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(CASE REPORT)

Pseudohypoparathyroidism revealed by Fahr syndrome: A case report

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Abstract

We report the case of a 19-year-old female patient with a history of epilepsy since the age of six, who was admitted to the emergency department for tetany episodes. Clinical examination revealed facial dysmorphia and dental dysgenesis. Initial laboratory workup showed severe hypocalcemia, and a brain CT scan revealed calcifications in the basal ganglia, suggestive of Fahr syndrome.

Keywords: Pseudohypoparathyroidism; Fahr syndrome; Hypocalcemia; Parathyroid hormone resistance; Brain calcifications

1. Introduction

Pseudohypoparathyroidism (PHP) encompasses a spectrum of disorders characterized by resistance to the action of parathyroid hormone (PTH), with significant clinical and genetic variability. We report a case of PHP that was initially misdiagnosed as idiopathic epilepsy but was eventually revealed through the manifestation of Fahr syndrome.

2. Case Report

The patient is a 19-year-old female born from a consanguineous marriage, with a history of macrosomia at birth, obesity since childhood, poor academic performance, and two cases of mental retardation in her family. She had been followed for epilepsy since the age of six and was treated with phenobarbital. She was admitted to the emergency department for tetany crises with muscular contractions of the hands, manifesting as the "obstetrician's hand." Clinical examination revealed a weight of 57 kg, a height of 1.50 m (-2SD compared to the target height), a BMI of 25.3, and facial dysmorphia characterized by a moon face, hypertelorism, a short broad neck, and dental dysgenesis (Figure 1).

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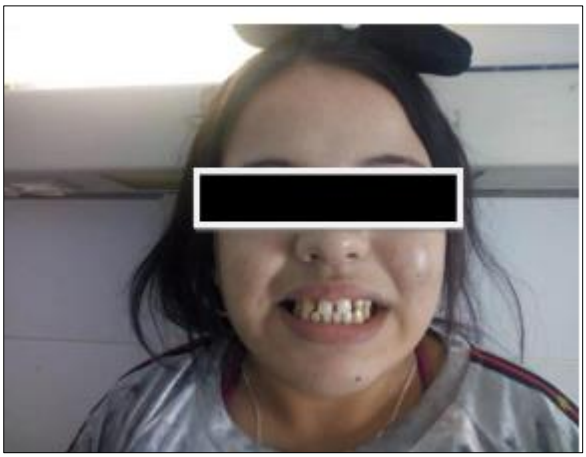

Figure 1 The patient's face showing facial dysmorphia, dental dysgenesis, and a short neck

Both Chvostek's and Trousseau's signs were positive, indicating hypocalcemia, which was confirmed by laboratory tests showing severe hypocalcemia (57 mg/L) and hyperphosphatemia (68 mg/L). An emergency ECG revealed a prolonged QT interval, and intravenous calcium gluconate was administered. A non-contrast brain CT scan revealed bilateral, symmetrical caudolenticular calcifications suggestive of Fahr syndrome (Figure 2).

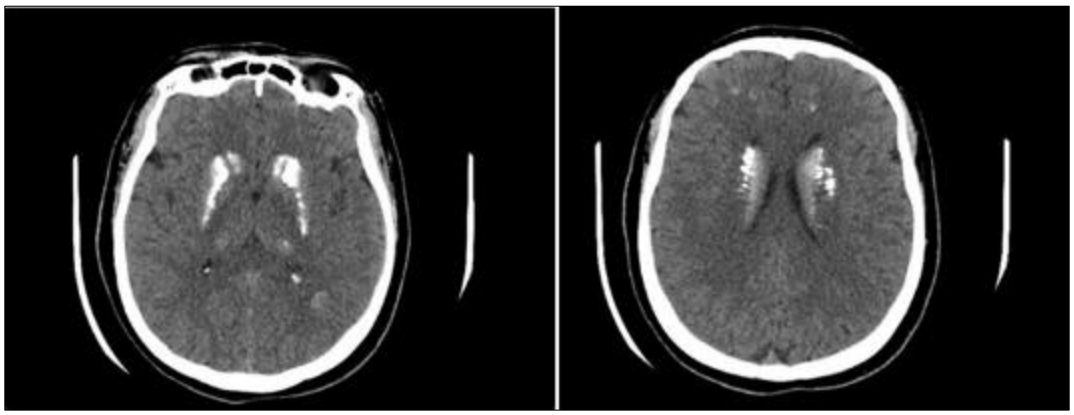

Figure 2 Brain CT scan showing caudolenticular calcifications

The etiological workup of hypocalcemia revealed normal renal function (urea: 0.18, creatinine: 6), normal 25-OH Vitamin D levels, normal magnesium levels, and a PTH level more than ten times the normal value (697 pg/mL), leading to the diagnosis of pseudohypoparathyroidism.

