Case Report

Fahr's disease with epilepsy, deafness, schizophreniform psychosis and autoimmune polymyositis: a case report

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Competing interests
None declared

Authors' contribution
Both authors have substantial contributed to conception and design, acquisition of data, or analysis and interpretation of data. Dr Viteva had a substantial role in drafting the article

Received: 4 September 2014
Accepted: 10 March 2015

The Rare Diseases and Orphan Drugs Journal has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under Grant Agreement n. 305690 RARE-Bestpractices project www.rarebestpractices.eu.
Sole responsibility lies with the authors and the European Commission is not responsible for any use that may be made of the information contained therein.

Abstract

Fahr's disease is a rare sporadic or inherited neurodegenerative disorder characterized by symmetrical bilateral calcifications in the basal ganglia and some other brain structures – dentate nucleus, thalamus, cerebral cortex, subcortical white matter, and hippocampus.

We report a patient with Fahr's disease who was monitored for 11 years. The case is of interest for clinical practice because of the following features: 1. the patient fulfills the Fahr's disease criteria with the exception of family history consistent with autosomal dominant inheritance; 2. early disease onset (20 years of age) with a generalized tonic-clonic seizure; 3. despite calcifications in the region of the basal ganglia on CT scans, there are no clinical signs of extrapyramidal system abnormalities; 4. rare epileptic seizures (4 generalized tonic-clonic seizures for the whole period of observation); 5. generalized paroxysmal activity of delta waves on only one EEG which could not be regarded as a specific finding; 6. autoimmune polymyositis as a concomitant disease, which improved by specific treatment; 7. diagnosis of complete deafness 6 years after Fahr's disease onset; 8. typical psychotic symptoms 9 years after the first epileptic seizure; 9. Fahr's disease evolution was proven 11 years after initial symptoms by CT scan visualization of new bilateral symmetrical calcifications in the cerebellar hemispheres and respective clinical manifestations – static and locomotor ataxia. We found no case reports in the literature with a similar combination of clinical manifestations and progression.

In conclusion, this case report provides additional information about the clinical characteristics and management of patients with Fahr's disease.

Key words

Fahr's disease, epilepsy, psychosis, polymyositis, deafness.

Introduction

Fahr's disease (familial idiopathic calcification of the basal ganglia) was first described by the German neurologist Theodor Fahr in 1930 [1]. It is a rare (prevalence of <1/1,000,000) sporadic or inherited neurodegenerative disease characterized by symmetrical bilateral calcifications in the basal ganglia and some other brain structures – dentate nucleus, thalamus, cerebral cortex, subcortical white matter, and hippocampus [1, 2]. It has been recognized as a sporadic or inherited disease with identified loci in chromosomes 2, 8 and 14q and autosomal dominant type of inheritance [2-4].

The most frequent initial symptoms are associated with extrapyramidal system disorders [1], including Parkinson syndrome [2], choreoathetosis [5] and dystonia [6]. Other symptoms include coordination impairment [1, 2], dysarthria [1, 2], psychiatric disorders (depression, anxiety, visual, auditory hallucinations, delusions, mania, personality and behavior problems, schizophreniform psychoses, delirium) [1-3, 7-9], cognitive impairment as a part of subcortical dementia (impaired verbal, visual-spatial memory, planning, attention, concentration, visual constructive abilities) [10-11]. Epileptic seizures (complex partial seizures) [2, 12], stroke-like incidents [2], vertigo [2], headache [2], paresis [2], orthostatic hypotonia [1, 2] have been rarely described.

Diagnostic methods: 1. CT scan – a basic method, more effective than MRI; 2. SPECT – it shows increased blood flow in both temporal lobes; 3. EEG – there is no specific EEG pattern [13].

The modern modified criteria of Manyam 2005 for Fahr's disease can be summarized as follows [1]:

1. bilateral calcification of the basal ganglia on neuroimaging. Other brain regions may also be involved;
2. progressive neurologic dysfunction, usually including a movement disorder and/or neuropsychiatric manifestations. Age of onset is typically in the fourth or fifth decade, although this dysfunction may also present in childhood;
3. absence of biochemical abnormalities and somatic features suggestive of a mitochondrial or metabolic disease or other systemic disorder;
4. absence of an infectious, toxic or traumatic cause;
5. family history consistent with autosomal dominant inheritance.

