

Letter to the Editor

Fahr's syndrome with hyperparathyroidism revealed by seizures and proximal weakness



1. Introduction

Fahr's syndrome is a rare anatomic and clinical entity characterized by non-arteriosclerotic, bilateral and symmetrical intracerebral calcifications, localized in the central gray nuclei [1–4]. The pathophysiological mechanisms that contribute to these intracerebral calcifications are not well known, and are probably multi factorial [1,5,6]. Biochemical analysis of the intracerebral calcifications shows that these are composed of an organic matrix constituted of neutral and acidic mucopolysaccharides as well as mineral elements (calcium, phosphorus, iron, sulfur, magnesium, aluminum, zinc) [1,7]. This disease is usually associated with phosphocalcic metabolism disorders, principally hypoparathyroidism [1,4]. The clinical presentation of Fahr's syndrome involves first neuropsychiatric features. Other possible neurological manifestations include cognitive impairment, intellectual disability, mental retardation, extrapyramidal features, generalized or partial seizures, and rarely pyramidal syndrome and intracranial hypertension are found. Dermatological lesions related to the deficiency in parathormone are possible [4].

Fahr's syndrome is to differentiate from Fahr's disease, which is an autosomal dominant disorder caused by mutations in the *BGCI* gene located on chromosome 14q. It does not cause phosphocalcic metabolism impairment [5,8] while the presence of this defect defines Fahr's syndrome [9].

2. Observation

F. K, a 26-year-old male who was born from a normal pregnancy and delivery was seen for seizures and walking difficulty. He had normal psychomotor development until recently.

Symptoms started back in 2000 (at 10 years old) when he presented with generalized tonic clonic seizures. He had several spells after which he was put on Phenobarbital 100 mg per day with no success. Few months later, he presented with abnormal movements in four limbs and language disorder. Despite no specific treatment, abnormal movements had disappeared a year later.

He underwent bilateral eye surgery in 2008 for cataracts, and in 2014, abnormal movements started up again but interested left limbs only. In April 2015, he was referred to our Neurogenetics Clinic to explore a genetic cause because of the persistence of the seizures and the adjunction of walking difficulty.

No similar case in the family and no known consanguinity between parents were reported.

Neurological examination found myopathic syndrome with a proximal weakness worse at pelvic girdle, a cerebellar syndrome, choreic movements of left limbs, stiffness and cortical irritation syndrome. He scored 23/30 in the MMS test, consistent with a cognitive impairment, especially for calculation. EEG confirmed active seizures with a slow and symmetric background activity at 6 Hz, paroxysmal abnormalities

of brief bursts of generalized spikes and poly-spikes waves.

Brain CT-scan showed spontaneous, bilateral and symmetrical hyperdensities in the central gray nuclei, the dentate nuclei of the cerebellum, the oval center and frontal lobes. In addition, these lesions do not take the injected contrast (Fig. 1A and B). These findings were consistent with Fahr's disease or syndrome.

Blood chemistries showed high parathormone (PTH: 186 ng/l; Normal = 15–65) and creatine kinase (CK: 2131 UI/l; Normal = 30–200). However, ionized calcium levels were low (0.60 mmol/l Normal = 1.12–1.32 mmol/l); confirming the diagnostic of Fahr's syndrome. Thyroid hormones, 25-hydroxy-vitamin D, creatinine and blood glucose were normal. A summary of clinical and laboratory findings are found in Table 1.

Treatment included sodium Valproate 1000 mg, Clonazepam 1 mg, Calcium 1000 mg, and Haloperidol 10 mg per day.

After six months of treatment, the patient has improved: choreic movements, the myopathic syndrome and seizures disappeared. In addition, CK levels dropped to 769 UI/l.

3. Discussion

Fahr's syndrome affects both sexes with the same ratio, and usually occurs in adolescence or the middle age [7]. Our patient presented the first neurological symptoms at age 10.

This disease has an endocrine origin, more often hypoparathyroidism or pseudo hypoparathyroidism [2], [4–7]. Its association with hyperparathyroidism, as seen in our patient, was rarely reported.

