Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 10/04/2018
Approved on: 04/20/2020

ORIGINAL ARTICLE

# Fahr's syndrome in adolescence: a case report

Karla Souza da Costa[1], Jamson Barreto Nunes Junior[1], Guilherme Truppa Giunzioni[1], Maria de Fatima Valente Rizzo[1], Gabriela Paladini[1]

**Keywords:**
Calcinosis,
Basal Ganglia,
Seizures,
Adolescent.

## Abstract

We present here a case of Fahr's disease in the pediatric age group. Fahr's disease is a neurological, degenerative and rare disease, especially in this age group. It differs from Fahrs syndrome, which is associated with infectious pathologies, such as human immunodeficiency virus infection and metabolic causes, such as hypoparathyroidism. In contrast, Fahr's disease has an idiopathic or familial cause and is related to neuropsychic symptoms. However, the differentiation of these terms is still poorly established in the literature. It has an unknown prevalence and affects individuals of both sexes in any age group, and individuals from the 4th decade are more likely to develop it. It has polygenic etiology being autosomal dominant, characterized by abnormal deposits of minerals, including mainly calcium and phosphate in the basal ganglia. It presents extra-pyramidal, psychiatric and epileptic manifestations. It is an incurable disease with progressive and irreversible evolution. Due to the involvement of the central nervous system, the prognosis is reserved and eventually fatal. The patient in question was MF, 15-years-old, male, with severe holocranial headache and convulsive crisis with findings of calcifications in the base ganglia bilaterally tomography of the skull.

[1] Medical School of Jundiaí, Pediatrics Department - Jundiaí - São Paulo - Brazil.

**Correspondence to:**
Karla Souza da Costa.
Faculdade de Medicina de Jundiaí (Departamento de Pediatria). R. Francisco Teles, 250 - Vila Arens II, Jundiaí - SP, Brazil.
CEP: 13202-550. E-mail: karlacostamed@gmail.com

## INTRODUCTION

Fahr's disease (DF), eponymous to idiopathic basal ganglia calcification, refers to bilateral idiopathic basal ganglia calcification (IBGC), sporadic or familial, supposedly an autosomal dominant disease. Despite being named after Theodor Fahr, the disease has been known since 1850, many years before his description in 1930. Theodor Fahr reported the case of an 81-year-old man with epileptic seizures and diffuse calcification of brain vessels and basal ganglia, probably related to hypoparathyroidism, and therefore not idiopathic, with a probable relationship with infections, such as Epstein-Barr, immunodeficiency by the HIV virus, lupus erythematosus, perinatal hypoxia, radiation or chemotherapy, carbon monoxide poisoning and prolonged use of anticonvulsants[1]. Some authors use the term Fahr's syndrome to describe pathological calcification of the basal ganglia that can be caused by diseases of different etiologies[2] but the differentiation between syndrome and disease is not yet well established, and there is no consensus about it in the literature.

It is a rare disease, with manifestations of a variable combination of abnormal movements, parkinsonism, dementia, seizures and cerebellar dysfunction. The diagnosis is usually clinical, associated with hypocalcemia and calcification of the basal ganglia in imaging exams. It is an incurable disease, with progressive and irreversible evolution. Due to the involvement of the central nervous system, the prognosis is poor and eventually fatal[3].

The causes of intracranial calcifications are multiple and can be physiological, primary (idiopathic, familial) or secondary. These are more frequently associated with parathyroid dysfunction (primary, post-surgical, idiopathic hypoparathyroidism, pseudo-hypoparathyroidism, pseudo-pseudo hypoparathyroidism, hyperparathyroidism), in addition to other causes[4].

Four primary family cerebral calcification genes have been identified, on chromosome 14q for Fahr's disease, among them SLC20A2, PDGFB, PDGFRB and XPR1, with pathogenic variants, which can present incomplete penetration in patients, leading to a great diversity in age and symptoms[5,6]. Mutations in SLC20A2 and PDGFB, which encodes the phosphate-2 transporter, is the main cause of IBGC, showing high levels of inorganic phosphate in the cerebrospinal fluid, which can be a good biomarker for Fahr's disease[7,8].

A study carried out in 2007 found that among 1,569 healthy individuals, 0.8% had calcifications in the basal ganglia on CT, apparently without any symptoms, inducing the authors to consider them "physiological" intracranial calcifications. When these findings are present in individuals under 40 years of age, simultaneously involving the pale globe, putamen, cerebellar dentate nucleus and white matter, they are considered pathological[9].

## CASE REPORT

MF, male, 15 years old, admitted to the Children's Emergency Room of the Jundiaí University Hospital (HU), Jundiaí, São Paulo, with severe holocranial headache, vertigo, visual scotoma and divergent strabismus of the right eye. He had no fever, nausea, vomiting or sphincter release. He had had fatigue for about 5 days preceding the condition. No episode of headache and previous seizures. During the initial treatment, he presented a brief episode of head deviation to the right side, tremor in the R hand and R eye consecutively, which ceased spontaneously. On physical examination, he was collaborative, with isochoric and photoreactive pupils, without meningeal signs, and without motor and sensory deficits. As a hypothesis, he was diagnosed with a focal seizure crisis, and carbamazepine was introduced without recurrence. A contrasted skull computed tomography scan showed important and symmetrical calcifications of the basal ganglia, suggesting a diagnosis of Fahr's disease, as shown in Figure 1.

