eISSN (Online): 2598-0580

**Bioscientia Medicina: Journal of Biomedicine & Translational Research**

Journal Homepage: www.bioscmed.com

# Progressive Fahr's Syndrome with Severe Hypocalcemia in a Woman with Uncontrolled Type 2 Diabetes Mellitus and Coronary Artery Disease: A Case Report

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**ARTICLE INFO**

**Keywords:**
Basal ganglia calcification
Coronary artery disease
Diabetes mellitus
Fahr's syndrome
Hypocalcemia

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All authors have reviewed and approved the final version of the manuscript.

*https://doi.org/10.37275/bsm.v10i8.1644*

**A B S T R A C T**

**Background.** Fahr's syndrome denotes bilateral, symmetric calcification of the basal ganglia and other deep cerebral structures arising from an identifiable secondary cause, most commonly a disorder of calcium–phosphate metabolism. Its association with diabetes mellitus and systemic vascular calcification is increasingly recognized but seldom documented in a single patient.

**Case presentation.** A 58-year-old woman presented with one month of intermittent confusion, bilateral resting hand tremor, intermittent muscle cramps, and gait imbalance. Three months earlier she had a first-ever generalized tonic–clonic seizure coinciding with a new diagnosis of type 2 diabetes mellitus, after which she was non-adherent to insulin therapy. Examination revealed a fine resting tremor, a positive Trousseau sign, and impaired finger-to-nose testing. Investigations showed severe hypocalcemia (4.4 mg/dL), $HbA_{1c}$ 9.7%, and electrocardiographic anterior ischemia with cardiomegaly on chest radiography. Non-contrast cranial computed tomography demonstrated extensive bilateral symmetric calcification of the basal ganglia, cerebellum, thalami, and corona radiata–centrum semiovale. She was diagnosed with Fahr's syndrome with hypocalcemia, type 2 diabetes mellitus, and coronary artery disease, and managed with insulin, calcium lactate, vitamin $D_3$, aspirin, simvastatin, and bisoprolol, with symptomatic improvement by the third hospital day.

**Conclusion.** Bilateral intracranial calcification warrants a structured search for secondary causes, particularly calcium–phosphate disturbance. The coexistence of uncontrolled diabetes, coronary artery disease, and progressive brain calcification supports a panvascular contribution and underscores the need for sustained metabolic control and longitudinal neurological follow-up, given that no curative therapy currently exists.

## 1. Introduction

Fahr's disease is a rare neurodegenerative disorder defined by abnormal, bilateral, and symmetric deposition of calcium and other mineral salts within the basal ganglia, and frequently extending to the thalami, dentate nuclei, cerebellum, and subcortical white matter.[1,2] The condition is uncommon and typically becomes clinically manifest in mid-to-late adulthood, although it may also be detected in younger patients or among asymptomatic relatives.[3,4] Because the calcification is dense and accumulates slowly, it is most often discovered on non-contrast cranial computed tomography (CT), which has superior sensitivity for calcium and has become the practical reference standard for detecting and mapping the deposits.[1,5]

A clinically important distinction separates Fahr's disease from Fahr's syndrome, even though the two terms are often used interchangeably and share an identical radiological appearance. Fahr's disease, also termed primary familial brain calcification (PFBC), refers to idiopathic or genetically determined calcification occurring in the absence of an identifiable metabolic, infectious, or toxic cause; it is associated with pathogenic variants in genes that govern phosphate homeostasis and the integrity of the neurovascular unit, including *SLC20A2*, *PDGFB*, *PDGFRB*, and *XPR1*, with additional recessive genes such as *MYORG* and *JAM2* described more recently.[6-8] By contrast, Fahr's syndrome denotes morphologically indistinguishable calcification that is secondary to an identifiable systemic disorder—most characteristically a derangement of calcium–phosphate metabolism such as hypoparathyroidism or pseudohypoparathyroidism, but also a range of infectious, metabolic, toxic, and vascular conditions.[9-11]

The pathogenesis of pathological brain calcification, regardless of cause, converges on dysfunction of the perivascular environment that normally keeps phosphate and calcium below their precipitation threshold. Disruption of phosphate transport, as occurs with *SLC20A2* variants encoding the type III sodium-dependent phosphate transporter PiT-2, and loss of pericyte support with consequent blood–brain barrier compromise, as occurs with *PDGFB* dysfunction, each tilt the balance toward mineralization.[6,8,12] The resulting deposits can impair regional microcirculation and provoke progressive tissue injury, reflected clinically in a strikingly heterogeneous phenotype: movement disorders such as parkinsonism, tremor, dystonia, and cerebellar ataxia predominate, but cognitive decline, neuropsychiatric disturbance, and seizures also occur, and severity tends to track the anatomical extent of calcification.[2,13,14] No therapy halts or reverses the calcifying process; management is symptomatic and, where a secondary cause is found, directed at that underlying disorder.[11,15]

Diabetes mellitus has emerged as a biologically plausible accelerant of vascular and intracranial calcification. Chronic hyperglycemia, advanced glycation end-products, and oxidative stress drive endothelial dysfunction and the osteogenic transdifferentiation of vascular smooth muscle cells, the same final pathway implicated in coronary and peripheral arterial calcification.[16,17] Markers and mediators of this process correlate with coronary calcium burden, and diabetic microvascular disease affects small vessels throughout the body, including the brain.[18-20] Despite this mechanistic rationale, the simultaneous occurrence of progressive Fahr's syndrome, severe hypocalcemia, uncontrolled diabetes, and coronary artery disease in one patient is rarely documented, and the interplay among these processes is incompletely characterized.

