CASE REPORT

Fahr's disease: bilateral symmetrical striopallidodentate calcification in two brothers with two distinct presentations

Abdalla Bowirrat,¹ Mustafa Yassin,² Faozi Artoul,³ Suheil Artul⁴

¹Department of Neuroscience, EMMS Nazareth Hospital, Nazareth, Israel

²Department of Orthopaedic, Rabin Medical Center, Tel-aviv, Israel

³Department of Nuclear Medicine, Meir Hospital, Kfar Saba, Israel

⁴Department of Radiology, EMMS Nazareth Hospital, Nazareth, Israel

Correspondence to

Professor Bowirrat Abdalla, Prof.Bowirrat@yahoo.com

SUMMARY

Bilateral striopallidodentate calcinosis, commonly known as Fahr's disease is a rare clinical entity present mainly with extrapyramidal signs and accompanied with metabolic, biochemical, neuroradiological and neuropsychiatric situations. It is characterised by the symmetrical and bilateral intracranial deposition of calcium associated with cell loss in the basal ganglia, cerebral cortex and cerebellum. In this study, we discussed two brothers' cases of Fahr's diseases who presented with different symptomatology. The first presented with walking difficulty, cramps and dysarthria and moderate memory impairment whereas the second with vertigo, ataxia, forgetfulness and headache. CT scans of both patients revealed intracranial diffuse bilateral calcifications in the basal ganglia and the cerebellum. The second patient revealed progressive cerebral atrophy but reduction in the calcification. Fahr's disease, although encountered rarely, should also be taken into account in the differential diagnosis of cases with abnormal intracranial calcifications along with other familial, congenital and metabolic diseases and syndromes.

BACKGROUND

In this unique study, we described two brothers with Fahr's disease (FD), which emphasises the fact that FD can be present in various heterogeneous manifestations even in the same family and can be met also in patients with unknown family history of disease based on a suggestive calcification pattern correlated with neuropsychiatric manifestations, in absence of biochemical abnormalities, infectious, toxic or traumatic causes.

CASE PRESENTATION

Case reports

The first brother case (March 2013)

A 52-year-old married man was referred for the evaluation of 1 year history of continuous headache, moderate memory impairment, dysarthria and difficulty walking accompanied by frequent cramps. Except for these symptoms, the patient's medical history was unremarkable. There was no family history of mental illness, dementia or major physical illness. He did not have depressive or psychotic symptoms. He scored 27/30 in his Mini-Mental State Examination (MMSE) and was able to maintain normal independent daily living activity. He had deficits on frontal lobe tasks including verbal fluency and task shifting. No parietal lobe signs, and nor any clinical features suggestive of hypoparathyroidism were found.

The second brother case

In May 2013, a 45-year-old married man presented to the emergency room with a history of ataxia, headache, forgetfulness, dizziness and vertigo. Extensive investigations began and neurological examination had confirmed the patient's findings. He did not have depressive or psychotic symptoms. He scored 28/30 in his MMSE and was able to maintain normal independent daily living activity.

INVESTIGATIONS

First brother's laboratory investigations including whole blood count, urine analysis, sedimentation rate, fasting blood glucose, blood electrolytes, thyroid hormones, blood serum iron, ferritin, and total iron binding capacity showed no abnormality. Blood calcium 8.19 mg/dL (8.2–10.2 mg/dL), blood phosphate 3.7 mg/dL (3–4.5 mg/dL), blood ceruloplasmin 28 mg/dL (20–45 mg/dL) and parathyroid hormone levels 36.306 pg/mL (15–65 pg/mL) were in normal limits. IgM and IgG for toxoplasma gondii were negative. On neurological examination the patient had rigidity of the lower limbs with gait instability and moderate dysarthria characterised by slurred or slow speech that can be difficult to understand. Non-contrast axial CT scan of the brain was performed and showed coarse calcification in the basal ganglia and the thalamus (figure 1).

Physical examination of the second brother's case was unremarkable. Laboratory and endocrinological

Figure 1 Non-contrast axial CT scan of the head showing subcortical coarse calcification in the basal ganglia and thalamus.

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investigations were within normal range: whole blood count, urine analysis, sedimentation rate, fasting blood glucose, blood electrolytes, thyroid hormones, blood serum iron, ferritin, and total iron binding capacity showed no abnormality. Blood calcium 8.78 mg/dL (8.2–10.2 mg/dL), blood phosphate 3.4 mg/dL (3–4.5 mg/dL), blood ceruloplasmin 24 mg/dL (20–45 mg/dL) and parathyroid hormone levels 45.376 pg/mL (15–65 pg/mL) were in normal limits.

