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Our cases of Fahr's disease and review of the literature

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Abstract

Fahr's disease is defined as idiopathic basal ganglia calcification. Calcinosis develops in the basal ganglia and cerebral cortex due to impaired calcium and phosphorus metabolism. Calcium deposition or mineralization usually develops in vascular and perivascular areas. It results in vascular obliteration, perivascular neuronal degeneration, and gliosis in the brain. Intracranial calcifications are symmetrical and occur primarily in the basal ganglia, dentate nucleus, thalamus, and centrum semiovale. If intracranial calcifications develop due to a known cause, it is called Fahr syndrome. It is an inherited or sporadic neurological disorder and is thought to be rare. It is more common in males than females and occurs mainly in the fourth decade of life. The disease may present with clinical signs such as slurred speech, gait instability, involuntary movements, or muscle cramps. It may be accompanied by neuropsychiatric symptoms such as psychosis and personality changes. Because of the symptoms, it may be confused with other neurological diseases and misdiagnosed. This retrospective study was planned to evaluate the frequency of patients in our region and their clinical findings.

Keywords: Neurologic disorder, Fahr's disease, Fahr's syndrome, intracranial calcification

Introduction

Fahr disease (FD) is a rare neurodegenerative disorder characterized by bilateral symmetrical intracranial calcification due to calcium and phosphorus metabolism disorders. Fahr's disease was first reported by German neurologist Karl Theodor Fahr in 1930. Fahr's disease is generally thought to affect people in their fourth and fifth decades.The disease frequency is reported to be <1/1,000.000 [1]. Although genetic evidence has been found, the prevalence of this disease is not well known because first degree relatives of patients have not been adequately investigated. Patients are generally healthy in their youth. They tend to develop neurodegenerative diseases with advancing age. FD may have a benign course or may cause life-threatening clinical pictures. However, it usually has a slow course. Calcium deposition or mineralization usually develops in vascular and perivascular areas. It results in vascular obliteration, perivascular neuronal degeneration, and gliosis in the brain. Intracranial calcifications are symmetrical and occur primarily in the basal ganglia, dentate nucleus, thalamus, and centrum semiovale. Four genes (SLC20A2, PDGFRB, PDGFB, and XPR1) that have been proven to be associated with Fahr disease have been identified [2]. It is generally thought to be inherited in an autosomal dominant manner. However, genetic history is not available in most patients. The terms Fahr disease and Fahr syndrome (FS) are often used interchangeably in the literature. However, over time, the terms Fahr disease and Fahr syndrome have been proposed for primary basal ganglia calcifications of unknown etiology and secondary basal ganglia calcifications, respectively. The etiology of Fahr syndrome may include parathyroid disorders, perinatal/intrauterine infections, tuberous sclerosis, brucellosis, and tuberculosis. Fahr's disease should be considered in the differential diagnosis in patients presenting with neuropsychiatric disorders, calcium and phosphorus metabolism disorders, and unexplained neurologic complaints, especially in the presence of intracranial calcification in the basal ganglia that cannot be attributed to any cause of radiologic imaging.

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Material and Methods

Patient Population

Between January 2024 and January 2025, patients who applied to the Neurology Outpatient Clinic and underwent cranial imaging were evaluated. Among these patients, patients whose imaging findings were compatible with the diagnosis of Fahr's Disease were identified. The following diagnostic criteria were used to diagnose Fahr's disease.

- Bilateral calcification in the basal ganglia on neuroimaging.
- Progressive neurologic dysfunction, which generally includes a movement disorder and/or neuropsychiatric manifestations. The age of onset is typically in the fourth or fifth decade.
- The absence of biochemical abnormalities and somatic features suggests a mitochondrial or metabolic disease or other systemic disorder.
- An infectious, toxic, or traumatic cause is not detected.
- Family history is consistent with autosomal dominant inheritance [3].

Method

The study was planned to be retrospective, cross-sectional, and descriptive. Retrospectively, the files and hospital automation system were scanned, and the diagnosed patients were identified. Patients diagnosed with Fahr's disease in the system were re-evaluated according to the diagnostic criteria. Possible etiologic investigations for Fahr syndrome and differential diagnosis of Fahr Syndrome-Fahr's Disease were reviewed. Demographic data, medical history, clinical complaints, examination findings, and laboratory tests (calcium, phosphorus, magnesium, alkaline phosphatase, parathormone) were noted. Neurological imaging (cranial computed tomography and magnetic resonance imaging) of the patients were re-evaluated. They were checked for possible Fahr's disease/syndrome. Descriptive values of the obtained data were determined as mean, standard deviation, number, and percentage frequency. The statistical significance level was 5%, and the Statistical Package for Social Sciences (IBM SPSS for Mac 26.0) program version 26 was used for statistical analysis.

Patients whose clinical information could not be obtained from medical records, pediatric patients under 18 years of age, and patients who were followed up with suspected Fahr's disease but received a different diagnosis were excluded from the study.

Consent was obtained from patients diagnosed with Fahr, and the Declaration of Helsinki was followed at all stages of the study. Ordu University Non-Invasive Scientific Research Ethics Committee approval was obtained, date: 07.03.2025, No: 2025/74.