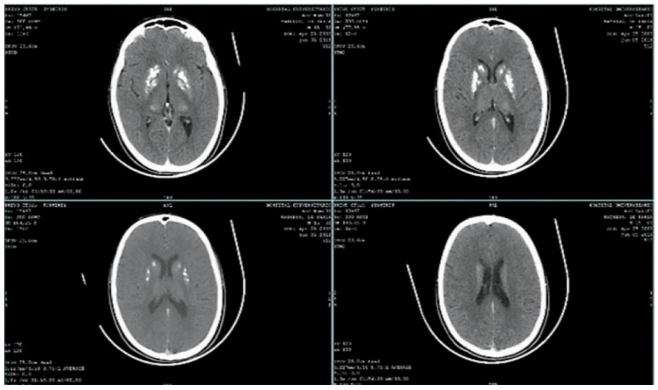


**Figure 1.** Skull contrasted CT scan showing bilateral calcifications in the basal ganglia

During the hospitalization period, he developed a generalized tonic-clonic seizure crisis, and after being medicated with Diazepam®, he improved. The patient spent the period of hospitalization without any other seizure episode. We continued with complementary laboratory tests to rule out infectious, systemic and endocrine causes. He had leukocytosis, without left shift and borderline vitamin D level.

The patient remained hospitalized for 5 days, asymptomatic, using carbamazepine. He was then discharged for outpatient follow-up with a neuropediatrician. The skull CT findings, laboratory tests without changes and clinical history suggested a diagnosis of Fahr's disease.

## DISCUSSION

The reported case deals with Fahr's disease, or idiopathic calcification of the basal ganglia, which was recently called primary familial brain calcification (PFBC), a rare polygenic and probably autosomal dominant condition,

characterized by abnormal mineral deposits, including mainly calcium and phosphate in the brain, especially in the basal ganglia, with manifestations of movement disorders, neuropsychiatric symptoms and epilepsy in a small number of patients[7,8].

The prevalence of this disease is still unknown, it affects individuals of both sexes, in any age group, and those with 4o years of age onwards are the most susceptible to the development of the disease[3,5].

There are but a handful of reports of childhood cases in the scientific literature: in a child under 2 years of age, from Bangladesh, with delayed motor development[10]; and two male and female siblings in China, whose first manifestation was extrapyramidal movement disorder, in the first at 15 years of life, and seizure in the second at 2 years of age. Both evolved with deterioration of motor function in adulthood, a condition from which they obtained the definitive diagnosis of Fahr's disease[11]. In Brazil, the presentations found refer only to clinical conditions in adults.

This case report portrays a rare condition described in the literature, the presentation of Fahr's disease in a 15-year-old adolescent, who presented with headache, holocranial tremors, focal seizure crisis and, consecutively, tonic-clonic seizure crises.

Fahr's disease can present in an "asymptomatic" way. However, when symptomatic, it presents with variable clinical picture, ranging from neurological symptoms, including impairment of cognitive function (dementia), motor and language changes, seizures, headache, muscle hypertonia, as well as extrapyramidal manifestations such as parkinsonism, dystonia and tics[12,13,14]. Clinical manifestations may be associated with disease duration and the injury sites initially involved. The patient in this case report presented an episode of tremor in the right hand right eye, focal seizure and tonic-clonic seizure in the initial examination. The most common clinical condition is movement disorder, which affects about 55% of cases (parkinsonism in 57% of cases, chorea in 19%, tremor in 8%, dystonia in 8% and orofacial dyskinesia in 3% of cases)[15].

Calcification may worsen with advancing age, concomitantly with symptoms, progressing to degenerative disorder, which prognosis is variable and poor.[1,13,16]

Abnormal bilateral calcifications in the basal ganglia, seen on computed tomography can be used as a reliable diagnosis clue, whatever the clinical condition of the patient. Pathology studies demonstrate that calcium is the main element present. There are also mucopolysaccharides, traces of aluminum, copper, iron, among others[17]. These deposits, especially calcium, are responsible for the aspect observed in the neuroimaging.[4] The electroencephalogram can be used to accurately classify epilepsy in a patient with primary familiar cerebral calcification.[7] The patient in this case report had no previous history of seizures, being the first occurrence to the diagnosis of calcifications in the basal ganglia, during his hospitalization. We could not do an electroencephalogram, due to the unavailability of the equipment in our service, and upon discharge, the patient was referred for evaluation and monitoring by a neurologist.

