# Case Presentation- pseudohypoparathyroidism

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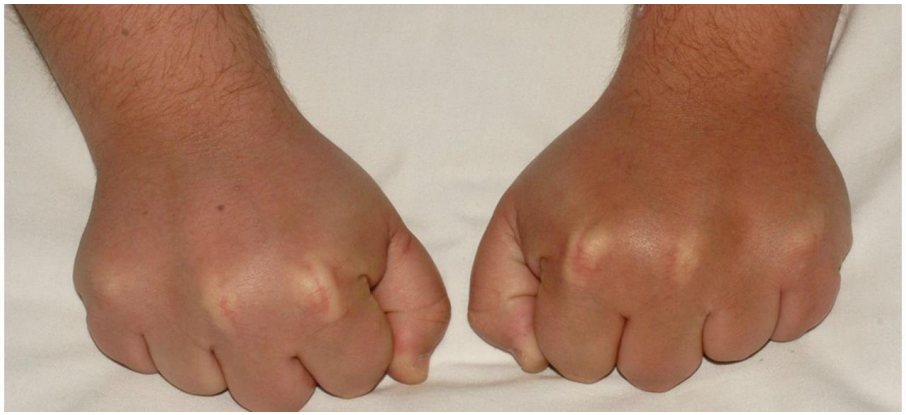
- **Girl born in 2009**
- Born at the 38. week, resuscitation, 1 day of mechanical ventillation, CPAP, iv. atb.
  - 1 month: on the chest appeared a small, hard nodule, weeks later on the forehead
- **May of 2010, Szeged:**
  - 1-2 cm big nodules all over the body- biopsy- osteoma cutis
  - Subclinical hypothyreosis- starts to take L-thyroxin (TSH: 14,0 mIU/L, fT4: 14,0 pmol/l)
  - Laboratory: Ca: 2,4 mmol/l, P: 2,03 mmol/l, PTH: 10,8 pmol/L, ALP: 274 U/L
  - Wrist X-ray: wider and shorter metacarpi
- **Albright's herediter ostodystrophy (AHO)?**