Toxoplasmosis was excluded by examining the levels of IgM and IgG, which were negative. No thyroid disease or vitamin deficiency could be found. Brain non-contrast axial CT scan documented marked and symmetrical calcification in the dentate nuclei of the cerebellum (figure 2). The CT scan findings when correlated with typical clinical history and normal blood chemistry were suggestive of FD.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes Parkinson's disease, Huntington's chorea, Wilson's disease, oligodendroglioma, low-grade astrocytoma, Binswinger's disease, also infectious disease (*Brucella*, Epstein-Barr virus infections, tuberculosis, AIDS), and parathyroid disorders. All the aforementioned differential diagnoses were effectively ruled out in our cases. Therefore, FD or BSPDC is a diagnosis of exclusion.

TREATMENT

There is neither a cure for FD, nor a standard course of treatment. The prognosis is variable and hard to predict.

OUTCOME AND FOLLOW-UP

The present paper presents two distinct cases belonging to two family members and in turn emphasises the fact that FD can be present in various heterogeneous manifestations even in the same family and can also be met in patients with unknown family history of disease based on a suggestive calcification pattern correlated with neuropsychiatric manifestations, in the absence of biochemical abnormalities, infectious, toxic or traumatic causes. We also observed that CT scan is considerably more sensitive device than X-rays and MRI to detect intracerebral calcifications.

Figure 2 Non-contrast axial CT scan of the head showing subcortical coarse calcification in the cerebellum.

DISCUSSION

FD is a rare, insidious, idiopathic neurodegenerative disease, which can be present in various heterogeneous manifestations and characterised by non-arteriosclerotic bilateral symmetrical calcification of cerebral vessels, with predilection for certain regions of the brain, such as basal ganglion, thalami, subcortical hemispherical white matter and deep cerebellar nuclei.¹

FD may have familial aggregation, with autosomal dominant or autosomal recessive transmission. Geschwind *et al*² have described a locus IBGC1 ('idiopathic basal ganglia calcification') on chromosome 14q involved in the IBGC1. One multigenerational family with linkage to the IBGC1 of chromosome 14 has been identified but the causal gene is still unknown. However, genetic studies on other families did not replicate these results.³

The expressivity within the family is variable and genetic heterogeneity and an anticipatory affect have been observed; age of onset is decreasing progressively with each transmission in the family in case of the autosomal dominant inheritance. There are also sporadic cases with no family history of disease, apparently with no genetic component. In the cases without modification of 14q chromosome, the neurological and psychiatric symptoms are moderately mild or absent.⁴

The most common sites of calcifications are basal ganglia and dentate nuclei of cerebellum. Hence, one of the other names of the disease is BSPDC. However, calcification can involve centrum ovale, thalami, cerebral cortex, subcortex and no part of the brain could be spared.^{5–6} FD has a broad spectrum of clinical manifestations in the form of neuropsychiatric disorders, neurological symptoms and cognitive involvement.^{7–8}

Patients can be presented with pyramidal and extrapyramidal symptoms, cerebellar dysfunctions, speech difficulties, executive and cognitive impairment, seizures and pain.⁶

The wide ranging of signs and various presentations, depend on which part of the brain was affected by the lesions. Usually, about 50% of patients with BSPDC have neurological features in the form of headache, vertigo, movement disorders, paresis, transient ischaemic attacks, seizures and syncope. Indeed, our first case presented with walking difficulty, cramps and dysarthria and moderate memory impairment, and the second case was presented with vertigo, ataxia, forgetfulness and headache.⁵

Manyam *et al*⁹ reported movement disorders in 56%, parkinsonism 57%, chorea 19%, tremor 8%, dystonia 8%, athetosis 5% and orofacial dyskinesia 3% and Konig¹⁰ reported that about 40% of patients with FD present initially with cognitive and psychiatric features. Mild-to-moderate cognitive impairments also were presented in our cases, with MMSE scores of 27/30 in the first case and 28/30 in the second.

Learning points

- ▶ Fahr's disease may have familial aggregation, with autosomal dominant or autosomal recessive or sporadic form.
- ▶ Familial cases may have different presentations of the disease.
- ▶ Fahr's disease has a wide range of clinical manifestations in the form of neuropsychiatric disorders, neurological symptoms and cognitive involvement. Furthermore, in the literature there were reported asymptomatic cases.
- ▶ CT scan was demonstrated to be the ideal device for the diagnosis.

Contributors AB: Conceived the study, and participated in its design and coordination and wrote almost all the article (introduction & discussion) and helped to draft the manuscript. MY: Carried out the study design and participating in writing and editing the case study. FA: Participated in the radiological analysis, and wrote and editing the manuscript. SA: Participated in the collections of data and study design, editing the manuscript and participated in writing part of the introduction. All coauthors have read and approved the final manuscript.

Competing interests None.

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