X-rays of the hands did not show brachydactyly, and other bone X-rays were unremarkable. Additional tests showed a TSH level of 7 uU/mL, LT4: 0.88 ng/dL, with negative anti-TPO and anti-Tg antibodies. No other hormonal resistances were identified.

Treatment was initiated with calcium (2 g/day) and 1-alpha-hydroxyvitamin D (1 mg/day), along with anticonvulsant therapy using sodium valproate. The patient showed good clinical and biochemical improvement, with follow-up focusing on maintaining calcium levels at the lower limit of normal, normal PTH levels, and normal urinary calcium excretion.

3. Discussion

Pseudohypoparathyroidism (PHP) is a very rare metabolic disorder characterized by resistance of target tissues to parathyroid hormone (PTH). This resistance is due to molecular defects in the PTH – PTHrP signaling pathway. PHP is classified into several types depending on the presence or absence of dysmorphic features, resistance to other hormones, and the response of hormonal signaling pathways to exogenous PTH administration :

Type 1A PHP (Albright's Hereditary Osteodystrophy) is caused by a GNAS mutation, which disrupts the production of the stimulatory G-protein (Gs) that links the PTH receptor to the effector unit producing cAMP. Clinically, it is characterized by short stature, obesity, a round face, brachymetacarpia, and cognitive impairment. Type 1B PHP, caused by an abnormality in the syntaxin gene, a functional partner of Gs, does not involve phenotypic abnormalities. Type 1C PHP results from downstream alterations in cAMP production, while pseudopseudohypoparathyroidism corresponds to Albright's Hereditary Osteodystrophy without metabolic abnormalities.

In our patient, the diagnosis is consistent with type 1A PHP, as evidenced by her short adult stature relative to the unaffected parent (a major criterion according to [2]), obesity, and a round face compared to her siblings (additional criteria according to [2]).

In the majority of PHP patients, hypocalcemia is the most common symptom, resulting from the resistance of target organs to PTH. The severity of hypocalcemia varies among patients. In patients with PHP1A, PTH resistance is generally absent at birth and develops over time (from 2 to 22 years) [3,4,5], with clinical manifestations typically occurring later. These data suggest that PTH resistance begins in early childhood, and changes in serum calcium and phosphorus levels develop progressively at some point in adulthood [4,6,7]. The first biochemical abnormalities to appear are elevated serum levels of PTH and phosphorus, followed by hypocalcemia. In cases of hypocalcemia, urinary calcium levels are low, while calcitriol levels may be either low or normal [3]. The time between the onset of elevated PTH and phosphorus levels and the development of hypocalcemia can be up to 4 to 5 years [8]. This explains the diagnostic delay of hypocalcemia and its symptoms in our patient.

This hypocalcemia can lead to bilateral and symmetrical striato-pallido-dentate brain calcifications, which define Fahr syndrome, a rare entity with etiologies dominated by parathyroid disorders, particularly hypoparathyroidism. However, the association of Fahr syndrome with pseudohypoparathyroidism is exceptional, making this case particularly noteworthy.

In addition to PTH resistance, other hormonal resistances may be associated, with TSH resistance being the most common. Patients with PHP1A almost always present with elevated serum TSH levels and normal or slightly low thyroid hormone levels [9]; in our patient, this level was 7 uUI/L. Some patients may have manifest clinical hypothyroidism. Elevated TSH levels due to TSH resistance can be present at birth and detected during neonatal screening [9].

Treatment is based on calcium and 25 OH vitamin D supplementation, along with hormone replacement therapy in cases of TSH resistance. Monitoring involves tracking serum calcium and urinary calcium levels.

4. Conclusion

Our case report describes the exceptional case of pseudohypoparathyroidism revealed by Fahr syndrome and emphasizes the importance of investigating metabolic abnormalities in the presence of brain calcifications and considering potential cerebral complications in cases of chronic hypocalcemia.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The present research work does not contain any studies performed on animals or human subjects by any of the authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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