From a public-health standpoint, such cases are particularly instructive in regional and resource-limited settings, where non-contrast CT is increasingly accessible but the specialized biochemical and genetic assays required to characterize a secondary cause may not be.[5,11] A clinician may readily detect bilateral calcification yet struggle to complete the etiological work-up, and the temptation to label the finding idiopathic—or to overlook it as incidental—is real. The patient described here exemplifies this tension: an unambiguous and extensive radiological abnormality, a clear and dangerous biochemical clue in the form of severe hypocalcemia, and a partially constrained work-up that nonetheless permitted rational, life-improving treatment.

The novelty of this report lies in its depiction of clinically progressive Fahr's syndrome in a woman in whom three distinct mineral-handling and vascular derangements coincide—profound hypocalcemia, poorly controlled type 2 diabetes mellitus, and coronary artery disease—offering a single-patient illustration of how systemic metabolic disease may both unmask and aggravate bilateral intracranial calcification. The aim of this report is to describe the clinical course, diagnostic reasoning, and management of this patient, and to synthesize the mechanistic links between calcium–phosphate

dysregulation, diabetic vascular calcification, and the progressive neurological syndrome that resulted.

## 2. Case Presentation

A 58-year-old woman was brought conscious to the emergency department of Sanjiwani Regional General Hospital, Gianyar, Bali, in May 2026. Her family reported that, over the preceding month, she had become intermittently confused, with episodes of slowed and inappropriate responses to conversation that fluctuated in severity throughout the day. During the same period she had developed a bilateral hand tremor and intermittent cramping of all four limbs, and on several occasions she had lost her balance and nearly fallen. She remained ambulant but increasingly hesitant. There was no fever, no focal weakness, and no new headache.

Approximately three months earlier, in January 2026, the patient had been hospitalized for a first-ever generalized tonic–clonic seizure lasting around ten minutes, occurring without an identifiable precipitant. At that admission she denied any tremor, involuntary movements, or balance disturbance, and type 2 diabetes mellitus was diagnosed for the first time, concurrent with the seizure presentation. She was commenced on insulin. After discharge, however, she did not attend any outpatient follow-up and did not use insulin as prescribed. By the time of the current presentation she had had no further seizures, but the movement and cognitive complaints described above had appeared and progressed. She denied any chronic movement disorder, visual disturbance, or chronic headache, and had no history of thyroid disease or thyroid surgery. There was no family history of seizures or similar neurological complaints, no head trauma, and no hallucinations or delusions.

The history was notable as much for what was absent as for what was present. There was no antecedent thyroid surgery or neck irradiation that might point to acquired hypoparathyroidism, no chronic headache or visual disturbance to suggest raised intracranial pressure or a mass lesion, and no hallucinations, delusions, or personality change to indicate a primary neuropsychiatric process—although subtle cognitive slowing was evident to the family. The absence of a family history of seizures, movement disorders, or unexplained neurological illness reduced, without eliminating, the prior probability of a hereditary primary brain calcification. Taken together, these negatives helped to narrow the differential toward an acquired, metabolically driven syndrome and shaped the subsequent, biochemically oriented work-up.

On examination the vital signs were within normal limits and the general physical examination, including the cardiorespiratory and abdominal systems, was unremarkable. Neurological examination revealed no neck stiffness, no cranial nerve palsy, and no limb weakness. A fine resting tremor was evident in both hands. The Trousseau sign was positive, consistent with neuromuscular irritability from hypocalcemia. Finger-to-nose testing demonstrated impaired coordination, indicating cerebellar dysfunction. The remainder of the motor and sensory examination was normal.

Laboratory and ancillary investigations are summarized in Table 1, and the narrative values below correspond exactly to that table. Hematological testing showed a leukocyte count of 10.47 × $10^3$/µL and hemoglobin of 11.7 g/dL. Metabolic testing on the current admission revealed a random blood glucose of 162 mg/dL, while the value recorded during the January admission had been markedly elevated at 237 mg/dL with a glycated hemoglobin ($HbA_{1c}$) of 9.7%, confirming chronically poor glycemic control. The most striking abnormality, detailed in Table 1, was a serum calcium of 4.4 mg/dL, indicating severe hypocalcemia. Renal indices showed a mildly elevated urea of 63.7 mg/dL with a normal creatinine of 1.0 mg/dL. Parathyroid hormone, serum phosphate, and magnesium could not be measured because of reagent and equipment limitations at the treating facility, a constraint that bears directly on the completeness of the etiological work-up discussed below.

