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Research Article

Fahr Syndrome and Dysparathyroidism

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Abstract

Fahr Syndrome (FS) is a rare clinicopathological syndrome defined by the presence of bilateral and symmetrical intracerebral calcifications, usually associated with hypoparathyroidism. We report seven cases of FS with hypoparathyroidism. Mean age was 36 years. There were five women and two men. Famial history of FS was found in one case. Clinical manifestations included: seizures (n=5), cognitive impairment (n=4), tetany (n=4), epileptic disorder (n=1), extrapyramidal symptoms (n=1), psychiatric disorders as schizophrenia (n=1). We found a cataract in 6 patients. One patient had postpartum hemorrhage due to uterine atony. Etiologies were dominated by primary idiopatic hypoparathyroidism (n=5), secondary hypoparathyroidism after a total thyroidectomy (n=1), and familial pseudo-hypoparathyroidism (n=1). Treatment was based on calcium and vitamin D therapy (alfacalcidiol) associated to a symptomatic treatment leading to seizures regression, but persistence of calcifications and cognitive impairment disorders.

Introduction

Fahr Syndrome (FS), as defined by Theodor Fahr in 1930, is a rare clinicopathological syndrome, defined by the presence of bilateral and symmetrical intracerebral calcifications [1]. It is usually associated to a phosphorcalcic metabolism disorder. Hypoparathyroidism is the most common etiology. A combination of FS with hyperparathyroidism or a pseudohypoparathyroidism was more rarely reported [2].

The physiopathology of intracerebral calcifications is poorly understood and probably multifactorial. Most authors incriminate anoligoglial cells metabolic disorder with deposits of mucopolysaccharides and occurrence of secondary vascular lesions [3].

We report seven cases of F-Sand describe clinical, etiological and therapeutic features.

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Material and Methods

We describe retrospectively seven cases of FS observed over a period of seven years (2008 to 2015). Were included patients who had basal ganglia calcifications on CT scan and primary or secondary hypoparathyroidism. Cognitive impairment evaluation was based on Mini Mental State Examination (MMSE) in 3 patients; it was subjectively evaluated in the other cases.

Results

Mean age was 36 years. There were five women and two men. We found a familial history of FS in one case (Table 1). Clinical manifestations included: seizures (n=5), cognitive impairment (n=4), tetany (n=4), epileptic disorders (n=1), extrapyramidal symptoms (n=1), psychiatric disorders as schizophrenia (n=1). We found a cataract in 6 patients. One patient had postpartum hemorrhage due to uterine atony.

Calcifications of basal ganglia were found in all patients CT scans. Few patients had also subcortical and cerebellar calcifications (Table 1; Figures 1 and 2).

Mean calcium level in blood was 49 mg/l, the parathyroid hormone rate was low in 6 patients (<15 pg/ml) and high in one patient (174 pg/ml for normal <68 pg/ml).

Etiologies were dominated by primitiveidiopatic hypoparathyroidism in 5 patients, secondary hypoparathyroidism after a total thyroidectomy in one patient, and familial pseudo-hypoparathyroidism in one patient.

Treatment was based on calcium (carbonate of calcium) and vitamin D therapy (alfacalcidiol). Symptomatic treatment was indicated in all cases: antipsychotics and / or anti epileptic therapy, none of our patient had subcutaneous parathormone or lithium therapy. At follow up, all patients had clinical and biological monitoring (calcium, urinary 24h calcium). We noticed, at the follow up, a regression of seizures in all cases, but persistence of calcifications patients and cognitive impairment disorders.

Discussion

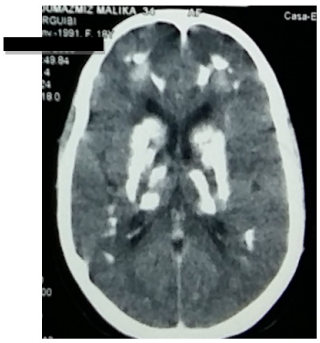
Fahr Syndrome is a rare clinicopathological syndrome [1]. Its clinical symptoms may include: Neuropsychiatric disorders such as personality disorders and / or behavior, confusional or delirious syndrome, cognitive disorders, extrapyramidal syndrome as observed in one of our patients. Partial or generalized seizures can also happen in FS, rarely cerebellar or pyramidal syndrome, cranial nerves impairment and chorea [4]. Usually psychiatric manifestations precede neurologic symptoms [5]. And more rarely FS may remain asymptomatic [4].

A variety of conditions can cause intracerebral calcification: endocrinedisorders, infectious diseases, degenerative or systemic diseases and tumors. In these cases, the calcifications are not bilateral, symmetric or localized to the basal ganglia as observed in FS [6]. Idiopathic FS is called Fahr's disease, especially if there is a familial history consistent with autosomal dominant inheritance [7].

