Hypocalcemia caused by Pseudohypoparathyroidism Type 1b

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Introduction

The pseudohypoparathyroidism (PHP) encompasses a heterogeneous group of diseases characterized by end-organ resistance to parathyroid hormone (PTH). Pseudohypoparathyroidism type 1b (PHP1b) presents with PTH resistance at the renal proximal tubule, sometimes with TSH resistance, usually in the absence of Albright´s hereditary osteodystrophy (AHO) clinical features.

Case Report

64 year-old male, caucasian

Referred to an endocrinology appointment due to hypocalcemia

Third of eight children of non-consanguineous parents
Unremarkable psychomotor development

✓Stroke at the age of 50
✓Hypertension
✓Dyslipidemia
✓Anxiety disorder

Arthralgia, muscle contractures and paresthesias.

PHYSICAL EXAMINATION

Weight: 76kg | **Height:** 1.60m | **BMI:** 29.7kg/m^2
BP 141/76mmHg, **HR** 82bpm
Rounded face, short neck
Nonpalpable thyroid
Cardiac auscultation: rhythmic, without murmurs
Pulmonary auscultation: normal
Normal abdominal examination
No articular deformities, brachydactyly or subcutaneous calcifications
Negative *Chvostek's* and *Trousseau's signs*
Normal neurologic examination

LABORATORY TESTS

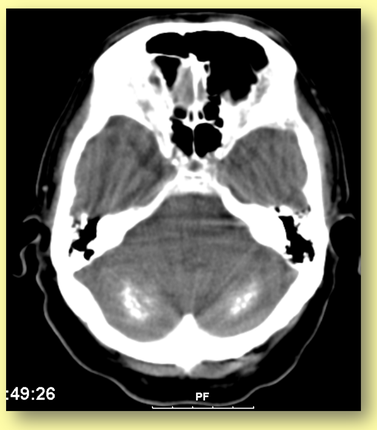
*Albumin 41g/L (38-51)
*Total calcium 2.2mmol/L (2.1-2.6)
***Ionized calcium 0.9mmol/L (1.13-1.32)**
***Inorganic phosphorus 5.7mg/dL (2.7-4.5)**
***25-OH-Vitamin D 17ng/mL(>30)**
***PTH 287.3pg/mL (10-65)**
*24 hour urinary calcium 5.9mEq/L (0.5-19)
***24 hour urinary phosphorus 251.7mg/L (300-1300mg/24h)**
***ALP 134U/L (30-120)**
*Urea 31mg/dL (10-50), creatinine 1.15mg/dL (0.8-1.3)
*TSH 3.54µUI/mL (0.35-4.94); FT4 0.97ng/dL (0.70-1.48)
*Total testosterone 3.81ng/mL (2.8-8.0), free testosterone 11.18pg/mL (5.6-19)

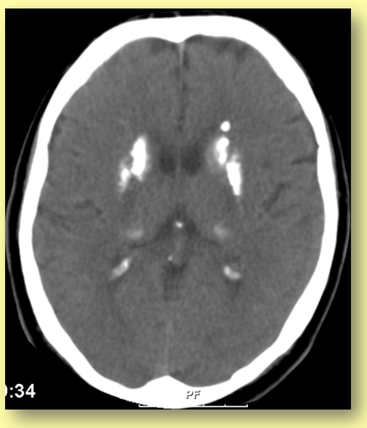
IMAGIOLOGY

SPINAL X-RAY
Osteophytosis with ossification of the posterior longitudinal ligament

RENAL ULTRASOUND
Bilateral nephrolithiasis. The largest calculus in the left kidney with 9mm and another one in the right with 7mm. No renal parenchymal calcification were observed.

CEREBRAL CT
Calcification of basal ganglia, *corona radiata*, cerebellum and thalamus.





FAMILY HISTORY

✓ Healthy parents

✓ 1 brother, died at the age of 42 of brain cancer
↳ Analytical study in our hospital showed **hypocalcemia and hyperphosphatemia**:
*Albumin 43.1g/L (38-51)
***Total calcium 1.3mmol/L (2.1-2.6)**
***Ionized calcium 0.51mmol/L (1.13-1.32)**
***Inorganic phosphorus 6.1mg/dL (2.7-4.5)**
*Urea 59mg/dL (10-50)
*Creatinine 0.89mg/dL (0.8-1.3)

✓ 34 year-old healthy child (normal calcium, phosphorus and PTH)

GENETIC TESTING

Abnormal methylation pattern of exon A/B in GNAS1 gene associated with **heterozygous deletion within STX16** (the gene encoding syntaxin-16), cause of **PHP1B, AUTOSOMAL DOMINANT**

The patient is treated with **calcitriol** and **elemental calcium**
↳ Normal levels of serum calcium, phosphorus and vitamin PTH 168.3pg/mL (10-65)

Conclusion

PHP1b is an uncommon disorder that should be considered in the presence of hypocalcemia, hyperphosphatemia and elevated PTH, particularly in the absence of physical findings consistent with OHA. The autosomal dominant familial form is relatively rare and its recognition may allow early diagnosis and treatment of the disease in other family members.

Bibliografia: Pseudohypoparathyroidism: Diagnosis and Treatment. JCEM, October 2011, 96(10):3020–3030; Pseudohypoparathyroidism Type 1b due to Paternal Uniparental Dissomy of Chromosome 20q. J Clin Endocrinol Metab, January 2013, 98(1):E103–E108. Pseudohypoparathyroidism and *GNAS Epigenetic* Defects: Clinical Evaluation of Albright Hereditary Osteodystrophy and Molecular Analysis in 40 Patients. Clin Endocrinol Metab, February 2010, 95(2):651–658.