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Case Report

Fahr syndrome - an incidental finding in a patient with lymphocytic meningitis ☆☆☆

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ABSTRACT

Fahr syndrome is a rare condition mainly characterized by symmetric and bilateral calcification of basal ganglia and cerebellar nuclei. Herein, we report a case of a 67-year-old woman with a history of parathyroidectomy and Parkinsonism, who was admitted to hospital with suspected neuroinfection, and imaging features that were consistent with Fahr syndrome. The objective of this study is to teach clinicians about a neurologic illness that requires comprehensive medical and neurologic investigation due to the manifestations of lymphocytic meningitis might distract you from Fahr syndrome symptoms.

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Introduction

Fahr syndrome is a rare inherited or sporadic neurodegenerative condition associated with symmetric intracerebral calcifications of the basal ganglia and adjacent parenchyma most easily visualized on CT scan. Around these calcifications neuronal degeneration and gliosis occur [1,2,3]. Clinical symptoms of this disorder are varied, ranging from progressive movement disorders including Parkinsonism, chorea and dystonia to neuropsychiatric abnormalities of memory, and concentration [4]. The variety of symptoms may resemble many other diseases, for example neurologic, cardiologic, urologic, and psychiatric illnesses [5]. A positive family history is important when considering the diagnosis of Fahr syndrome [6]. We present a case of Fahr syndrome incidentally diagnosed in a patient with lymphocytic meningitis with a prior history of parathyroidectomy and parkinsonism.

Case presentation

A 67-year-old woman with a history of parathyroidectomy (10 years earlier) and Parkinsonism was admitted to the hospital with suspected neuroinfection. The day before hospitalization she lost consciousness and also had a few days history of personality and mood changes. In anamnesis, the patient was disorientated. Physical examination also revealed symptoms of dehydration, meningeal signs (nuchal rigidity and Kernig sign), unsteady gait, moderate rigidity, and resting tremor of both upper limbs. The laboratory tests showed: hypokalemia, 2.97 mmol/L (norm: 3.5-5.0 mmol/L), hypomagnesemia, 0.7 mmol/L (norm: 0.8-1.0 mmol/L), hypocalcemia, 1.59 mmol/L (norm: 2.12-2.62 mmol/L), hyperphosphatemia, 5.8 mg/dL (norm: 2.8-5.0 mg/dL), leukocytosis, $17.6 \times 10^3/\mu\text{L}$ (norm: $4.0\text{-}10.0 \times 10^3/\mu\text{L}$), increased values of CRP, 45.6 mg/L (norm: 0-5.0 mg/L), and ESR, 36 mm/hr (norm: 12-17 mm/hr). The cerebrospinal fluid (CSF) was macroscopically clear with inflammatory features: cytosis – 26 cells/mm³ (norm: 0-8 cells/mm³) and protein – 0.584 g/L (norm: 0.15-0.45 g/L), while glucose level was within normal range. Direct examination of CSF showed no organisms after Gram stain. Viral meningitis was suspected. Serologic examinations for human immunodeficiency virus (HIV), herpes simplex virus (HSV), tick-borne encephalitis (TBE), and *Treponema pallidum* were negative. A blood and CSF culture were negative. One day after admission, the patient's mental status became progressively worse, she experienced severe impairment of memory functions and reduced psychomotor speed. Computed tomography (CT) and magnetic resonance imaging (MRI) of the head showed symmetrical calcifications in the both hemispheres of the brain, located in subcortical and paraventricular regions (ie in the caudate nucleus and lenticular nucleus), and in the both cerebellar hemispheres (Fig. 1). Based on the classical imaging findings, a diagnosis of Fahr syndrome was made.

From the first day of patient's stay, her initial management consisted of intravenous rehydration and empiric antimicrobial therapy immediately after lumbar puncture to cover all potential organisms (combination of vancomycin, ampicillin,

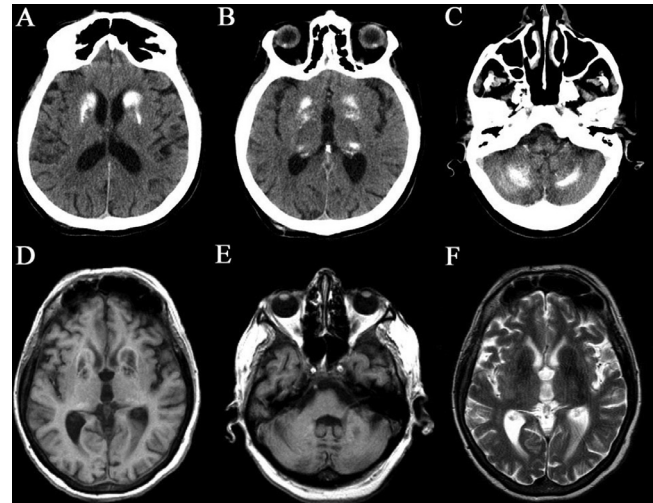


Fig. 1 – Axial non-enhanced brain CT (A-C): massive, relatively symmetrical and coarse calcifications located in the caudate nuclei, putamina, lateral globi pallidi and in the pulvinae of both thalami (A, B) and in both cerebellar hemispheres (C). Cortical and subcortical atrophy in supra- and infratentorial region. Corresponding axial non-enhanced brain MRI (D-F) showing calcifications of bilateral basal ganglia and thalami (D, E) and in both cerebellar hemispheres (F), but to a lesser extent than CT.

ceftriaxone and acyclovir), until receiving above-mentioned microbiology test results. Due to features of parkinsonism, the combination drug carbidopa-levodopa was started additionally. The rehydration therapy led to return of full consciousness by day 4 after admission. After 3 weeks the patient was discharged home. Features of dehydration and meningeal signs resolved, however bilateral, but currently mild rigidity, and resting tremor of both upper limbs persisted.