Results

In the specified date range, 628 patients were examined in the general neurology outpatient clinic. Cranial imaging was indicated in 248 of these patients. Of the patients, 111 (45%) were male, and 137 (55%) were female, with an age range of 18-92 years (mean 55±3.2). Six patients who complied with the diagnostic criteria for FD/FS were identified in the patient group. (Frequency 0.95%) FD was considered in five patients. Hypoparathyroidism was detected in one patient and was interpreted as FS. Demographic characteristics, complaints at presentation, and results of the investigations are presented in Table 1. Three of the diagnosed patients were female, and three were male. While one patient was in the third decade, the others were diagnosed at older ages (6th, eighth, and ninth decades). One patient was diagnosed in the third decade, while the other patients were diagnosed at older ages (6th, eighth, and ninth decades). All patients complained of chronic headaches. Headache was the sole symptom reported by all patients. All patients' findings differed (gait disturbance, oral dyskinesia, seizures). Motor examinations showed no pathology. Elderly patients had neurologic complaints and a history of presentation to a neurology outpatient clinic.In the history of elderly patients, it was learned that they had neurologic complaints and hospital admissions. However, imaging and examination findings in the past years could not be reached.All our patients had bilateral calcifications of varying severity (CT images are presented in Figure 1). Imaging reports of the patients are presented in Table 2. Genetic testing was not available in the patient group.

Table 1. Demographic characteristics of the patients, complaints at presentation and results of investigations

Patient no	Gender	Age	Clinic	Ca (8.6-10.4 mg/dL)	P (2.5- 4.5 mg/dL)	Mg (1.6-2.6 mg/dL)	ALP (0 – 140 IU/L)	Vit D (ng/mL)	PTH (10-65 pg/ml)
1	M	63	Headache, daytime sleepiness	9.8	4.1	1.9	61	16	36
2	M	61	Headache	9.1	3.02	2.02	90	37	40
3	F	63	Headache, Paresthesia, oral dyskinesia	8.6	3.7	2	94	17	35
4	F	88	Headache, gait disturbance	9.4	3.5	1.8	77	24	72
5	F	92	Headache, Dementia	8.7	3.4	2.3	89	22	50
6	M	33	Headache, seizure, loss of cognition,	6.5	4.35	1.7	92	17	3.55

M: male, F: female, Ca: calcium, P: phosphorus, Mg: magnesium, ALP: alkaline phosphatase, Vit D: vitamin D, PTH: parathormone

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Table 2. Cranial imaging results of the patients

Patient no	Cranial computed tomography reports
1	Diffuse calcifications at the level of bilateral cerebellar hemispheres, mesencephalon and pons, basal ganglia and centrum semioval
2	Calcifications in all bilateral basal ganglia, subraventricular white matter, cerebellum dentate nuclei
3	Symmetrical calcifications at the level of both basal ganglia and in both cerebellar hemispheres
4	Calcifications in bilateral basal ganglia, periventricular white matter and cerebellar nucle
5	Rough calcifications were observed in both basal ganlia and left occipitotemporal lobe
6	Symmetric hyperdense calcified appearance in bilateral cerebral and cerebellar hemispheres

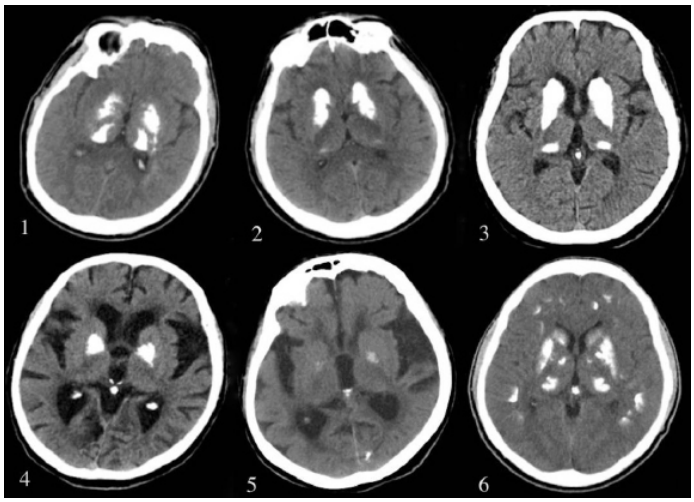

Figure 1. Cranial imaging of the patients (Patients 1-6)

Discussion

It is generally reported in the literature that FD is detected in the 4th or 5th decade. Clinically, patients may present with movement disorders, neuropsychiatric symptoms, or neurologic symptoms such as seizures, spasticity, speech impairment, myoclonus, and chronic headaches. Parkinsonism, ataxia and cognitive decline are the most common symptoms [3,4].

