FAHR SYNDROME SECONDARY TO HYPOPARATHYROIDISM AND PSEUDOHYPO-PARATHYROIDISM

Violeta Hoxha[1], Klodiana Poshi[2*], Dorina Ylli[3], Adela Haxhiraj[4], Tea Shehu Kolnikaj[5], Agron Ylli[6]

Abstract

Background: Fahr's Syndrome, also known as striopallidodentate calcinosis is a rare form of neurological disorder characterized by abnormal calcifications in the basal ganglia, cerebellum, and cerebral cortex. Its prevalence goes from 2 to 12.5 %. It can be primary (idiopathic) or secondary (from metabolic disorders especially from hypoparathyroidism and pseudohypoparathyroidism).

Cases descriptions: The first patient is a 61 years old woman who came to the Emergency Unit with complaints of body weakness, severe fatigue, left-side numbness, and headache. That's why she got a head injury with an open bleeding wound. A head CT was performed where diffuse cerebral and cerebellar calcifications were noticed. Biochemical analysis demonstrated hypocalcemia due to primary hypoparathyroidism, vitamin D deficiency, and Hashimoto thyroiditis. Immediate treatment with IV calcium (2000mg/day) and Vit D3 (2000UI/day) was started and the patient was advised for further follow-up. The second patient is a 37 years old man who presented in the Emergency Unit with epileptic generalized tonic-clonic seizure. He was known to suffer from epilepsy since 4 months of age but a head CT was performed for the first time where diffuse bilateral brain calcifications were noticed. Biochemical analysis showed hypocalcemia with low/normal Vit D levels and high PTH levels. Diagnose of pseudohypoparathyroidism probably type 1 was made. The patient was treated with IV calcium and Vit D3. On follow-up, levels of serum ionized calcium and 24h calcinuria were improved.

Conclusions: Fahr's Disease is a neurological complication of chronic hypoparathyroidism and pseudohypoparathyroidism. In most cases, the diagnosis is clinical-radiological with calcifications in the basal ganglia. No significant differences are shown between hypoparathyroidism and pseudohypoparathyroidism on CT images. After confirming the diagnosis, the patients should start treatment with cholecalciferol or ergocalciferol (firstly to fill the depots), calcium supplements, and rocatrol.

Keywords: calcium, PTH, hypoparathyroidism, pseudohypoparathyroidism, brain calcifications

[1,2*,3,5,6]Department of Endocrinology, Diabetes and Metabolic Disease, University Medical Center ``Mother Teresa``, Tirana, Albania.
[1,3,6]Faculty of Medicine, University of Medicine Tirana, Tirana, Albania.
[2*,,4,5]Faculty of Technical Medical Sciences, University of Medicine Tirana, Tirana, Albania.
[4]Salus Hospital, Tirana, Albania.
[2*]Aldent University, Tirana, Albania.

***Corrrespondence Author:** Klodiana Poshi Phd
*Department of Endocrinology, Diabetes, and Metabolic Diseases, Faculty of Medical Technical Sciences, University of Medicine, Rruga e Dibres, 372, Tirana, 1000, Albania

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Introduction:

Fahr's Syndrome, also known as striopal-lidodentate calcinosis is a rare form of neurological disorder characterized by abnormal calcifications in the basal ganglia, cerebellum, and cerebral cortex. Its prevalence goes from 2 to 12.5 % (1). It can be primary (idiopathic) or secondary (from metabolic disorders especially from hypoparathyroidism and pseudohypoparathyr-oidism). Low activity of parathyroid hormone results in calcium deposits in soft tissues, including brain tissue. Affecting mostly the basal ganglia, the patients have neurological manifestations like chorea, tetany, disorientation, loss of balance, seizure, or even dementia (2). Generally, the patients are diagnosed after brain imaging findings of the calcification. The vast variety of the causes and the subtle course of the disease requires an accurate differential diagnosis.

We present a case series of two patients presented with basal ganglia calcifications and low levels of calcium, later diagnosed with hypoparathyroidism and pseudohypoparathyroidism.