The differential diagnosis includes a variety of inflammatory, toxic, anoxic, metabolic conditions associated with basal ganglia calcifications.

There is no specific treatment [2]. The symptomatic treatment includes antipsychotic drugs [3, 6], antiepileptic drugs [1], antidepressants [1], anxiolytic agents [1].

Generally, the disorder worsens over time and progressive neurological deterioration results in disability and death.

Case report

A 21-year-old male patient was first admitted to the Neurology Clinic at the University Hospital St. George in Plovdiv, Bulgaria, in 2004 with the purpose of diagnosis and adequate treatment.

The patient was born with asphyxia, with subsequent normal neuropsychological development, without clinically significant diseases in childhood. In July 2003, he had a first unprovoked generalized-tonic-clonic seizure, and carbamazepine therapy (daily dose of 300 mg) was initiated. Swelling of the ankles started in October 2003. In April 2004, the patient was admitted to Multiprofile Hospital for active treatment (Plovdiv). He was diagnosed with reactive hepatitis caused by carbamazepine treatment. Carbamazepine was replaced with oxcarbazepine. Then thyroid ultrasound was performed, that was normal. TSH was within reference values.

In November 2004, ankles swelling reappeared. It was accompanied by lower extremities weakness and pain in the leg muscles. The patient became less self-sufficient and that was the reason for which he was admitted to the Neurology Clinic. There was no family history for any disease.

Physical examination

Asthenic habitus, swelling of lower legs, ankles and feet. Subfebrile temperature (37.5 °C) during the first days of hospitalization. Examination of other systems showed no abnormalities.

