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Fahr's Syndrome and Neuropsychiatric Manifestations: A Case Report

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Abstract **Case Report**

Fahr's syndrome is characterized by bilateral and symmetrical intracerebral calcifications, primarily affecting the basal ganglia, and is often associated with phosphocalcic metabolism disorders. In this study, we present the case of a 50-year-old man diagnosed with hypoparathyroidism revealed by Fahr's syndrome and neuropsychiatric symptoms. This case highlights the importance of investigating phosphocalcic metabolism disorders in neuropsychiatric manifestations to detect hypoparathyroidism or other causes of Fahr's syndrome, and to adopt appropriate therapeutic measures.

Keywords: Fahr's syndrome, phosphocalcic metabolism disorders, hypoparathyroidism, irritability.

INTRODUCTION

Fahr's syndrome is a rare condition with a prevalence of less than 0.5% [1]. First described in 1930 by Karl Theodor Fahr [2], it is radiologically defined by bilateral and symmetrical intracerebral calcifications, non-arteriosclerotic in nature, localized to the basal ganglia [3-6]. The disease typically presents between the 3rd and 5th decades of life, but can appear in childhood or later in life [7]. It is more commonly observed in patients with parathyroid disorders, particularly hyperparathyroidism [8, 9], and less frequently in hypoparathyroidism or pseudohypoparathyroidism (PHP) [10-13]. Clinical manifestations range from mild behavioral changes to severe neuropsychiatric symptoms [13]. In this report, we describe a 50-year-old patient who presented with psychiatric symptoms and was diagnosed with Fahr's syndrome.

CLINICAL CASE

The patient, a 50-year-old married man with four children and no personal or family history of note, worked as a trader and had good social and occupational adaptation. Three years prior, without any triggering factors, he developed feelings of sadness, irritability, and an inability to cope with frustration. He became aggressive towards those around him, displaying destructive behavior. He experienced motor slowing, withdrew to his room neglecting familial responsibilities, and had significant loss of appetite and sleep. He also started frequently missing work. This situation led to excessive fear and pessimistic thoughts about his future. His condition prompted his first psychiatric consultation, during which he was prescribed escitalopram and a benzodiazepine with no improvement. Subsequently, he was put on paroxetine, which resulted in substantial clinical improvement. Some months later, he began experiencing anterograde memory disturbances and information processing delays.

Given these cognitive symptoms, the patient underwent biological and radiological assessments, which revealed bilateral and symmetrical intraparenchymal calcifications affecting the basal ganglia and cerebellar hemispheres (see Figure 1) on a cerebral computed tomography scan. Blood tests showed normal complete blood count, renal and hepatic functions, but revealed hypocalcemia at 70 mg/L and hyperphosphatemia at 53 mg/L. Parathyroid hormone (PTH) levels were within the normal range. Notably, the patient did not report clinical signs of hypocalcemia such as convulsive seizures. Neuropsychological evaluation indicated no global intellectual impairment but revealed slight deficits in episodic memory, social cognition, and information processing speed.

A diagnosis of Fahr's syndrome revealing pseudohypoparathyroidism was established, with a possibility of associated early-onset dementia. The patient was referred to an endocrinology clinic. Further investigations included an electroencephalogram (EEG) without anomalies and an ophthalmological examination that identified a posterior subcapsular cataract in the left eye. Substitutive treatment was initiated, combining 1.5 g of calcium daily.