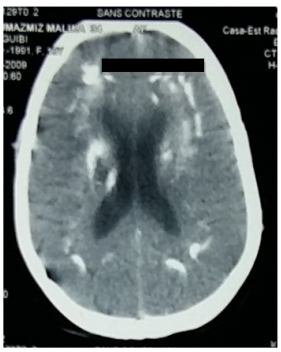
	Sex	Age (Year)	Time of Evolution Years	Clinical-Features	Ca Rate (mg/l)	Ph Rate (mg/l)	PTH (pg/ml)	CT Scan	Etiology	Therapy
Case 1	F	36	31	Seizures and tetany Mild cognitive impairment	60	50,4	1,2	Basal ganglia, periventricular and subcortical calcifications	HPT	Calcitherapy and vitamin D atypical neuroleptic Antiepileptic (SV)
Case 2	M	47	1	Generalized seizures Muscle cramps Appendages disorders	44	72	63	Basal ganglia calcifications	HPT	Calcitherapy and vitamin D Antiepileptic (VS)
Case 3	M	30	10	Partial seizures Bone pain Paresthesia	46	45	174	Basal ganglia and subcortical calcifications	PHPT	Calcitherapy and vitamin D Antiepileptic (CBZ)
Case 4	F	26	1	Behavioral disorders Extra pyramidal syndrome Cognitive impairment Seizures and tetany Candidiasis and skin pustulosis	39	80	10	Basal ganglia calcifications	HPT	Calcitherapy and vitamin D Antiepileptic (SV) Neuroleptic
Case 5	F	31	NM	Tetany Deafness Severe cognitive impairment Growth and puberty delay	59	NM	NM	Basal ganglia calcifications Cerebellar subcortical occipital calcifications	HPT	Calcitherapy and vitamin D Antiepileptic (SV)
Case 6	F	50	1 month	Generalized seizures Tetany	54	NM	NM	Basal ganglia and subcortical calcifications	HPT post thyroidectomy (3 years)	Calcitherapy and vitamin D Antiepileptic (SV)
Case 7	F	33	1 week	Postpartum Hemorrhage due to uterine atony Delirium, delusions Mild cognitive impairment	43	60	3,82	Basal ganglia calcifications	HPT	Calcitherapy and vitamin D

Table 1: Clinical, biological, therapeutic and outcomes of different cases.

Ca: Calcium, CBZ: Carbamazepine, HPT: Hypoparathyroidism, NM: Not Mentioned, Ph: Phosphore, PHPT: Pseudo Hypoparathyroidism, PTH: Parathyroid Hormone, SV: Sodium Valproates



Figures 1: Calcifications of the basal ganglia.



Figures 2: Calcifications of the parenchyma.

Hmami F [8] reported 5 cases of adolescence-onset epilepsy with unsuccessful antiepileptic therapy, who had hypoparathyroidism in three cases and pseudohypoparathyroidism in the other two. The patients were treated with oral calcium and active vitamin D (1-alphahydroxy vitamin D3). Seizure frequency progressively decreased and serum calcium levels returned to normal. Seizures were the most commonly symptoms found in our patients.

Yurekli et al. [9] diagnosed a case presenting with dementia, and observed a reduction in the dementia symptoms after treatment.

Simone et al. [10] reported a case of a 69-year-old male with repeated episodes of transient loss of consciousness and minimal cognitive and behavioural disturbances. With a diagnosis of pseudo hypoparathyroidism, whose correction led to a significant clinical improvement. Unfortunately we hadn't similar results.

Prescribing thiazide diuretic may be helpful by increasing serum calcium without causing hypercalcaemia. Subcutaneous administration of synthetic parathormone also can significantly reduce calcium and vitamin D intake and hypercalciuria, but it is not permitted for this indication currently.

Hypomagnesemia must be systematically investigated and corrected in all cases so that the calcium and vitamin D treatment can be effective [7].

Other pharmacological treatments, such as clonazepam and atypical antipsychotics (quetiapine), can be useful to improve anxiety, depression and obsessive compulsive disorders and can also reduce

dystonia. One of our patient's had quetiapine with an improvement of movement disorders.

Lithium should be provided carefully because it can increase seizures risk in patients with FS [11].

Conclusion

Fahr syndrome is a rare entity which is not overlooked. There is an agreement that FS must be considered in the diagnosis of patients displaying nonspecific neuropsychiatric symptoms accompanied by calcium metabolism disorders in order to allow an appropriate treatment and to prevent high morbidity neurological damage.

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