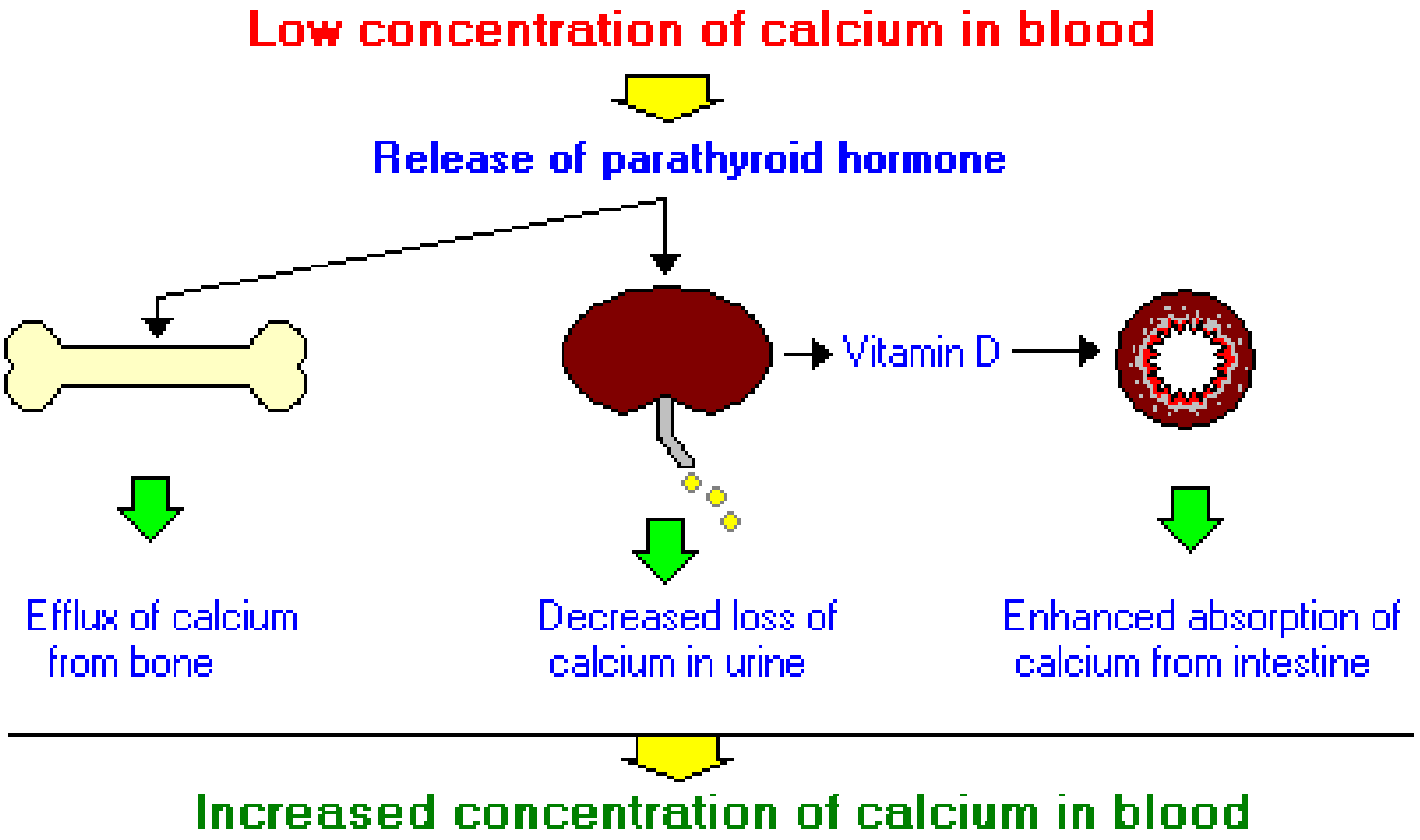
- **December of 2013, Debrecen**
  - Genetics consultation: AHO? sclerosis tuberosa? von Recklinghausen's?
  - Laboratory parameters: higher P, normal Ca, normal PTH, good TSH, fT4 with the hormone therapy
  - 2014.03. head MRI : At the site of corpus pineale a 7x5x 7 mm septated cyst (accidental finding)
- **February of 2015, Gyula, endocrinology**
  - Laboratory: higher P, normal Ca, normal PTH, good TSH, fT4 with the hormone therapy
  - Deceber, 2015: higher P, normal Ca, increasing PTH
  - February 2016: PTH: 304,6 pg/mL
  - May 2016: Ca: 2.08 mmol/L, P: 1.92 mmol/L, PTH: 1037.00 pg/mL (norm: 10-65 pg/mL) -> sended to our Hospital for confirmation of the diagnosis

- **June, 2016: 2nd Dept. of Pediatrics:**
- Physical examination:
  - Weight: 28.6 kg (pc: 90-97, SD: 2.6 )
  - Height: 117.1 cm (pc: 10-25, SD: 1.6)
  - Face: round, slight hypertelorizm
  - Short fingers, short IV. metacarpus
  - Skin: cartilage-hard, slightly elevated lesions. Above the right eyebrow a 3 cm big, on the right side of the chest 5 cm big, chest, belly, back: multiple 0,5 cm big lesions
  - Mentally normal, age-appropriate communication



- Laboratory:
  - Ca: 2.42 mmol/l, iCa 1.02 mmol/L, P: 1.73 mmol/l, PTH: 504 pg/mL (norm: 10-65 pg/mL) , D3-vitamin 10.1 ng/mL
  - Normal kidney function
  - Neck US:  thyroid gland hypoplasia
- Wrist xray: bone-age 7 years and 6 months = biological age.