Table 1. Laboratory and ancillary investigations.

| Parameter | Result | Reference range |
|---|---|---|
| ***Hematology*** | | |
| Leukocytes | 10.47 × $10^3$/μL | 4.0–11.0 × $10^3$/μL |
| Hemoglobin | **11.7 g/dL** | 12.0–15.0 g/dL |
| ***Glycemic status*** | | |
| Random blood glucose (Jan 2026) | **237 mg/dL** | < 200 mg/dL |
| Random blood glucose (May 2026) | 162 mg/dL | < 200 mg/dL |
| $HbA_{1c}$ (Jan 2026) | **9.7 %** | < 5.7 % (≥ 6.5 % = diabetes) |
| ***Calcium and renal indices*** | | |
| Serum calcium | **4.4 mg/dL** | 8.5–10.5 mg/dL |
| Urea | **63.7 mg/dL** | 15–40 mg/dL |
| Creatinine | 1.0 mg/dL | 0.6–1.1 mg/dL |
| ***Cardiac evaluation*** | | |
| Chest radiograph | Cardiomegaly, CTR 59%; clear lungs | CTR < 50% |
| Electrocardiogram | Anterior ischemia; PVC; no QT prolongation | Normal sinus rhythm |
| ***Not assessed (facility limitation)*** | | |
| Parathyroid hormone, phosphate, magnesium | Not performed | — |

*Notes: Values in red are outside the reference range. Reference ranges follow the treating laboratory's standards for adult women. CTR, cardiothoracic ratio; $HbA_{1c}$, glycated hemoglobin; PVC, premature ventricular complex.*

Cardiac evaluation, also itemized in Table 1, disclosed coexisting cardiovascular disease. The chest radiograph showed cardiomegaly with a cardiothoracic ratio (CTR) of 59% and clear lung fields. The electrocardiogram demonstrated anterior myocardial ischemia and premature ventricular complexes, without QT-interval prolongation despite the profound hypocalcemia. On the basis of these findings the patient was considered to have coronary artery disease in addition to her metabolic derangements; this designation rested on electrocardiographic and radiographic evidence rather than on coronary angiography or a coronary calcium score, neither of which was available.

Non-contrast cranial CT, performed during the January 2026 admission, was the pivotal investigation. As shown in Figure 1, there was dense, bilateral, and symmetric calcification involving the cerebellar hemispheres (Figure 1A) and the lentiform nuclei of the basal ganglia (Figure 1B). Figure 2 demonstrates that the calcification extended symmetrically into the thalami and adjacent deep gray matter (Figure 2A) and further into the corona radiata and centrum semiovale of the periventricular white matter (Figure 2B). The distribution—basal ganglia, cerebellum, thalami, and corona radiata–centrum semiovale—is the classic topography of Fahr's disease/syndrome and is far more extensive than the incidental, isolated pallidal flecks frequently seen in asymptomatic individuals.[1,5]

Integrating the imaging with the biochemical and clinical findings, the patient was diagnosed with Fahr's syndrome accompanied by hypocalcemia, type 2 diabetes mellitus, and coronary artery disease. The temporal evolution of her illness—from an unheralded first seizure with newly diagnosed diabetes, through a period of treatment non-adherence, to the emergence and progression of tremor, cognitive slowing, cramps, and imbalance—is set out chronologically in Table 2.

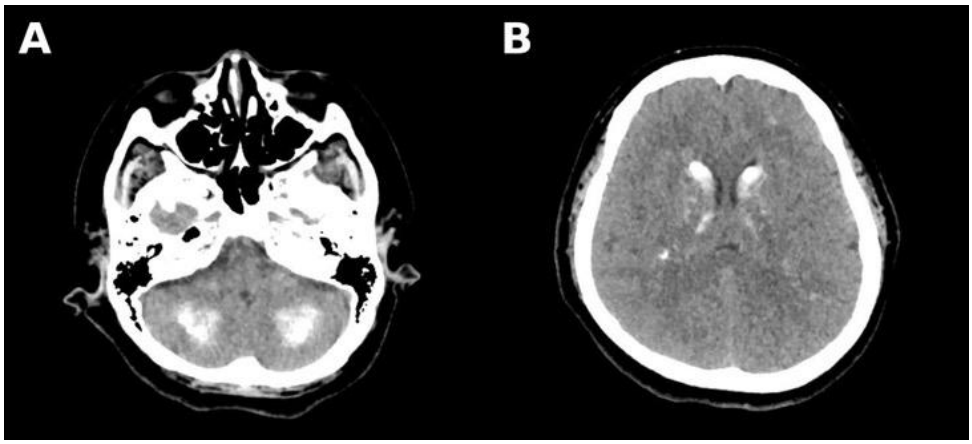


*Figure 1. Non-contrast axial cranial computed tomography. (A) At the posterior fossa level, dense bilateral and symmetric calcification of the cerebellar hemispheres. (B) At the level of the basal ganglia, symmetric calcification of the lentiform nuclei (globus pallidus and putamen). The deposits are markedly hyperdense and bilaterally symmetric, characteristic of Fahr's disease/syndrome.*

