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Case Report

A Case Report on Fahr's Syndrome: Complex Presentation and Diagnostic Challenges

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ABSTRACT

Fahr's syndrome, an exceedingly rare neurogenetic disorder characterized by abnormal bilateral calcium deposition in the brain, primarily affects individuals in their 30s and 40s. This case report details a 55-year-old female with Fahr's syndrome presenting generalized seizures, extrapyramidal features, and left basal ganglia calcification. Despite months of sodium valproate treatment, seizures persisted. Initial assessment revealed elevated blood pressure, hypocalcemia, hyperglycemia, and positive Chvostek's sign. Intravenous calcium, midazolam, and nitroglycerin were administered, resulting in significant improvement. Laboratory investigations highlighted metabolic abnormalities and radiological examination confirmed symmetrical bilateral basal ganglia calcification, gliotic changes, and mild cerebral atrophy. The case aligns with Fahr's syndrome, emphasizing the need for close monitoring and tailored therapeutic interventions to manage its diverse clinical spectrum and potential complications. The pathophysiology, linked to calcium and phosphorus imbalances, underscores the complex nature of this disorder. Comprehensive understanding and diligent care are crucial for effectively addressing Fahr's syndrome, given its rarity and the challenges associated with its diagnosis and management.

Keywords: Fahr's syndrome, Basal ganglia calcification, Generalized seizures, Neurogenetic disorder, Metabolic abnormalities.

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INTRODUCTION

Fahr's syndrome, also recognized as primary familial brain calcification, stands as an exceedingly rare neurogenetic degenerative disease characterized by abnormal symmetrical bilateral calcium deposition in the basal ganglia, thalamus, cerebral cortex, dentate nucleus, and cerebellum.[1-3] Initially documented in 1930 by the German neurologist Karl Theodor Fahr, this syndrome exhibits a sporadic prevalence of less than 1 per 1,000,000 and primarily affects individuals in their 30s and 40s.[2,4] The etiology of Basal Ganglia Calcification (BGC) remains unknown,[5] and they are associated with various metabolic disorders and neurological, such as parkinsonism,[1] hypoparathyroidism, pseudohypoparathyroidism, hypoglycemia, and others.[6,7]

Diagnosing Fahr's syndrome requires the identification of bilateral striato-pallido-dentate calcification on neuroimaging, progressive cognitive dysfunction, and movement disorders without biochemical, infectious, toxic, or traumatic causes.[8] Clinical manifestations in Primary Familial Brain Calcification (PFBC) patients encompass chorea, ataxia, dystonia, and seizures.[1] Remarkably, individuals aged over 50 may exhibit a certain degree of BGC, and this finding could be coincidental in 15-20% of asymptomatic patients undergoing Computed Tomography (CT) scans.[9,10]

Effective management of movement disorders and seizures associated with Fahr's syndrome may involve correcting calcium and phosphate levels. Symptomatic relief for individuals with Fahr's syndrome might include the use of clonazepam and atypical antipsychotics. However, caution is advised regarding the use of lithium, as it may elevate the risk of seizures. Furthermore, strategies employing carbamazepine, benzodiazepines, and barbiturates should be approached with care, as they may aggravate underlying gait disorders. Therefore, these therapeutic interventions require judicious administration in the treatment of patients with Fahr's syndrome. In this report, we present the case of a hyperglycemic patient exhibiting generalized seizures and extrapyramidal features, accompanied by left BGC.[4]

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CASE REPORT

A 55-year-old female patient presented to the emergency department following a recent episode of seizures. During a generalized tonic seizure, she experienced a 15 min period of unconsciousness. The patient reported symptoms of dyspnea, headache, vertigo, sleep disturbances, and decreased appetite. Despite three to four months of sodium valproate treatment with strict adherence, the seizures remained uncontrolled. On assessment, her vital signs revealed elevated Blood Pressure (BP) at 228/110 mmHg, a pulse rate of 140 beats per minute, a respiratory rate of 20 breaths per minute, SpO_2 at 73%, and a body temperature of 37.3°C.

Neurological examination showed clear consciousness with no evidence of cognitive impairment or cranial nerve dysfunction. Systemic and general physical examinations were unremarkable, except for a positive Chvostek sign. Notably, after the physical examination, her BP increased, likely attributed to the breathlessness she was experiencing.

Initial investigations into the metabolic causes of seizures revealed hypocalcemia and hyperglycemia, as detailed in Table 1. The patient had no prior medical history of autoimmune diseases, hypertension, stroke, infections of the central nervous system, or head trauma. Furthermore, there was no relevant family history concerning her seizure condition.

The patient was administered calcium gluconate intravenously, comprising 20 mL of a 10% calcium gluconate solution diluted in 50 mL of dextrose, with the infusion spanning a duration of 20 min. Simultaneously, an injection of midazolam (75 mg twice daily) and an injection of nitroglycerin 5mg/ml, along with the injection of clopidogrel 75 mg, were administered to prevent clot formation in blood vessels. Following the patient's recovery of consciousness, the midazolam dosage was modified to 75 mg administered once daily.