# Parathyroid Hormone



- **Hypoparathyroidism**:
- **Low PTH, low Ca, high P levels**
- Symptoms: paresthesia, tetany, cramps (Chvostek's sign), abdominal pain, fatigue, headache, in severe case: seizures, heart arrythmy, bronchospasm

- **Hyperparathyroidism**:
- **High PTH, high Ca, low P levels**
- Symptoms: kidney stones, weak bones, bone pain, depression
  - **Primary**: caused by higher production of PTH of the parathyroid gland
  - **Secondary**: caused by kidney disease, kidney failure, vitamin D deficiency (the kidney does not excrete the P, insoluble Ca-P forms and removes Ca from the circulation)

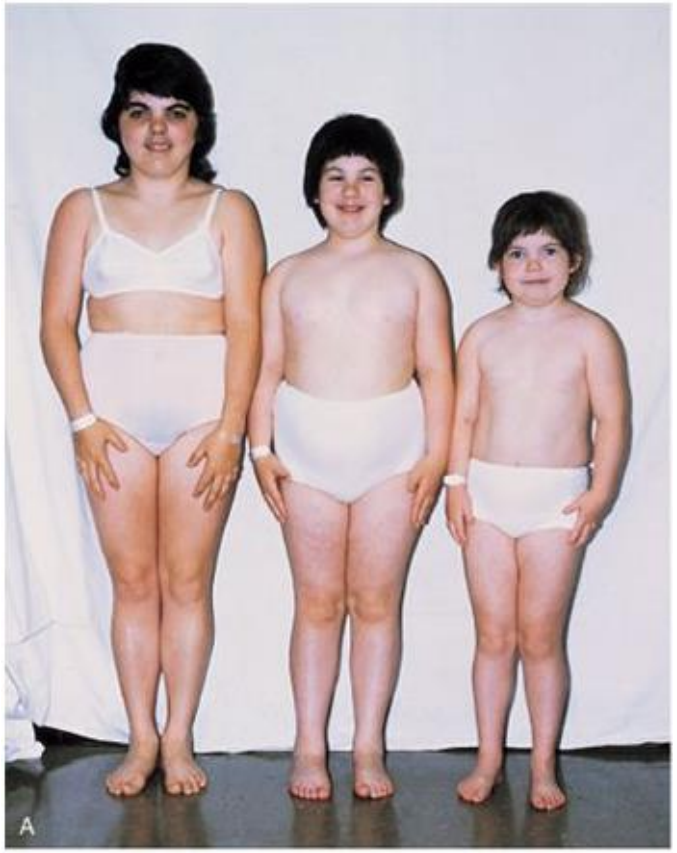
- **Pseudohypoparathyroidism**- the target organ (kidney) is insensible to PTH

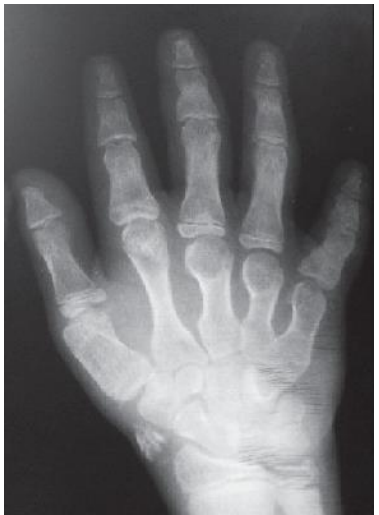
- Ca level is low (the kidney does not reabsorb the Ca)
- PTH level is high (low Ca levels triggers the PTH excretion)
- P level high (coming from the bone together with Ca because of the PTH)
- Calcifications because of the insoluble Ca-P particles

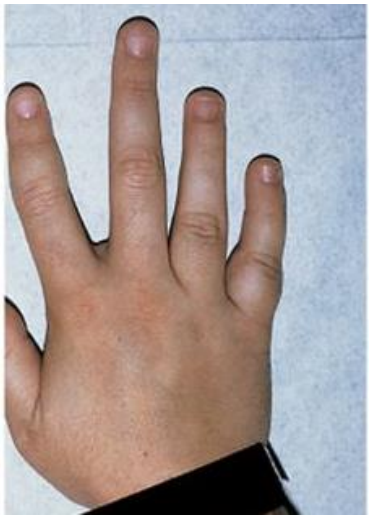
- **Pseudohypoparathyroidism Ia-** next to the receptor of the PTH other hormon receptors are also dysfunctional (TSH, LH, FSH)
- **Pseudohypoparathyroidism Ib-** PTH receptor insensitivity
- **Albright's herediter osteodystrophy-** pseudohypoparathyreosis + typical phenotype
- **Pseudo-pseudohypoparathyroidism-** Albright's phenotype without PTH resistency