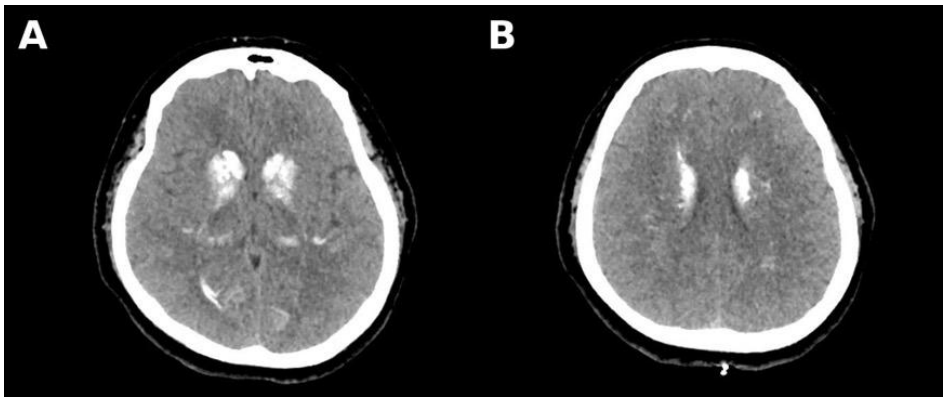


*Figure 2. Non-contrast axial cranial computed tomography in the same patient. (A) Symmetric calcification involving the thalami and adjacent deep gray matter. (B) Extension of calcification into the corona radiata and centrum semiovale of the periventricular white matter. Together with Figure 1, the findings define an extensive, symmetric distribution far exceeding the isolated pallidal flecks seen incidentally in asymptomatic individuals.*

Table 2. Chronology of the clinical course and symptom progression.

| Timepoint | Clinical events | Key findings |
|---|---|---|
| January 2026 (~3 months prior) | First-ever generalized tonic–clonic seizure (~10 min) without identifiable trigger; no tremor or balance disturbance at this stage; new diagnosis of type 2 diabetes mellitus; insulin started. | RBG 237 mg/dL; $HbA_{1c}$ 9.7%. Non-contrast CT: bilateral symmetric calcification of basal ganglia, cerebellum, thalami, and corona radiata–centrum semiovale. |
| February–April 2026 (interval) | No outpatient follow-up; insulin not taken as prescribed (treatment non-adherence). | Not reassessed during this interval. |
| May 2026 (admission) | Intermittent confusion and slowed responses; 1-month bilateral resting hand tremor; intermittent cramps in all four limbs; gait imbalance with near-falls; no recurrent seizure. | Fine resting tremor; positive Trousseau sign; impaired finger-to-nose test. Serum calcium 4.4 mg/dL; RBG 162 mg/dL. CXR cardiomegaly (CTR 59%); ECG anterior ischemia and PVC. |
| Hospital day 3 | Symptomatic improvement with reduced tremor frequency and clearer sensorium; discharged with outpatient follow-up arranged. | Treatment: insulin, calcium lactate, vitamin $D_3$, aspirin, simvastatin, bisoprolol. |

*Notes: CT, computed tomography; CXR, chest radiograph; ECG, electrocardiogram; PVC, premature ventricular complex; RBG, random blood glucose.*

Management was directed simultaneously at the metabolic, mineral, and cardiovascular components of her presentation. She received short-acting insulin 6 IU every 8 hours and long-acting insulin 12 IU every 24 hours for glycemic control, together with calcium lactate 500 mg every 24 hours and vitamin $D_3$ 5,000 IU every 24 hours to correct the hypocalcemia and address the presumed underlying calcium–phosphate disturbance. For the coronary artery disease and associated cardiovascular risk she was given acetylsalicylic acid 80 mg every 24 hours, simvastatin 20 mg every 24 hours, and bisoprolol 1.25 mg every 24 hours. No antiepileptic drug was added, as there had been no seizure recurrence. After three days of inpatient care her condition improved: the frequency of her tremor diminished compared with admission and her sensorium was clearer, and she was discharged with arrangements for outpatient neurological and endocrine follow-up and counseling on the importance of treatment adherence.

## 3. Discussion

This case brings together, in one patient, several strands of contemporary neurology and internal medicine that are usually considered separately: the radiological recognition of bilateral intracranial calcification, the metabolic interrogation of severe hypocalcemia, the vascular biology of diabetes, and the cardiology of coronary artery disease. Considering them jointly is not merely an academic exercise; it changes how the patient is investigated and treated, because the threads are mechanistically linked through the shared theme of disordered mineral handling. The discussion below moves from classification and pathophysiology, through the specific contributions of hypocalcemia and diabetes, to the clinical phenotype, diagnosis, and management, before acknowledging the limitations of a single observation.

### *Disease versus syndrome: classifying bilateral intracranial calcification*

The first and most consequential decision in any patient with bilateral symmetric intracranial calcification is whether the calcification represents primary familial brain calcification (Fahr's disease) or a secondary process (Fahr's syndrome), because the two diverge sharply in work-up, counseling, and the potential for treating an underlying cause.[9,10] In this patient the diagnosis of a syndrome rather than a primary disease rested on the discovery of severe hypocalcemia in the appropriate clinical context, the absence of any family history of similar neurological illness, and the coexistence of uncontrolled diabetes and coronary disease—features that point toward an acquired metabolic and vascular contribution. A structured framework for this differential is presented in Table 3, which also documents how each category was addressed in the present case.

