PSEUDOHYPOPARATHYROIDISM TYPE 1b, A RARE DIAGNOSIS IN ADOLESCENTS

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Introduction

Pseudohypoparathyroidism (PHP) is a rare group of disorders characterized by end-organ resistance to parathyroid hormone (PTH), and other hormones, such as TSH, and absence of any features of Albright's hereditary osteodystrophy. PHP-Ib is the result of defects in the methylation pattern of the complex GNAS locus and it can be inherited in an autosomal-dominant manner or it may occur sporadically.

Case Description

A 14-year-old boy presented at the hospital because of an episode of fever and signs of hypocalceamia (positive Trousseau sign).

Physical examination:

On physical examination he was a fully pubertal adolescent with normal examination except for positive Trousseau sign. There were no dysmorhic features appreciated.

Laboratory findings:

Laboratory investigation revealed:

low serum calcium
elevated PTH and
vitamin D deficiency.

High serum phosphate
Normal serum TSH
normal serum magnesium
normal ALP

ECG showed prolonged corrected QT interval

Patient's history

Patient's history reported that he was hospitalized three years ago, because of knee metaphyseal dysplasia, with no signs of Albright's hereditary osteodystrophy dysplasia. The laboratory results had revealed mild hypocalcaemia and the rest had been quite similar with the present ones. He was treated with alphacalcidol daily, but hediscontinued therapy and he was lost to follow-up.

Patient's family history

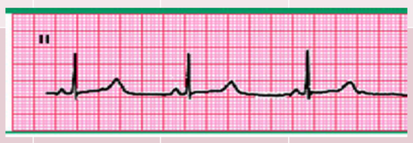
Family history reported that mother has sporadic episodes of hand numbness and her grand mother had carpal spasms and multiple fractures.

Treatment

The patient was treated with intravenous and oral calcium and alphacalcidol. Moreover a molecular genetic analysis was performed and confirmed the diagnosis of PHP typelb.

Table 1 Clinical and laboratory changes

Day of treatment	first	second	third	fourth	fifth	sixth	eighth	Normal ranges
Ca (mg/dl)	5,3	6	6,7	7,5	7	7,4	8	8,6-10,6
P (mg/dl)	5,6	6	6,2	5,6	5,5			3,5-7.0
Mg (mg/dl)	1,6	2	1,9	1,9	1,9			1,6-2,6
Albumin (g/dl)	4,7	4,7	4,8	4,6				3,8-5,4
Total protein (g/dl)	7,3	6,7	6,9	6,9				5,9-8,0
ALP	340	290						Up to 500
urea(mg/dl)	25	22						5-45
Creatinine (mg/dl)	0,8	0,7						0,5-1,2
Ca/creat urine	0,0012				0,0007			0,014-0,24
HCG QTc msec	443		429	471				350-430
Blood gas	normal				normal			



Picture 1: Biochemical presentation of the Most Common Causes of Hypocalcaemia

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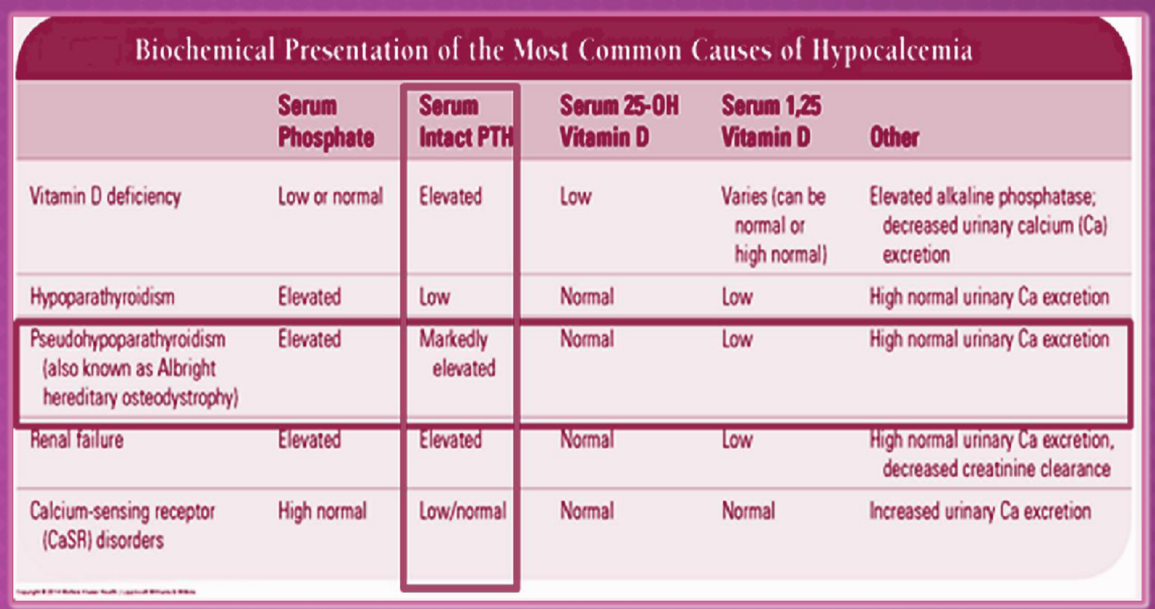