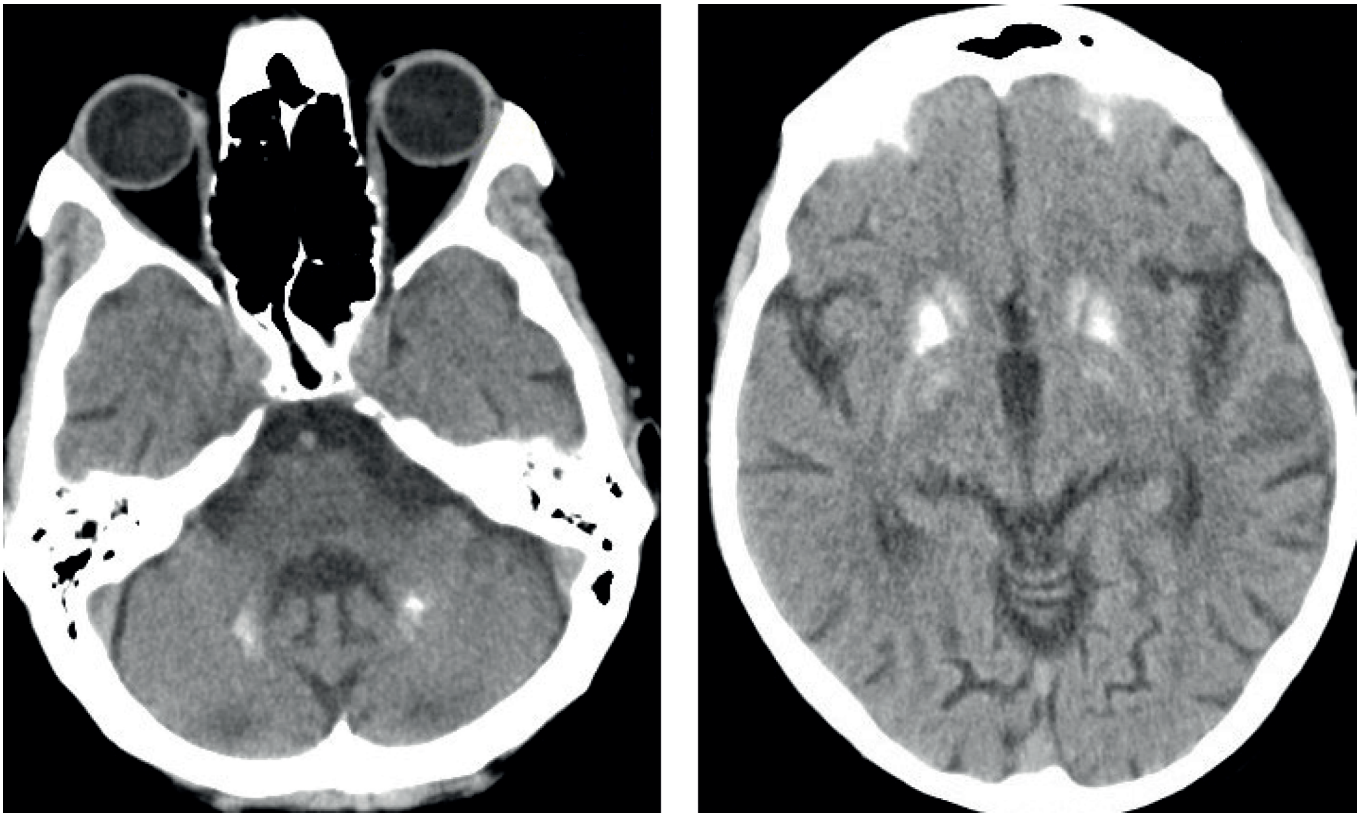
Neurological examination

Conscious, without psychotic manifestations. Amyotrophic syndrome, more severe for the proximal muscles of extremities: reduced power of the legs – reduced power of thigh muscles, limited plantar flexion and impossible dorsal flexion of feet; normal Achilles reflexes; areflexia for triceps and styloradial reflexes, hyporeflexia for biceps reflexes. Spontaneous and palpatory pain of hip and leg muscles. Distal hypesthesia for pain, temperature, and touch of the lower extremities.

Laboratory investigations

1. Within reference values: full blood count, differential blood count, erythrocyte sedimentation rate, blood glucose, cholesterol, total protein, albumin, urea, creatinine, total and direct bilirubin, electrolytes/sodium, potassium, calcium, coagulogram, troponin, serum IgA, IgM, IgG, reversed Ehrlich reaction, cerebrospinal fluid test, serum and urine uroporphyrins and coproporphyrins, Lyme borreliosis test /-/, HIV /-/, Wassermann /-/, HBV antigen /-/ and anti-HCV /-/, LE cells /-/, antinuclear antibodies /-/; parathyroid hormone (30 pg/ml).
2. Abnormal results: AST 105 U/l, 79 U/l; ALT 67 U/l, 37 U/l; alkaline phosphatase 250 U/l, 211 U/l; LDH 1298 U/l, 872 U/l; HBDH 557 U/l, 442 U/l, creatine kinase 1242 U/l, 653 U/l; MB fraction of creatine kinase 124 U/l , GGT 39 U/l, 32 U/l; cholinesterase 3516 U/l, anti Jo-1 /ELISA/ 1:32 /+/. Flow cytometry of the lymphocyte population: mild decrease in T-lymphocytes. Decreased T-killer cells. T-suppressor cell percentage near the upper reference value. Decreased percentage of T-helper cells decreased ratio CD4/CD8: a sign of immune dysbalance.

- X-ray of the lungs showed no active pulmonary disease.
- ECG showed no clinically significant abnormalities.
- CT scan: bilateral symmetrical calcifications in the region of caudate nucleus, putamen, and thalamus.
- EEG showed no abnormalities.
- EMG: on needle EMG test of all investigated muscles /mm. biceps brachii, mm. deltoidei, mm. quadriceps femoris/ we recorded spontaneous denervation activity at rest /fibrillations, fasciculations, multiple positive acute waves/ and action potentials with myopathic (myositis) characteristic during muscle contraction. The disease history, clinical progress, and the recorded denervation activity and reduced conduction of peripheral motor neurons of both proximal and distal segment of legs are consistent with secondary distal, mainly axonal peripheral disorder which we accepted as secondary to chronic polymyositis.
- Abdominal ultrasound: steatosis of the liver. The treatment with carbamazepine was accepted as the most possible explanation for this finding.
- Fibrogastroscopy: chronic gastroduodenitis with erythema and exudates.
- Echocardiography: suspected secondary myocarditis.



Symmetrical small calcifications in both cerebellar hemispheres.

Treatment

Pentoxyfilline 800 mg daily, milgamma N (benfotiamine/pyridoxine hydrochloride/cyanocobalamine) 3 tablets daily, pyridostigmine bromide 2×60 mg daily, oxcarbazepine 300 mg daily, amantadine sulfate i.v. 200 mg/500 ml.

Clinical progress

The patient improved and at the end of hospitalization he was able to stand without help.

