic basis and pathophysiological mechanisms linking Fahr's disease to cerebrovascular events and exploring potential therapeutic strategies to mitigate these complications.

Conclusion

Fahr's disease is a rare condition characterized by intracranial calcification predominantly within the basal ganglia. CT scans are pivotal in identifying the characteristic symmetrical calcification patterns in these areas. Acute ischemic stroke is an uncommon manifestation of Fahr's disease. The exact relationship between Fahr's disease and cerebrovascular events needs further investigation to clarify the underlying mechanisms. Additionally, exploring treatment options for managing both Fahr's disease and its neurological complications is essential for improving patient outcomes.

Ethical approval

Our institution doesn't require ethical approval for reporting individual case report or case series.

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editorin-in-Chief of this journal on request.

Sources of funding

No financial support was received from any organization for the submitted work.

Author's contribution

A.M., B.D., and S.B.K. were responsible for taking the history and conducting the examination of the case. A.M. and N. N. contributed to drafting the manuscript. B.D., S.B.K., N.P. N., and A.M. assisted with manuscript writing. All authors reviewed and approved the final version of the manuscript individually.

Conflicts of interest disclosure

Not applicable.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Narayan Prasad Neupane.

Provenance and peer review

Not commissioned.

Data availability statement

All the required information is within the manuscript itself.

Assistance with the study

Not applicable.

Presentation

Not applicable.

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