The patient's condition remained stable and within normal limits. Intravenous fluids included normal saline (100 mL) and a half bottle of dextrose and sodium chloride, administered at a rate of 50 mL per hour (200 mL per day for 3 days). Additionally, the patient received an injection of ceftriaxone (1.5 mg) and an injection of ondansetron 2mg/mL twice daily for three days.

By the third day of admission, the patient showed significant improvement and successfully recovered. Upon discharge, the prescribed oral medications included 500 mg sodium valproate twice daily, 600 mg calcium citrate twice daily, and 50,000 IU vitamin D_3 once weekly for six weeks.

Radiological examination

Imaging protocol

A comprehensive evaluation of the brain was performed through a plain CT scan, utilizing axial sections with a thickness of 5 mm. The imaging protocol aimed to capture detailed insights into the patient's intracranial structures (Figure 1).

Table 1: Laboratory investigation report.

Investigation	Result	Normal Range	Unit
BSL	258	<140	mg/dL
WBC	28100	10000-26000	cells/µL
Hemoglobin	15.7	14-22	g/dL
Platelets	4.39	1.0-4.5	Lakh/Cumm
Blood urea	20	10-50	mg/dL
Serum creatinine	0.6	up to 1.2	mg/dL
Serum bilirubin	0.8	0.1-1.2	mg/dL
SGOT	29	0-40	u/L
SGPT	34	0-41	u/L
Alanine transaminase	11.5	10-50	u/L
Alkaline phosphatase	66	35-104	u/L
Serum albumin	4.57	3.5-5.0	g/dL
Serum calcium	4.79	8.0-10.0	mg/dL
Magnesium	2	1.5-2.5	mg/dL
C reactive protein	3.4	0-6	mg/dL
ESR	29	0-20	mg/hr

BSL: Blood sugar level; **ESR:** Erythrocyte sedimentation rate; **SGOT:** Serum glutamic oxaloacetic transaminase; **SGPT:** Serum glutamic pyruvic transaminase; **WBC:** White blood cell.

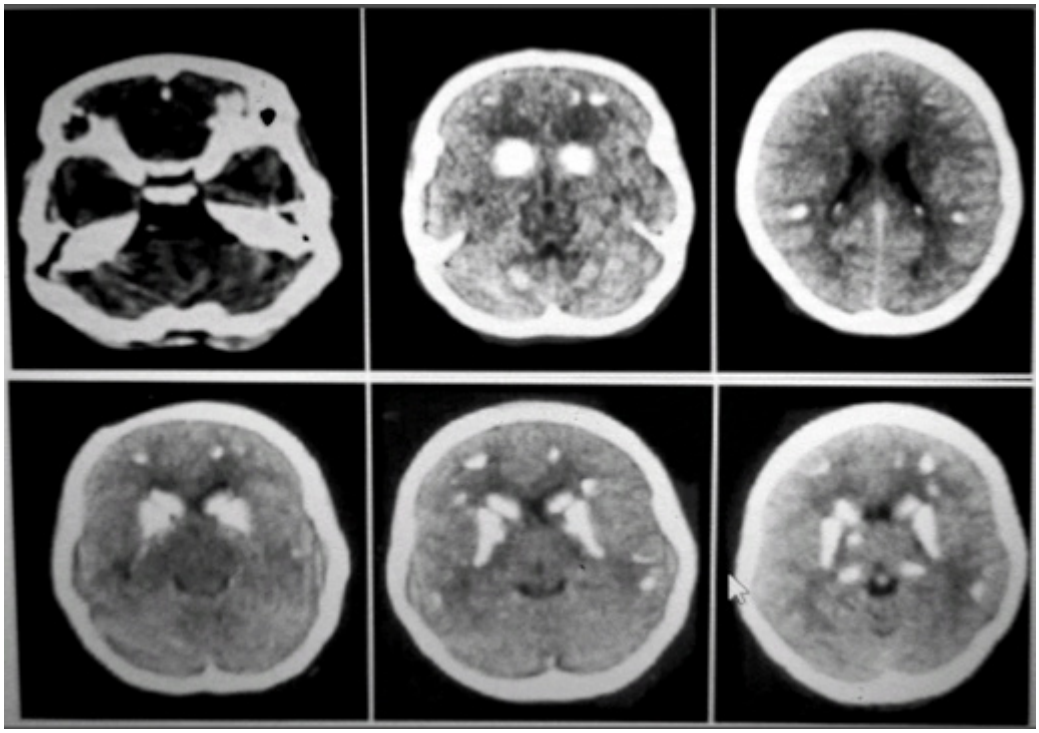

Figure 1: A computed tomography scan of the brain.