In our study, all patients except one were older. The frequency of visits to neurology outpatient clinics for various reasons increases with age. Since only the last one or two years of data were available, no clear information about the date of the first diagnosis could be obtained. The advanced age of our patients may be related to this reason or the progression of the neurodegenerative process with age in this patient group. Various studies have suggested that FD can be classified in two different clinical forms: early onset (under 40 years of age) and late-onset (over 50 years of age) [5,6]. Failure to differentiate between late presentation and delayed diagnosis is one of the limitations of our study. Our clinical findings were consistent with the cases reported in the literature as case reports. Despite the advanced age of the patients, various complaints other than movement disorders were detected.

The pathophysiology of FD has not been fully elucidated. Molecular and genetic evidence is limited. It is thought to be related to the possible dysfunction of cortico-basal connections and interhemispheric relations [7]. Most studies show that mutations in the SLC20A2 gene (40%) cause dysregulation of calcium and phosphate metabolism and decreased phosphate transport. Mutations in the PDGFRB (Platelet Derived Growth Factor Receptor Beta) genes have also been identified. These genes are important in the protection of the blood-brain barrier [8]. Neuropathologic findings suggest a common neuropathologic pathway involving pericytes and endothelial media in both FD and FS. Since we could not perform genetic analysis in our patients, it was not possible to comment. The most common endocrine disorders associated with intracerebral calcification are idiopathic hypoparathyroidism, secondary hypoparathyroidism (after thyroidectomy), and pseudohypoparathyroidism. Serum calcium, phosphorus, and parathormone analysis should be performed to exclude parathyroid abnormalities. In addition to endocrine disorders, neuroinfectious diseases should also be considered in the differential diagnosis. Possible etiologies include tuberculosis, brucellosis, and HIV positivity. Serum analysis of five of our patients for possible etiology did not reveal any pathologic values. Investigation for secondary diseases did not reveal any additional disease. Young patient number six had hypoparathyroidism. His blood picture was consistent and appropriate treatment was arranged in consultation with the endocrinologist. This patient was considered as FS. Patient number four was diagnosed with lung cancer during follow-up and had a mild elevation in creatinine. The high PTH value was thought to be secondary to these and the patient was considered in favor of FD.

Cranial computed tomography is valuable for diagnostic imaging in FD. All our patients had bilateral calcifications of varying severity (CT images are presented in Figure 1). MR/MR diffusion studies performed to identify possible hemorrhagic or ischemic problems did not detect these pathologies.

Fahr's disease should not be considered only as an intracranial calcification. The pathogenesis, clinical manifestations, and treatment approaches are diverse and complex. It is even difficult to determine the incidence of the disease. The literature has case reports, usually consisting of a single case. The literature reports its frequency as rare, but Chen et al. reported an estimated prevalence rate of 2.1 to 6.6/1000 people [9]. Movement disorders and extrapyramidal symptoms are common. However, numerous case reports report unusual clinical findings [10-12].

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In our study, we planned to draw attention to Fahr's disease. However, our limitations include our study's cross-sectional, retrospective nature, lack of access to the patient's past data, and lack of genetic analysis.

Conclusion

In conclusion, we think that FD/FS is a more common and under-recognized disease than known. It should be considered in the presence of appropriate clinical and radiological findings.

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.

Ethical Approval
Ordu University Non-Invasive Scientific Research Ethics Committee; 07.03.2025 Decision no: 2025/74.

References

1. Saleem S, Aslam HM, Anwar M, et al. Fahr's syndrome: literature review of current evidence. Orphanet J Rare Dis. 2013;8:156.
2. Lemos RR, Ramos EM, Legati A, et al. Update and mutational analysis of SLC20A2: a major cause of primary familial brain calcification. Hum Mutat. 2015;36:489-95.
3. Manyam BV. What is and what is not 'Fahr's disease'. Parkinsonism Relat Disord. 2005;11:73-80.
4. Amisha F, Munakomi S. Fahr Syndrome. 2023 Aug 13. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–.
5. Iqbal S, Nassar M, Chung H, et al. Fahr's disease with late onset: a case report. Cureus. 2022;14:e23316.
6. Choayb S, El Harras Y, Lahfidi A, et al. A rare case of Fahr disease revealed by an epileptic seizure. Radiol Case Rep. 2023;18:1954-6.
7. Lamessa A, Tesfaye K, Woyimo TG, Gebremichael EH. First-time seizure revealing late-onset Fahr's disease: a case report and brief literature review. Front Hum Neurosci. 2024;18:1456610.
8. Donzuso G, Mostile G, Nicoletti A, Zappia M. Basal ganglia calcifications (Fahr syndrome): associated conditions and clinical features. Neurol Sci. 2019;40:2251-63. Erratum in: Neurol Sci. 2019;40:2265.
9. Chen SY, Ho CJ, Lu YT, et al. The genetics of primary familial brain calcification: a literature review. Int J Mol Sci. 2023;24:10886.
10. Ayoub B, Chakib C, Khalil M, Hicham B. Fahr´ s disease presenting with epileptic seizures: a case report. PAMJ Clinical Medicine. 2020;3:55.
11. Adekanmi AJ, Bisi, Ayotunde I, Akinyemi R. Fahr's disease: Clinicoradiological findings of a rare disease in an adult Nigerian. West Afr J Radiol. 2020;27:155-8.
12. 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.