First Case: The patient L.J. 61 years old, from Pogradec, Albania, came to the emergency room with complaints of body weakness, severe fatigue, left-side numbness, and headache. The patient mentioned several similar episodes during the years. A month ago, she got a head injury, with an open bleeding wound because of disorientation and extreme fatigue. The patient was being treated only for Arterial Hypertension with Irdapin (Irbesartan/Amlodipine) 150/5 1 tablet/day.

At the emergency room, a computed tomography (CT) of the head was performed to exclude acute cerebral damage. During the examination, diffuse cerebral and cerebellar calcifications were seen and identified as FAHR Disease. (Figure 1) The patient was first hospitalized in the Neurology Department where she was treated for her immediate symptoms. During her hospital stay her blood test came as shown below: A blood test and biochemical parameters within normal range. Other tests resulted as shown in table 1.

Table1

During the thyroid ultrasound, it was evident a heterogeneous bilateral structure favored Hashimoto's thyroiditis.

A normal electroencephalogram was obtained. The patient was later transferred to our department because of the new-found diagnosis: Primary Hypoparathyroidism, FAHR Disease, and Hypovitaminosis D.

The patient began treatment with intravenous Calcium and in just a few days her symptoms became less evident. She was discharged from the hospital with oral Calcium (2000 mg/day) and Vitamin D3 (2000 UI / day) and was advised to check in with her endocrinologist for future follow-up.

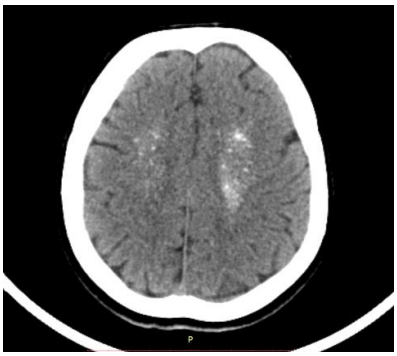

Figure 1: Head CT of the first patient

Second case: The second patient is 37 years old man who presented in the Emergency Unit with epileptic generalized tonic-clonic seizure. The patient is known to suffer from epilepsy since 4 months of age (a time when he was diagnosed with acute meningoencephalitis) and he is under treatment with carbamazepine 200 mg TTD. The patient had never realized head imaging; therefore, a head and neck CT was performed where diffuse bilateral cortical cerebellar, frontal subcortical and parietal periventricular, basal ganglia, and thalamic nuclei calcifications were noticed. (Figure 2) The patient was transferred to the Neurology department and underwent detailed biochemical blood analysis as shown in table 2.

Table 2

Other tests were normal. Based on severe hypocalcemia and very high PTH, with normal Vitamin D, phosphoremia, magnesium, hepato-renal function, and diffuse basal ganglia calcification, a diagnosis of pseudohypoparathyroidism was made. His clinical features with a round face, short stature, and short fourth and fifth metacarpals suggested pseudohypoparathyroidism probably type 1.

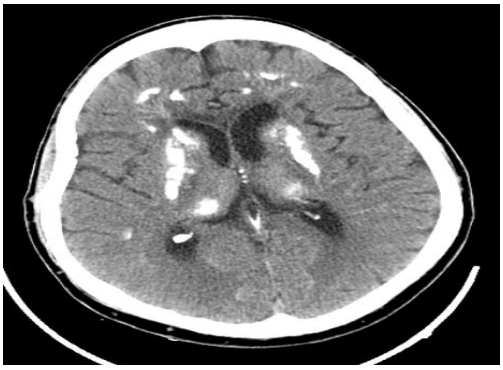

Figure 2: Head CT of the second patient

The patient was treated with IV calcium and then with calcium supplements (Ca carbonate 500 mg 3x2), Vit D3 2000UI/Day, and Rocatrol 0.25 mcg 2x1.
On follow up levels of serum ionized calcium and 24h calcinuria were improved.