One must rule out other causes of intracranial calcification, such as CMV infection, neurocysticercosis, toxoplasmosis, neurobrucellosis, neurotuberculosis, HIV infection, astrocytomas, calcified infarction, pseudo hypoparathyroidism, hyperparathyroidism due to lead poisoning, vitamin D hypervitaminosis, encephalopathic diseases and encephalopathies[18], and tuberous sclerosis, Down syndrome, Tay-Sachs disease and Cockayne syndrome[5]. The laboratory investigation carried out in the present case study, ruled out any infectious, metabolic causes, and calcium disorders, with the presence of borderline vitamin D values, and the absence of calcifications in the cerebral cortex. Therefore, we emphasize that Fahr's disease is a very probable diagnosis for this case, and it is therefore necessary to monitor the patient.

The therapeutic approach to Fahr's disease is based on the symptoms presented by the patient, who should receive supportive and long-term follow-up.[11] There is no definitive treatment for Fahr's disease. The patient addressed in this case report; we treated with carbamazepine for focal seizure and Diazepam® during tonic-clonic seizure.

## CONCLUSION

Fahr's disease is a rare condition, especially in the pediatric age group, which in the present case had holocranial headache, tremors, focal and tonic-clonic seizures, and it is important to stand out as a major differential diagnosis, in view of the disease progression and that it has no specific treatment. There are but a handful of reports in the national and international scientific literature.

## REFERENCES


1. Kümmer A, Castro M, Caramelli P, Cardoso F, Teixeira AL. alterações comportamentais graves em paciente com doença de Fahr. Arq Neuropsiquiatr. 2006;64(3-A):645-9.
2. aria AV, Pereira IC, Nanni L. Computerized tomography findings in Fahr's syndrome. Arq Neuropsiquiatr. 2004 Oct;62(3-B):789-92.
3. Malheiro A, Pestana N, Granito S, Pestana A, Costa AI, Brazão ML. Doença de Fahr: um caso clínico inesperado. Med Intern. 2017;24(1):33-5.
4. Conforto LB, Tiel C, Gasparetto E, Cavalcanti JLS, Engelhardt E. Doença de Fahr. Rev Bras Neurol. 2009;45(2):47.
5. Gaël N, Charbonnier C, Campion D, Veltrman JA. Estimation of minimal disease prevalence fron population genomic data: aplication familial brain calcification. Am Med Genet B Neuropsychiatr Genet. 2018 Jan;177(1):68-74.
6. Geschwind DH, Loginov M, Stern JM. Identification of a locus on chromosome 14q for idiopathic basal ganglia calcification (Fahr Disease). Am J Hum Genet. 1999 Sep;65(3):764-72.
7. Knowles JK, Santoro JTD, Porter BE, Baumer FM. Refractory focal epilepsy in a paediatric patient with primary familial brain calcification. Seizure. 2018 Mar;56:50-2.

8. Hozumi I, Kurita H, Ozawa K, Furuta N, Inden M, Sekine SI, et al. Inorganic phosphorus (Pi) in CSF is a biomarker for SLC20A2-associated idiopathic basal ganglia calcification (IBGC1). J Neurol Sci. 2018 May;388:150-4.
9. Savino E, Soavi C, Capatti E, Borrelli M, Vigna GB, Passaro A, Zuliani G. Bilateral strio-pallido-dentate calcinosis (Fahr's disease): report of seven cases and revision of literature BMC Neurol. 2016 Sep;16(1):165.
10. Rahman A, Begum R S, Hossain M Z, Ali MR, Rahman M. Fahr's disease: a rare neurodegenerative disorder in children. J Dhaka Med Coll. 2011;20(1):86-8.
11. Hong W, Bei S, Liuqing W, Qiang Y Fahr's disease in two siblings in a family: a case report. Exp Ther Med. 2015 May;9(5):1931-3.
12. Benke T, Karner E, Seppi K, Delazer M, Marksteiner J, Donnemiller E. Subacute dementia and imaging correlates in a case of Fahr's disease. J Neurol Neurosurg Psychiatry. 2004;75:1163-5.
13. König P. Psychopathological alterations in cases of symmetrical basal ganglia sclerosis. Biol Psychiatry. 1989 Feb;25(4):459-68.
14. Avrahami E, Cohn DF, Feibel M, Tadmor R. MRI demonstration and CT correlation of the brain in patients with idiopathic intracerebral calcification. J Neurol. 1994 May;241:381-4.
15. Gomille T, Meyer RA, Falkai P, Gaebel W, Kongshausen T, Christ F. Pravalenz und klinische Bedeutung computertomographisch gesicherter idiopathischer Stammganglienverkalkungen. Radiologe. 2001;4:205-10.
16. Brodaty H, Mitchell P, Luscombe G, Kwok JJ, Badenhop RF, McKenzie R, et al. Familial idiopathic basal ganglia calcification (Fahr's disease) without neurological, cognitive and psychiatric symptoms is not linked to the IBGC1 locus on chromosome 14q. Hum Genet. 2002;110(1):8-14.
17. Manyan BV, Walters AS, Narla KR. Bilateral striopalliododentate calcinosis: clinical characteristies of pacients seen in a registry. Mov Disord. 2001 Mar;16(2):258-64.
18. Malik R, Panday VK, Naik D. Fahr's disease. A rare neurodegenerative disorder. Int J Radiol Image. 2004;14:383-4.