Fahr's disease in the strict, genetic sense is dominated by variants in *SLC20A2* (encoding the phosphate transporter PiT-2), *PDGFB* and *PDGFRB* (which maintain pericyte coverage and blood–brain barrier integrity), and *XPR1* (a phosphate exporter), with autosomal dominant inheritance in most pedigrees and a positive family history in a substantial proportion of cases.[6,8,14] Cohort and mutation studies continue to broaden this spectrum—including recessive *MYORG*-related disease—and to refine genotype–phenotype correlations, as detailed in the differential framework of Table 3.[6,7] Our patient's lack of any familial neurological history and the presence of an alternative metabolic explanation argued against a primary genetic disease; however, in the absence of available genetic testing, a coexisting genetic predisposition cannot be entirely excluded, and this diagnostic humility is appropriate given that secondary triggers may simply unmask a latent tendency to calcify.[12,14]

An important corollary of this framework is that a clear secondary trigger does not rigidly exclude a contributory primary tendency. The threshold at which the perivascular environment begins to mineralize is likely determined by the sum of genetic susceptibility and acquired insults; a patient with a subclinical predisposition may remain radiologically silent for years until a metabolic stressor—chronic

hypocalcemia, sustained hyperglycemia, or both—pushes the system past its precipitation threshold.[14,21] This additive model reconciles the apparently discrete categories of Table 3 and cautions against assuming that the first identified abnormality is the sole explanation. It also has prognostic implications, because if part of the diathesis is fixed and genetic while another part is acquired and modifiable, then aggressive correction of the acquired component is the rational lever available to the clinician even when the constitutional substrate cannot be changed.[15]

Table 3. Framework for the differential etiology of bilateral symmetric intracranial calcification, with its application to the present patient.

| Category | Representative causes | Assessment in this patient |
|---|---|---|
| Primary familial brain calcification (Fahr's disease) | Pathogenic variants in *SLC20A2*, *PDGFB*, *PDGFRB*, *XPR1*, *MYORG*, *JAM2*; often autosomal dominant with positive family history. | No family history of similar illness; genetic testing unavailable, so a latent predisposition is not fully excluded. |
| Endocrine / calcium–phosphate disorders | Hypoparathyroidism, pseudohypoparathyroidism, hyperparathyroidism. | Severe hypocalcemia present; PTH, phosphate, magnesium not measured — the most likely secondary cause but unconfirmed. |
| Infectious / inflammatory | Congenital (TORCH) infection, neurocysticercosis, brucellosis, systemic lupus erythematosus. | No supportive history or clinical features. |
| Metabolic / mitochondrial | Mitochondrial cytopathies and other inherited metabolic disorders. | No suggestive systemic or family history. |
| Toxic / acquired | Lead or carbon-monoxide exposure, post-radiation, post-anoxic injury. | No relevant exposure identified. |
| Vascular / metabolic accelerant | Diabetic microangiopathy and panvascular calcification. | Uncontrolled type 2 diabetes mellitus with coronary artery disease — proposed contributor to progression. |

*Notes: PTH, parathyroid hormone; TORCH, toxoplasmosis, other, rubella, cytomegalovirus, herpes. The final diagnosis was Fahr's syndrome (secondary), given severe hypocalcemia and uncontrolled diabetes, with a primary genetic component not entirely excluded.*

***Distinguishing pathological from physiological calcification***

Not all intracranial calcification is pathological, and a deliberate effort to separate clinically meaningful deposits from benign, age-related ones is part of competent interpretation. Physiological calcification—of the pineal gland, choroid plexus, and dura, and small, often asymmetric flecks in the globus pallidus—is common, increases with age, and is generally of no consequence; modern high-resolution CT readily detects and characterizes such deposits.[5] What distinguishes the present case is the combination of features that mark calcification as pathological: it was bilateral and strikingly symmetric, it was dense and extensive, and it involved a constellation of structures—basal ganglia, cerebellar hemispheres, thalami, and subcortical white matter—that are not typically calcified in healthy aging, a pattern mirrored in reported Fahr's disease imaging.[1,4] As shown in Figure 1 and Figure 2, the deposits in this patient extended well beyond the isolated pallidal specks that might be dismissed as incidental, and their distribution correlated with her clinical signs, lending the imaging genuine explanatory power.[2,22] This clinico-radiological concordance is precisely what should prompt a secondary work-up rather than reassurance.

***Pathophysiology of pathological brain calcification***

Whatever the proximate cause, the deposition of calcium in the deep gray nuclei reflects a failure of the mechanisms that normally keep the perivascular

space mineral-free. Phosphate handling is central: *SLC20A2* encodes a sodium-dependent phosphate transporter, and functional and computational characterization of disease-associated variants shows how impaired transport raises local phosphate and favors precipitation.[6,12] In parallel, *PDGFB-PDGFRB* signaling maintains pericyte coverage and blood–brain barrier integrity, so that its dysfunction produces a leaky vasculature permissive to mineral deposition.[8,14] Crucially, calcification is increasingly understood as an active, cell-mediated process: experimental models show that mural and smooth-muscle-like cells can adopt an osteogenic program and that calcium–phosphate balance is locally regulated rather than passively determined.[15,17] The basal ganglia and dentate nuclei are especially vulnerable, plausibly because of their high metabolic demand and dense capillary network, which explains both the characteristic topography and the predilection for extrapyramidal and cerebellar signs.[13]

The recognition that calcification is cell-mediated rather than inert reframes how the deep gray nuclei come to mineralize. In peripheral vessels, smooth muscle cells exposed to a calcifying milieu release matrix vesicles that nucleate hydroxyapatite and adopt the transcriptional signature of bone-forming cells, a process demonstrated experimentally and linked to regulators such as MFG-E8 and protective factors such as CTRP3.[17,18] An analogous program executed by perivascular cells of the cerebral microvasculature is increasingly implicated in brain calcification, and studies in hypoparathyroidism show that the calcium burden tracks with both local and systemic metabolic mechanisms.[15,21] This conception is clinically liberating in one sense—because an active process is, in principle, targetable—and sobering in another, because by the time dense deposits are visible on CT the cellular changes are typically well established and not amenable to reversal.[15]