Differential diagnosis

1. Hereditary dystrophic myopathy. Rejected because of the rapid progress of amyotrophic syndrome, persisting muscle pains, fever, denervation activity on EMG.
2. Spinal muscular atrophy of Kugelberg Welander. Rejected for the lack of fasciculations from the neurological examination, preserved Achilles, distal hypesthesia of the lower extremities. The spontaneous activity on EMG is not consistent with the abnormal high and continuous action potentials during muscle contraction typical of spinal motor neuron disease.
3. Somatic disease (hepatic, hematological, of the thyroid and parathyroid gland, acute intermittent porphyria).

The diagnosis of autoimmune polymyositis complicated with secondary distal axonal polyneuropathy was based on the following criteria: fever, muscle pains, muscle atrophy, articular edema, increased enzymes, /+/ anti Jo-1, echocardiographic data about secondary myocarditis, EMG results, consultation with rheumatologist. The possibility of polymyositis secondary to carbamazepine and oxcarbazepine treatment was ruled out.

The patient was admitted to the Rheumatology Clinic and was treated with cortisone. The patient was discharged from hospital with significant improvement. Valproate was started for seizures treatment. Azathioprine and prednisone were recommended and initiated for supporting treatment of polymyositis.

Long-term follow-up of the patient

The patient had a second generalized tonic-clonic seizure in 2006. Valproate 1000 mg daily and oxcarbazepine 1200 mg daily were recommended and started. Later oxcarbazeline was discontinued.

The patient had a third generalized tonic-clonic seizure in 2009.

The patient has been with profound deafness since 2009, with externally worn hearing aid.

EEG 39/10.03.2010: a background activity of not well organized alpha rhythm, with weak reaction to eyes opening and photostimulation. Frequent generalized paroxysms of delta waves with duration up to 1 second and maximal amplitude in the frontal regions.

In 2012 the patient was admitted to a Psychiatry Clin-

ic because of anxiety, statements that he "hears noises and that everyone speaks about him and his parents on TV". He spoke more than usual and sought information about his relatives in the newspapers. He was aggressive. During hospitalization hyperbulia, accelerated thought with frequent topic change, paranoid ideation, and non-verbal auditory hallucinations were described. He was diagnosed with paranoid schizophrenia and treatment with haloperidol and biperiden hydrochloride was recommended and started.

The patient had a fourth generalized tonic-clonic seizure in 2014 (treated with valproate 1500 mg daily).

During a second hospitalization in the Neurology Clinic in 2014, impaired coordination with static and locomotor ataxia was found.

EEG 41/26.06.2014: decreased and not well organized brain activity without focal and paroxysmal activity.

CT scan in 2014 visualized massive, symmetrical, bilateral calcifications in the region of basal ganglia (caudate nucleus, lentiform nucleus) and thalamus (see Figure on page 36).

A daily treatment with valproate 1000 mg daily, betahistine 48 mg, vinpocetine 20 mg, azathioprine 50 mg, prednisone 15 mg, haloperidol 1.5 mg, biperiden hydrochloride 4 mg was recommended and started.

Discussion

The reported case is interesting for clinical practice because of the following features:

1. the patient fulfills the Fahr's disease criteria with the exception of family history consistent with autosomal dominant inheritance;
2. early disease onset (20 years of age) with a generalized tonic-clonic seizure;
3. despite calcifications in the region of the basal ganglia on CT scans, there are no clinical signs of extrapyramidal system abnormalities;
4. rare epileptic seizures: 4 generalized tonic-clonic seizures for the whole period of observation. Epilepsy was discussed as a separate condition, but no evidence for other etiology was found from disease history and investigations;
5. generalized paroxysmal activity of delta waves on only one EEG which could not be regarded as a specific finding;
6. autoimmune polymyositis as a concomitant disease, which improved by specific treatment;
7. diagnosis of complete deafness 6 years after Fahr's disease onset. The possibility of being a separate condition was discussed, but no explanation was found;
8. typical psychotic symptoms 9 years after the first epileptic seizure;
9. Fahr's disease progression was documented 11 years after initial symptoms by CT scan visualization of new bilateral symmetric calcifications in the cerebellar hemispheres and respective clinical manifestations (static and locomotor ataxia). We found no case reports in the literature with a similar combination of clinical manifestations and evolution.

Conclusions

In conclusion, this case report provides additional information about clinical characteristics and management of patients with Fahr's disease.

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