One of the main features of this disease is brain calcifications involving small vessels of the central gray nuclei [1,5].

In general, the clinical presentation is diverse and varied, making the disease clinically difficult to diagnose. Nonetheless, psychiatric symptoms are found in 45% of cases including intellectual disability, mental debility, behavioral disorders, and sometimes even delirious episodes [6,7]. Neurological symptoms, often understated compared to the extent of anatomic and radiological lesions, are fairly common. It can be seizures, pyramidal syndrome, akinetic hypertonic syndrome, cerebellar syndrome generally discreet, urinary problems, choreic athetotic movements, dysarthria or mumbling speech. However, seizures are rarely reported as revealing symptoms [10]. Cranial nerves involvement and bouts of benign intracranial hypertension are rare, while cases without neurological symptoms have been reported [1,7]. In addition to these symptoms, our patient had proximal weakness and high CK levels. The association of this myopathic syndrome with Fahr's syndrome has not been found in the literature. This could be stochastic or due to the osteomalacia secondary to the hyperparathyroidism and associating myopathic syndrome. The regression of these symptoms in addition to the decreased CK levels with calcium supplementation strengthen this hypothesis.

The diagnosis of Fahr's syndrome is based on brain CT-scan that

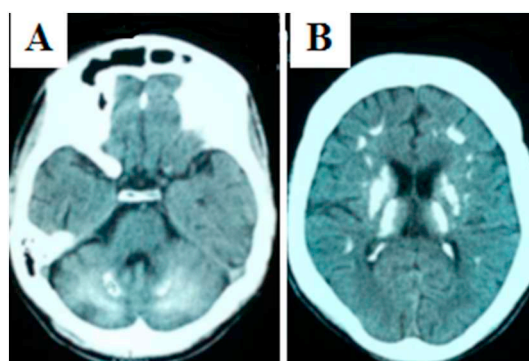


Fig. 1. Brain CT-scan showing cerebral calcifications. A) Calcifications in the dentate nuclei in the cerebellum, B) Calcifications in the central gray nuclei, the thalamus and white substance. Note that the calcifications are bilateral and symmetric.

Table 1

Summary of clinical and laboratory findings.

Clinical findings	Epilepsy	Generalized, tonic clonic seizures
	Myopathic syndrome	Proximal weakness, waddling gait
Laboratory findings	Hemi-chorea	Abnormal movements in left limbs
	Cerebellar syndrome	Dysarthria, unbalance
	Extrapyramidal signs	Rigidity
	Cognitive impairment	MMS: 23/30
	Brain CT-scan	Diffused calcifications: gray nuclei, dentate, oval center, frontal lobes
	EEG	Slow symmetric background activity, brief bursts of generalized spikes and poly-spikes waves
	Parathormone (PTH)	High (186 ng/l, N = 15–65)
	Inonized calcium	Low (0.60 mmol/l, N = 1.12–1.32)
	CK	High (2.131 UI/l, N = 30–200)

MMS: Mini-Mental-State, EEG: electroencephalogram, CK: creatine kinase.

shows intracerebral calcifications appearing as spontaneous bilateral and symmetric hyperdensities interesting the central gray nuclei, as seen in our patient [5,9].

Other diseases that could cause intracerebral calcifications including some endocrine diseases (hypothyroidism, hypogonadism), systemic diseases (systemic scleroderma, acute disseminated lupus erythematosus and celiac disease), brain infections (toxoplasmosis, neurocysticercosis, rubella) and some primary or secondary calcified brain tumors [1,4,5]. However, the intracerebral calcifications observed during these various diseases are not typically bilateral and symmetric, and not preferably in the central gray nuclei [1].

4. Conclusion

Our study shows that Fahr's syndrome can be associated with hyperparathyroidism and revealed by tonic clonic seizures. The clinical features are diverse; however, the diagnosis is first based on the presence of calcifications in the gray nuclei and phosphocalcic metabolism impairment. The presence of myopathy in our patient extends the diverse clinical spectrum of this disease.

Conflicts of interest

Authors declare no conflict of interest.

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