***Hypocalcemia and calcium–phosphate dysregulation in this patient***

The severe hypocalcemia documented here (serum calcium 4.4 mg/dL, the most abnormal value in Table 1) is the single most important secondary explanation for the patient's calcification and her acute neuromuscular signs. Chronic hypocalcemia, classically from hypoparathyroidism or pseudohypoparathyroidism, raises the calcium–phosphate product within the central nervous system microenvironment and promotes precipitation in the basal ganglia and beyond; a cross-sectional study of adult hypoparathyroidism confirms that basal ganglia calcification is associated with these local and systemic metabolic disturbances.[10,21] Hypoparathyroidism and its variants are among the most frequently identified causes of Fahr's syndrome.[9,11] The positive Trousseau sign is the clinical correlate of the same biochemical derangement, while seizures—as occurred at this patient's first presentation—are a recognized manifestation of hypocalcemia and of basal ganglia calcification.[23,24]

The relationship between hypocalcemia and the patient's index seizure deserves particular emphasis, because it links her first and most dramatic presentation to the same biochemical thread that runs through the rest of her illness. A calcium-deficient extracellular environment lowers the threshold for neuronal depolarization, predisposing to both the peripheral neuromuscular irritability captured by the Trousseau sign and the central hyperexcitability that can culminate in a generalized seizure; epilepsy with basal ganglia calcification and hypocalcemia is a well-described combination.[23,24] The fact that she had no recurrent seizures once calcium and glucose were being addressed, and required no antiepileptic drug, is consistent with a predominantly provoked, metabolically driven event rather than an independent epileptic disorder—an interpretation with direct therapeutic consequences, since correcting the metabolic derangement may obviate the need for chronic anticonvulsant therapy.[23,25]

A crucial limitation of the work-up was the inability to measure parathyroid hormone, phosphate, and magnesium, which precluded a definitive endocrine diagnosis. Distinguishing hypoparathyroidism from pseudohypoparathyroidism, or identifying a contributory hypomagnesemia, would normally guide

both the interpretation of the calcification and the long-term replacement strategy.[9,11] In their absence, the team appropriately treated the demonstrated hypocalcemia empirically with calcium lactate and vitamin $D_3$ while flagging the need for a complete metabolic panel at follow-up; experimental data indicate that calcitriol and calcium supplementation influence the calcification process, supporting this pragmatic approach.[15]

***Diabetes mellitus as an accelerant: vascular calcification and the osteogenic switch***

Beyond the calcium–phosphate axis, this patient's poorly controlled diabetes ($HbA_{1c}$ 9.7%) is likely to have actively promoted the calcifying process. Hyperglycemia, advanced glycation end-products acting through the receptor RAGE, and oxidative stress drive vascular smooth muscle cells to undergo phenotypic transdifferentiation toward an osteoblast-like state, depositing a mineralizing matrix within vessel walls.[16,17] This osteogenic switch is regulated by identifiable mediators—MFG-E8 promotes it, whereas factors such as CTRP3 restrain it—and the same programs operate in the small vessels affected by diabetic microvascular disease, providing a route by which diabetic vasculopathy in the brain could potentiate deposition in the deep gray nuclei.[17,18,20]

Reports linking hyperglycemia to the deep gray nuclei reinforce this rationale: non-ketotic hyperglycemia is itself a recognized cause of basal ganglia syndromes and has been described alongside Fahr's syndrome.[22] Importantly, emerging therapeutic data suggest the process is modifiable—sodium-glucose cotransporter-2 (SGLT2) inhibitors and incretin-based agents have been shown experimentally to attenuate vascular smooth muscle calcification by suppressing osteogenic differentiation—raising the possibility that aggressive metabolic control could, in principle, slow the vascular component of progression even though it cannot reverse established cerebral deposits.[26,27] For a patient who had been non-adherent to therapy, this mechanistic link transforms glycemic control from a generic recommendation into a disease-specific intervention.

It is worth being precise about the strength and the limits of the diabetes–brain-calcification link, so as not to overstate a single-patient inference. The cellular biology connecting hyperglycemia to osteogenic transdifferentiation is robust and reproducible in vascular tissue, and markers of the process correlate with coronary calcium burden.[16,17,18] The extrapolation to the cerebral deep gray nuclei specifically is more tentative, resting on mechanistic plausibility and the recognition that diabetic microangiopathy affects small vessels throughout the body, including the brain.[20] In this patient, the temporal coincidence of newly diagnosed, poorly controlled diabetes with the clinical emergence and progression of her syndrome is suggestive but not probative. What can be stated with confidence is that her diabetes was a modifiable amplifier of vascular pathology, that it independently mandated treatment, and that controlling it aligns with—rather than works against—the goal of limiting further calcification.[26]