Biochemical Presentation of the Most Common Causes of Hypocalcemia

	Serum Phosphate	Serum Intact PTH	Serum 25-OH Vitamin D	Serum 1,25 Vitamin D	Other
Vitamin D deficiency	Low or normal	Elevated	Low	Varies (can be normal or high normal)	Elevated alkaline phosphatase; decreased urinary calcium (Ca) excretion
Hypoparathyroidism	Elevated	Low	Normal	Low	High normal urinary Ca excretion
Pseudohypoparathyroidism (also known as Albright hereditary osteodystrophy)	Elevated	Markedly elevated	Normal	Low	High normal urinary Ca excretion
Renal failure	Elevated	Elevated	Normal	Low	High normal urinary Ca excretion, decreased creatinine clearance
Calcium-sensing receptor (CaSR) disorders	High normal	Low/normal	Normal	Normal	Increased urinary Ca excretion

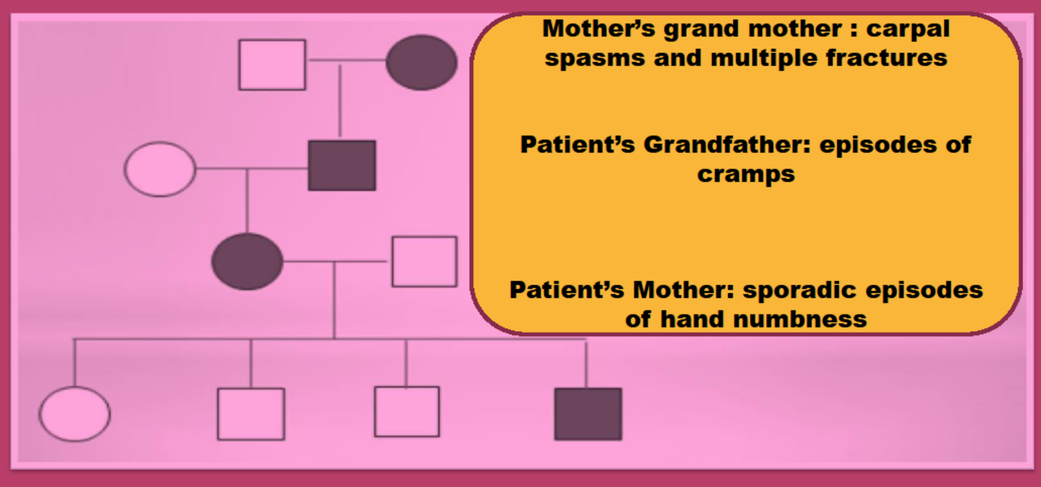
Discussion

The genetic defect for PHP_1b was mapped to chromosome 20q13.3.12 PHPIb is predominantly caused by the loss of imprinting at differentially methylated regions (DMR) on the GNAS gene which lead to decreased Gsα transcription in the renal proximal tubules, hence tissue resistance to PTH locally.

The genetic analysis on our patient revealed a complete loss of maternal methylation pattern at the GNAS exon consistent with reported loss of imprinting identified in PHP 1b.

Patients suffering from clinical disorders as a result of parathyroid hormone resistance, such as PHP, are quite rarely misdiagnosed. However, when symptoms are mild, diagnosis may be delayed due to the extreme rarity. Genetic counseling is important for the patient and the family, as well as the need for life-long treatment.

Picture 2: Patient's family tree



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