Observation

A small gliotic area was identified in the left basal ganglia region, accompanied by symmetrical bilateral BGC. Mild generalized cerebral atrophy was evident, manifested by a subtle prominence of the ventricular system and notable basal cisterns, sulcal spaces, and sylvian fissures. Additionally, bilateral ill-defined hypodensities in the paraventricular region raised suspicion of white matter ischemia. The ventricles appeared in midline alignment, with no discernible shift of midline structures. The brainstem and the remaining portions of both cerebral and cerebellar hemispheres displayed normal characteristics. Importantly, no signs of hemorrhage or space-occupying lesions were observed in the supra or infratentorial region.

DISCUSSION

Fahr's syndrome, characterized by calcification of the basal ganglia, is suspected based on brain imaging studies in patients presenting with neurological or psychiatric symptoms. The diverse signs and symptoms encompass seizures, dyskinesia, dementia,[11] impaired cognition, alterations in behavior and personality,[12] and depression.[11] Diagnosis typically involves the identification of prevalent parathyroid abnormalities (hyperparathyroidism, hypoparathyroidism, hypervitaminosis D) alongside BGC, in conjunction with other neurological or metabolic issues.[11]

While the precise pathophysiology of Fahr's syndrome remains elusive, established links exist with imbalances in calcium and phosphorus levels regulated by the parathyroid gland.[13] Associated diseases include tuberculosis, cytomegalovirus infection, toxoplasmosis, astrocytoma,[11] neuroferritinopathy, Kenny-Caffey syndrome type 1, intrauterine or perinatal infections (e.g., toxoplasma gondii, rubella), tuberous sclerosis complex, and brucella infection.[12]

In our presented case, the patient did not undergo neck surgery, and there were no features suggestive of other systemic diseases or developmental anomalies as discussed above. The physical examination unveiled significant signs, including Chvostek's sign (twitching of the upper lip on tapping the cheek along the course of the facial nerve) and Trousseau's sign (painful carpal spasm elicited by inflating the sphygmomanometer cuff 20 mm Hg above systolic BP for 3 min). Neurological manifestations beyond seizures encompass raised intracranial tension, papilledema, irritability, depression, psychosis, and extrapyramidal and cerebellar manifestations.[14-16]

Electroencephalogram findings, particularly in the presence of hypocalcemia, can reveal an evolution from alpha through theta and delta dominance, generalized spikes and sharp waves, and bursts of delta activity with sharp components.[17]

CONCLUSION

In this case report, a 55-year-old female presented with generalized seizures and extrapyramidal features, revealing left BGC. The patient exhibited elevated BP, hypocalcemia, hyperglycemia, and positive Chvostek's sign. Initial management involved intravenous calcium, midazolam, nitroglycerin, and clopidogrel. The patient responded well to treatment, and upon discharge, oral medications included sodium valproate, calcium

citrate, and vitamin D_3. Radiological examination revealed symmetrical bilateral BGC, gliotic changes, and mild generalized cerebral atrophy. The case aligns with Fahr's syndrome, a rare neurogenetic disorder characterized by BGC, often associated with parathyroid abnormalities. The pathophysiology, though not fully understood, implicates calcium and phosphorus imbalances. Neurological manifestations extend beyond seizures to include dyskinesia, dementia, and altered behavior. Close monitoring and tailored therapeutic interventions are crucial for managing Fahr's syndrome, considering its diverse clinical spectrum and potential complications.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

PATIENT CONSENT

The patient referenced in this case report has provided consent for publication, acknowledging the report's nature and understanding that their identity will be kept confidential.

ABBREVIATIONS

BGC: Basal ganglia calcification; **BP:** Blood pressure; **CT:** Computed tomography; **IU:** International Units; **mg:** Milligram; **ML:** Millimeter; **mm:** Millimeter; **mmHg:** Millimeters of mercury; **PFBC:** Primary familial brain calcification; **SpO_2:** Peripheral capillary oxygen saturation; **Vitamin D_3:** Cholecalciferol; **°C:** Degree Celsius.

SUMMARY

This case report delves into Fahr's syndrome, an uncommon neurogenetic disorder marked by bilateral calcium deposition in the brain. The patient, a 55-year-old woman, presented with generalized seizures and extrapyramidal features, accompanied by left BGC. Initial management involved addressing elevated blood pressure, hypocalcemia, and hyperglycemia. The patient's condition significantly improved with intravenous calcium, midazolam, nitroglycerin, and clopidogrel, leading to successful recovery by the third day of admission. Radiological examination revealed symmetrical BGC, gliotic changes, and mild cerebral atrophy. The case aligns with Fahr's syndrome, linked to calcium and phosphorus imbalances. While the syndrome's pathophysiology remains elusive, established associations exist with parathyroid abnormalities. Neurological manifestations extend beyond seizures to include dyskinesia and altered behavior. This report emphasizes the importance of close monitoring and tailored interventions in managing Fahr's syndrome due to its diverse clinical spectrum and potential complications.

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