***Diabetic panvascular disease: linking coronary and cerebral calcification***

The concurrent finding of coronary artery disease—electrocardiographic anterior ischemia and cardiomegaly—in a patient with extensive cerebral calcification is unlikely to be coincidental. Diabetes characteristically produces a panvascular phenotype in which atherosclerosis and calcification develop simultaneously across coronary, cerebral, and peripheral territories, sharing the common substrate of endothelial dysfunction, inflammation, and osteogenic matrix deposition.[16,19] Coronary artery calcification in type 2 diabetes is associated with adverse body-composition and metabolic markers and is a graded indicator of cardiovascular risk, and shared regulators of vascular calcification link the coronary and systemic beds.[18,19] Viewed through this lens, the patient's brain and heart are two windows onto the same systemic mineralizing diathesis, and her coronary disease both corroborates the panvascular interpretation and independently demands risk-factor modification.[28]

This framing has practical consequences. It justifies the antiplatelet and statin therapy she

received, aligns the cardiac and neurological problems under a unifying pathophysiology rather than treating them as unrelated coincidences, and emphasizes that the prognosis is determined as much by cardiovascular events as by the neurological syndrome itself. It also argues for surveillance of other vascular beds and for treating the diabetes as the shared upstream driver.[19,20]

***Clinical phenotype and the problem of symptom progression***

The patient's trajectory illustrates the characteristically progressive and heterogeneous phenotype of Fahr's syndrome. Her presentation evolved from an isolated seizure—an uncommon but well-described initial manifestation—to a composite of resting tremor, cerebellar incoordination, cognitive slowing, and gait instability, mirroring the extension of calcification from basal ganglia to cerebellum, thalamus, and white matter.[2,14] Movement disorders, including parkinsonism and other extrapyramidal phenomena, are among the most common features, and the cerebellar calcification evident in Figure 1A provides a direct anatomical explanation for the impaired finger-to-nose testing and balance disturbance.[13,22] Cognitive and neuropsychiatric symptoms—from subtle slowing to frank psychosis—are also part of the spectrum and can dominate the picture in some patients, underscoring the need for cognitive and psychiatric assessment in follow-up.[3,29,30] Seizures, though less frequent, are recognized and may be the heralding event, as they were here.[24,25]

Her age and sex are consistent with the typical demographic of symptomatic Fahr's syndrome, which most often becomes clinically manifest in mid-to-late adulthood, the period during which accumulated calcification tends to cross the threshold for producing symptoms.[3,4] The heterogeneity of the syndrome means that no two patients present identically, and the same anatomical lesion can be clinically silent in one individual and disabling in another, which complicates both diagnosis and prognostication.[13,14] In practice, this variability argues for individualized assessment and against rigid algorithms: the clinician must weigh the extent of calcification, the specific deficits elicited on examination, the identified secondary causes, and the patient's broader comorbidity in order to construct a sensible management plan.

The tempo of progression is clinically instructive. Calcification accrues slowly over years, yet this patient deteriorated noticeably within months, which suggests that superimposed, potentially reversible factors—uncontrolled hyperglycemia, persistent hypocalcemia, and treatment non-adherence—were driving the acceleration on top of the structural substrate.[16,22] This is a hopeful inference, because while the calcium deposits themselves are fixed, the metabolic accelerants are modifiable, and the symptomatic improvement observed after only three days of correction of hyperglycemia and hypocalcemia, as recorded in Table 2, supports the view that a meaningful portion of her acute decline was functional rather than purely structural.

***Diagnostic approach and management***

Non-contrast CT remains the cornerstone of diagnosis, offering superior sensitivity for calcium and allowing the symmetric, bilateral pattern to be recognized and mapped, as in Figure 1 and Figure 2.[1,5] Once calcification is identified, the essential next step is the systematic exclusion of secondary causes outlined in Table 3, with particular attention to the calcium–phosphate–parathyroid hormone axis, because an identifiable and treatable metabolic disorder changes management.[9,11] Where resources permit, genetic testing is reserved for patients with a suggestive family history or no secondary cause.[7] The present work-up was appropriately CT-led and biochemically oriented but was curtailed by the unavailability of parathyroid hormone, phosphate, and magnesium assays—a gap that should be closed at follow-up.

A practical question is whether magnetic resonance imaging (MRI) adds value once CT has shown calcification. CT is unequivocally superior for detecting and quantifying calcium, and in a resource-limited setting it is both sufficient and appropriate for establishing the diagnosis of bilateral

striopallidodentate calcinosis.[5] MRI can be complementary when an alternative or coexisting structural lesion is suspected, but it is not required to make the diagnosis and its appearance of calcium is variable and potentially misleading. In this patient, the CT findings were definitive, and the clinical priority shifted appropriately from further imaging to completing the biochemical work-up and instituting treatment.[1]

Because no treatment arrests or reverses the calcification, care is necessarily symptomatic and cause-directed.[11,15] In this patient the strategy was rational and multipronged: correction of hypocalcemia with calcium lactate and vitamin $D_3$; insulin to address the uncontrolled diabetes that plausibly accelerates calcification; and antiplatelet, statin, and beta-blocker therapy for coexisting coronary disease. Sustained, structured glycemic control is especially pertinent given the mechanistic link between hyperglycemia and vascular calcification, although the optimal intensity of control must be individualized, since glycemic variability and overly aggressive lowering carry their own cardiovascular and hypoglycemic risks.[26,31] Long-term, the patient requires reliable outpatient engagement—the very thing absent in her history—encompassing repeat metabolic profiling, neurological and cognitive surveillance, cardiovascular risk management, and adherence support.[20,28]