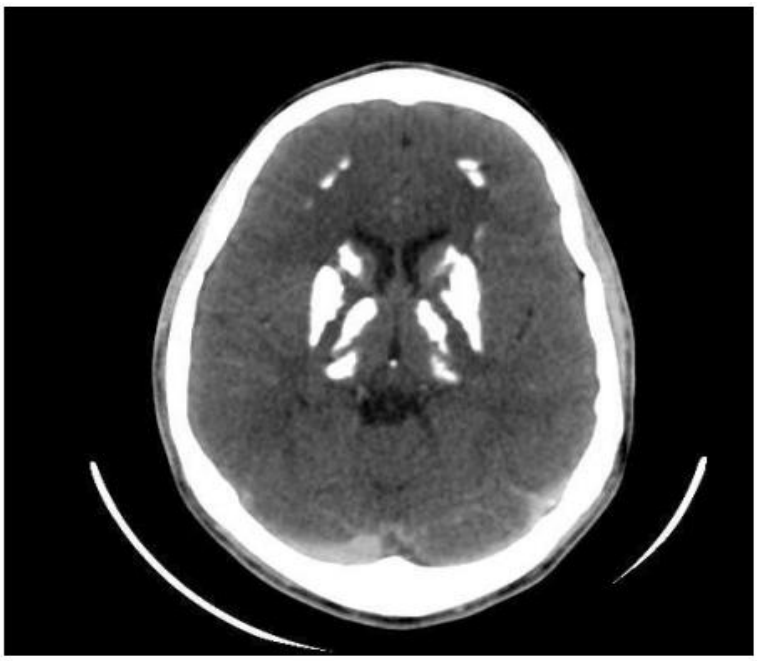

Figure 1: Brain CT scan of the patient shows dense calcification in the head of the caudate nucleus, basal ganglia, thalamus, and frontal cortex

DISCUSSION

The co-occurrence of Fahr's syndrome with hyperparathyroidism or pseudohypoparathyroidism (as in our patient's case) has rarely been described. The literature review revealed fewer than ten cases of hyperparathyroidism and/or PHP associated with Fahr's syndrome [14]. The pathophysiology of Fahr's syndrome remains partially understood. Most authors suggest a metabolic dysfunction in oligodendroglial cells, resulting in deposits of mucopolysaccharides and acids, along with minerals (calcium, phosphorus, iron, sulfur, magnesium, aluminum, zinc). Secondary vascular and perivascular lesions subsequently develop in the basal ganglia [14]. It is important to differentiate Fahr's disease from Fahr's syndrome; the former involves basal ganglia calcifications without phosphocalcic metabolism abnormalities, and it has an autosomal dominant hereditary origin due to a mutation on chromosome 14q [15].

PHP presents a similar clinical and biological profile but with a normal PTH level due to peripheral hormone resistance [14]. Different PHP subtypes exist, with PHP-Ia being associated with Albright's hereditary osteodystrophy and multiple hormone resistances due to a mutation in the GNAS1 gene encoding the α subunit of the stimulatory G protein (Gsα). PHP-Ib, characterized by isolated PTH resistance (without dysmorphia or multiple resistances), is often linked to a promoter abnormality in the PTH receptor gene. Rarer forms, PHP-Ic and PHP-II, resemble the clinical-biological phenotype of PHP-Ia but lack Gsα abnormalities [15].

Based on the provided information, our patient did not exhibit obesity, mental retardation, subcutaneous calcification, or shortening of the fourth and fifth metacarpals. These elements point toward PHP type Ib [15]. Molecular genetic analysis would be required to confirm this diagnosis [16]. While Fahr's syndrome can remain asymptomatic and be incidentally discovered during cerebral radiological investigations for other reasons [16], it can manifest with diverse and nonspecific neurological symptoms. Approximately 40% of patients initially exhibit neuropsychiatric symptoms [17]. Two clinical patterns are generally recognized: an early onset (mean age 30.7 years) with psychiatric symptoms and minimal movement disorders, and a late onset (mean age 49.4 years) associated with dementia and movement disorders [18].

Though our patient did not display movement disorders, he presented with a depressive syndrome, cognitive deficits including anterograde amnesia, and bradyphrenia. The basal ganglia play a crucial role in controlling motor functions and various cognitive processes via connections with the frontal cortex. They are involved in motivation, emotional impulse, planning, and cognition for goal-directed behaviors, as well as motor control through corticobasal and corticothalamic circuits [19].

Psychiatric symptoms in Fahr's syndrome could be explained by anomalies in the basal ganglia, which are central to the pathophysiology of psychiatric disorders, as well as disruption of the dorsolateral prefrontal circuit involving the thalamus [19]. To date, various treatments have been administered to Fahr's syndrome patients with the aim of achieving remission or stabilization. Treatment is symptomatic, involving calcium and alpha-hydroxyvitamin D3. Pharmacological treatment may address associated anxiety and depression. Given the

lack of controlled data, psychiatrists and neurologists must exercise caution when using conventional antidepressants and anxiolytics, as side effects may occur at very low thresholds in Fahr's syndrome patients [20].

CONCLUSION

This case underscores the importance of investigating phosphocalcic metabolism anomalies and cerebral calcifications in patients with neuropsychiatric symptoms to promptly diagnose Fahr's syndrome and initiate appropriate therapeutic measures.

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