Discussion:
Fahr's Disease is a rare, neurological complication of chronic hypoparathyroidism and pseudo-hypoparathyroidism. Its prevalence is higher in females and young to middle-aged adults (3). Calcifications are often present in brain tissues bilaterally and symmetrically mostly in the globus pallidus, caudate nucleus, and in a lesser probability, putamen, and thalamus (4). The areas of the brain affected are associated with motor activity resulting clinically in seizure, chorea, numbness, and tetany (5). In our cases, one of the patients had numbness and the other had a known diagnosis of epilepsy. Both patients had a long time with the symptoms. As suggested by other studies, it takes usually years from the onset of the disease to the final diagnosis, mostly because of the subtle and insidious way the disease presents itself (3). In our cases, the patients had a history of neurological disorders for which they were treated but not fully examined. None of the patients were evaluated before with a brain CT or the blood level of calcium and parathormone. In most cases the diagnosis is clinical-radiological. The calcifications in the basal ganglia are the main findings that suggest the syndrome. No significant differences are shown between hypoparathyroidism and pseudo-hypoparathyroidism in CT images (4). Both our cases had similar brain CT findings. Soft tissue calcifications in patients with disorders of mineral homeostasis are often explained by elevated calcium phosphate solubility products even in patients with hypocalcemia. The mechanism is not fully explained but it is emphasized the importance of PTH receptor 2, found in brain cells and mitochondrial superoxides (6). Differential diagnoses must be made with other conditions that result in hypocalcemia such as genetic diseases, myopathies, infectious diseases, or dermatological abnormalities (7). After confirming hypopar-athyroidism or pseudohypoparathyroidism, the patients should start treatment with cholecalciferol or ergocalciferol (firstly to fill the depots) and calcium supplements. Because PTH is required for the renal conversion of calcidiol (25-hydroxyvitamin D [25(OH)D]) to the active metabolite calcitriol (1,25-dihydroxy vitamin D [1,25D]), calcitriol is often regarded as the treatment of choice (8) Calcitriol is the most active metabolite of vitamin D. Other advantages of calcitriol include rapid onset of action (hours) and a biologic half-life of approximately four to six hours.
Maintaining the level of vitamin D and calcium within the normal range is essential in patients with a low level of PTH or peripheric insensitivity of it (9–11). As soon as treatment starts, the patient's symptoms improved and the risk of the spread of calcifications is lowered.

Conclusions:
Fahr's syndrome in hypoparathyroidism and pseudohypoparathyroidism is a rare but serious condition resulting in neuropsychiatric symptoms. Low activity of PTH favors abnormal deposition of calcium in soft tissues. We recommend blood tests of PTH, vitamin D, and Calcium in patients with basal ganglia calcifications and brain CT in patients diagnosed with hypoparathyroidism or pseudohypoparathyroidism. The latter should be tested regularly for calcium metabolism to maintain a normal level of calcium and to avoid acute or chronic complications.

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Tables

Parameter	Value	Normal Range	Comment
Thyroid-stimulating hormone (TSH)	3.241 U / ml	0.4 – 4 U / ml	Normal
Total calcium	3.3 mg/dl	8.6 – 10.2 mg/dl	Low
Phosphoremia	7.6 mg/dl	2.5 – 4.5 mg/dl	High
Blood Magnesium level	1.7 mg/dl	1.8 – 2.2 mg/dl	Low
Calcium in 24-hour Urine	8.7 mg/day	100 – 300 mg/day	Low
Phosphorous in 24-hour urine	14.2 mg/dl	400 - 1300	Low
Parathyroid hormone (PTH)	1.2 ng / l	15 – 65 ng/ l	Low
25 - OH - Vitamin D	15.24 ng/ml	> 30 ng/ml	Low

Table 1. Biological data from the first patient

Parameter	Value	Normal range	Comment
Natremia	143 mmol/L	(136-145)	Normal
Potassium	3.5 mmol/L	(3.5-5.1)	Normal
Chloremia	102 mmol/L	(98-107)	Normal
Total Calcium	6.1 mg/dl	(8.4-10.2)	Low
Ionized Calcium	0.58 mmol/L	(1.13-1.32)	Low
Phosphorus	4.2 mg/dl	(2.3-4.5)	Normal
Magnesium	1.6 mg/dL	(1.6-2.6 mg/dl)	Normal
Total protein	7 g/dL	(6.3-8.3)	Normal
Albumin	4.2 mg/dL	(3.5-5.2)	Normal
Vitamin D	29.8 ng/mL	(30-50 ng/ml)	Low/Normal
Alkaline phosphatase	117U/L	(40-150)	Normal
Parathyroid hormone	152.1 ng/L	(15-65)	High
24 h Calcinuria	55mg/24h	100-300	Low

Table 2. Biological data from the second patient