Discussion

The terms of Fahr syndrome, Fahr disease, and bilateral striopallidodentate calcinosis (BSPDC) are often used interchangeably but this is a mistake. Fahr disease is described as a primary, idiopathic form of basal ganglia calcifications. This denomination means the same as bilateral striopallidodentate calcinosis (BSPDC), primary familial brain calcification (PFBC), and calcinosis nucleorum. These terms could be used for basal ganglia calcifications without metabolic or other unidentified causes. On the other hand, Fahr syndrome is reported as secondary basal ganglia calcifications which are connected with hypoparathyroidism (for example after parathyroidectomy like in our patient), cerebrum infection, genetic mutations, and poisoning with toxins [7,8].

Typical clinical manifestations of this condition are neurologic symptoms: loss of consciousness, tetany, seizures, epileptic disorder, gait disorder, spasticity, speech impairment, dementia, myoclonus, coma, paroxysmal choreoathetosis, dys-

tonic choreoathetosis, papilledema of intracranial hypertension, pleocytosis of CSF. Other symptoms can be movement disorders, for example clumsiness, fatigability, unsteady gait, involuntary movements and muscle cramping; and also neuropsychiatric features like psychosis, depression, apoplexia, deterioration of intelligence, inability to make decisions [6]. The diagnosis of Fahr syndrome includes brain imaging and clinical symptoms. It is very important to exclude other causes of intracerebral deposits, which can be toxoplasmosis, parathyroid disorders, SLE, vascular lesions, and other diseases [9]. The prognosis of Fahr syndrome is incalculable, the clinical course can be variable. There is no independence between symptoms at onset, age of patients or range of calcifications with prognosis [8].

The epidemiology of Fahr syndrome is more or less unknown because investigations of patients' families are inadequate [8]. In our patient's family there was not any case of Fahr syndrome. Non-family history-based Fahr syndrome is infrequently described [6]. In reported cases the majority of patients are healthy in their childhood and the neurodegenerative disorder occurs in adulthood. The patient was 67 years old, which is unexpected, the Fahr syndrome is usually reported in age 40–50 [8].

Fahr syndrome is considered as an autosomal dominant disorder with deficient and age-related penetrance. However, Fahr syndrome can also be an autosomal recessive disease or appear sporadically. Four genes are involved in molecular base of Fahr syndrome: SLC20A2 (40%), PDGF β (11%), XPR1 (2%), PDGFR β (2%). Other gene mutations are unknown. Other locations associated with Fahr syndrome contain IBGC1 locus at chromosome 14q, a locus at chromosome 8, and the last 1 at chromosome 2q [8].

The pathophysiology of abnormal calcium deposition in Fahr syndrome (bilateral basal ganglia calcifications is common, particularly in elderly, but the calcifications in Fahr syndrome is coarser and more dramatic) is associated with atypical metabolism of calcium in cerebrum or metastatic deposition because of blood-brain barrier dysfunction. This tissue damage due to calcification is connected with free radicals and faulty iron transport. The calcium deposition begins in the walls of the capillaries, arteries, veins and perivascular space. It increases slowly to the whole neuron [8]. Components such as calcium phosphate and carbonate are discovered in deposits, as well as glyconate, mucopolysaccharide and metals (iron, magnesium, zinc, aluminum, copper, cobalt and silver) [6,10,11,12].

The most probable symptom attributable to dehydration was fever (38°C), which was caused by infection – mild lymphocytic meningitis, which is self-limiting disease led by unknown viruses (purulent meningitis was excluded). The dehydration and the fever may cause disorders of consciousness (especially in elderly). The rapid decline of functions was associated with lymphocytic meningitis, not with Fahr syndrome.

Furthermore, Parkinsonism accounts for over 50% of all movement disorders in the course of Fahr syndrome and it occurred in our patient. Clinical manifestations of Fahr syndrome are reported in the literature as individual case reports or as single-family reports due to rare occurrence of this condition [1]. Endocrine disorders, particularly hypoparathyroidism, are most commonly associated with Fahr syndrome.

CT and MRI revealed symmetrical calcific alterations in the subcortical and periventricular regions of cerebrum and in the both cerebellar hemispheres which are consistently reported in Fahr syndrome.

Conclusions

Fahr syndrome is an uncommon illness associated with many diseases, but with no identified particular etiologic agent [6]. Genetic mutations, which were found recently, help to differentiate between primary, and secondary disease [7]. This case report describes a presentation of Fahr syndrome in a patient who has parkinsonism and severe psychiatric manifestation related to this process. In our patient, the Fahr syndrome was secondary to endocrinopathy (parathyroidectomy), and to the neuroinfection. The purpose of this case is to educate doctors about an uncommon neurologic condition that necessitates extensive medical and neurologic assessment because symptoms of lymphocytic meningitis can distract you from the symptoms of Fahr syndrome.

Patient consent

An informed consent was obtained from the patient for publication of this case and any accompanying images. All patient identifying information has been stripped from the images. Additionally, no patient identifying information is used in the case report.

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