The cardiovascular limb of the regimen deserves to be defended explicitly rather than treated as routine. In a patient with electrocardiographic ischemia, cardiomegaly, and diabetes, antiplatelet therapy and a statin address a quantifiable, high risk of myocardial events, and the magnitude of that risk in diabetic patients with demonstrable vascular calcification is substantial.[19,28] The statin in particular is doubly rational here: it reduces atherosclerotic events and, mechanistically, intersects with the same vascular biology that links diabetes to calcification.[16] Beta-blockade was a reasonable choice given the ischemic findings and ventricular ectopy, with the dose kept deliberately low. None of these agents treats the brain calcification directly, but together they target the cardiovascular consequences of the shared panvascular process and may, over time, prove as important to the patient's survival as the neurological management is to her function.[19,20]

Follow-up imaging, although not performed in this case, would strengthen future management of similar patients. A repeat non-contrast CT after an interval would allow the radiological progression of calcification to be tracked against the clinical course and the adequacy of metabolic control, converting a static snapshot into a dynamic record.[5] Such longitudinal documentation is also valuable for the literature, because objective evidence of whether—and how fast—calcification advances under treatment is precisely what is needed to test the hypothesis that controlling diabetes and calcium status slows the process; until then, serial imaging should be regarded as a priority for this patient's ongoing care.[21]

***Prognosis, counseling, and the central role of adherence***

The prognosis of Fahr's syndrome is generally guarded, because the calcification is irreversible and tends to progress, and because the disability it produces—movement impairment, cognitive decline, and neuropsychiatric symptoms—accumulates over time.[3,14] Yet prognosis in an individual patient is not fixed by the imaging alone; it is shaped by how well the modifiable contributors are managed. This patient's course makes the point vividly. Her clinical deterioration over a few months was disproportionate to the slow biological pace of calcification and coincided precisely with a period of treatment non-adherence and uncontrolled metabolic disease, and her rapid symptomatic improvement once hypocalcemia and hyperglycemia were addressed indicates that a substantial fraction of her acute decline was functional and reversible.[16,24] The therapeutic implication is that consistent engagement with care—rather than any single drug—is the principal determinant of her trajectory.

This reframes adherence from a behavioral footnote into a central clinical objective. The patient had previously been started on insulin yet did not return for follow-up and did not take it as prescribed, and the consequences—persistent hyperglycemia, uncorrected

hypocalcemia, and symptomatic progression—were predictable. Effective long-term management therefore depends as much on adherence support, patient and family education, and reliable access to follow-up as on the pharmacological regimen itself.[28] Counseling should convey, in accessible terms, that although the brain calcification cannot be undone, controlling diabetes and maintaining normal calcium can reduce symptoms, lower the risk of further metabolic seizures, and protect the heart and other vascular beds. Coordinated, multidisciplinary follow-up spanning neurology, endocrinology, and cardiology—with periodic reassessment of the calcium–phosphate axis, glycemic indices, cognition, and cardiovascular status—offers the most realistic path to preserving function in a condition without a cure.[19,31]

### *Limitations*

Several limitations temper the conclusions that can be drawn from a single case. The etiological work-up was incomplete: parathyroid hormone, phosphate, and magnesium were not measured, so the precise calcium–phosphate disorder underlying the hypocalcemia—and therefore the definitive secondary cause of the syndrome—remains unconfirmed, and a contributory primary genetic predisposition could not be excluded in the absence of genetic testing.[7,9] Follow-up imaging was not available to document radiological progression in parallel with the clinical course, and the attribution of acceleration to diabetes and hypocalcemia, while mechanistically supported, remains inferential.[16] Finally, as with all case reports, causal and panvascular interpretations are hypothesis-generating rather than confirmatory; nonetheless, the constellation described here is clinically coherent and offers a practical lesson in the structured evaluation of bilateral intracranial calcification.

## 4. Conclusion

This case underscores that bilateral, symmetric intracranial calcification should never be dismissed as an incidental curiosity but should instead prompt a structured search for a secondary cause, with calcium–phosphate disturbance foremost among them. In this patient, severe hypocalcemia provided the principal secondary explanation for Fahr's syndrome, while uncontrolled type 2 diabetes mellitus and coexisting coronary artery disease pointed to a broader panvascular, mineralizing diathesis that plausibly accelerated her clinical progression. The prompt symptomatic improvement that followed correction of hypocalcemia and hyperglycemia suggests that, although the calcific deposits are irreversible, the metabolic accelerants are modifiable. Comprehensive etiological evaluation, sustained metabolic and cardiovascular control, and longitudinal neurological follow-up therefore remain the cornerstones of management for a condition that, to date, has no curative therapy.

## Declarations

### *Ethics approval and consent to participate*

Written informed consent for the publication of this case and the accompanying anonymized images was obtained from the patient. The report was prepared in accordance with the ethical principles of the Declaration of Helsinki, and patient identifiers have been removed to protect confidentiality.

### *Data availability*

The clinical data supporting the findings of this report are available from the corresponding author upon reasonable request, subject to constraints that protect patient privacy.

### *Conflict of interest*

The authors declare that there is no conflict of interest related to this report.


### *Funding*

This report received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

### *Acknowledgments*

The authors thank the staff of Sanjiwani Regional General Hospital, Gianyar, for their assistance in the care of the patient.


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