# Albright's Phenotype

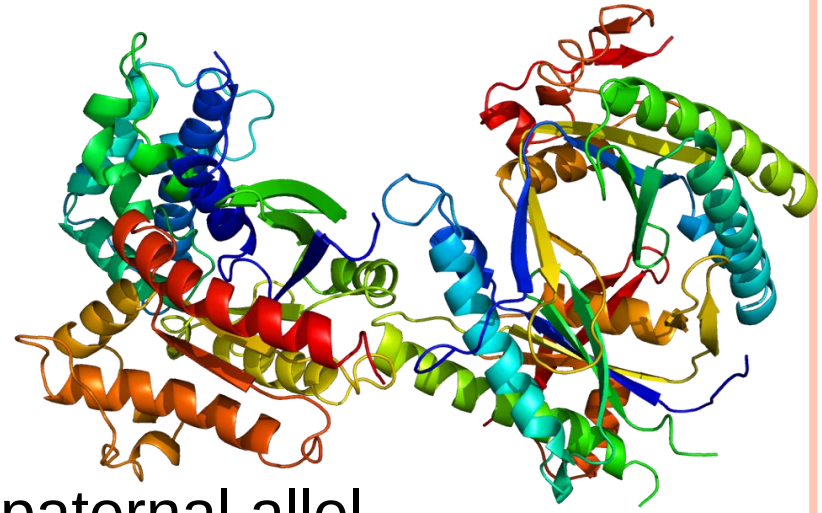
- Short statue
- Obesity
- Round face
- Brachydactily
- Short IV. metacarpus
- Subcutanous ossifications
- Sexual infantilism
- (mental retardation)





# Genetics- GNAS gene



- 20q13.2-13.3- Gsα
- Inheritance of the maternal or paternal allel mutation
- Maternal mutation: PHPT1a, paternal: PPHPT, both- PHPT1b (or imprinting error)
- tissuespecific imprinting of the GNAS gene – in the kidney tubuli, thyroid gland, pituitary gland- only maternal genes are transcripted, the paternal are silenced by methylation.
- The symptoms appear after years – the paternal methylation appears later

| | | AHO-phenotype + | AHO-phenotype - |
|---|---|---|---|
| Hormonresistency | + | **PHP1A**: maternal GNAS1 (Gsα)<br>Tissue specific monoallelic expression<br>**PHP1C**: extremly rare, ~1a, not PTH | **PHP1B**: renal resistency, Imprinting error<br><br>**PHPII**: gene defect in the GNAS signaling pathway |
| | - | **PPHP**: paternal GNAS1 (Gsα) | Vitamin D deficiency<br>CaSR activating mutation<br>DiGeorge sy<br>APECED<br>Bartter és Gittelman |

- In case of our patient the diagnosis of AHO was stated
- For the genetical proving, blood was taken for verifying the GNAS gene mutation. 2nd Dept. Of Internal Medicine
- Medicine taken: Euthyrox 50 ug, Vitamin D 2000 IU daily

- **Therapeutical goal:** Normalisation of the serum calcium level by giving Vitamin D and Calcium (avoiding the hypercalcaemia – lowering the PTH level, kidney stones, cutaneous ossifications, avoiding osteopenia)

# AHO – WHAT YOU HAVE TO KNOW

- Diagnosis suggested by dermatologist
- Hypothyroidism is observed early
- Laboratory:
  - First the PTH increases
  - Second: P level increases
  - The last: Ca level decreases (normocalcaemia is observed for a long time)
- Possibility for a molecular diagnosis (GNAS gene)
- Therapy: Vitamin D till the normalization of the Ca level and hormontherapy for hypothyroidism.