Variable phenotype and genetic findings in a cohort of patients with pseudohypoparathyroidism.

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Background

Pseudohypoparathyroidism is a group of rare disorders characterized by tissue insensitivity to multiple hormones (PTH, TSH, GHRG, LH, FSH) and Albright hereditary osteodystrophy (AHO) due to inactivating mutations or epigenetic defects of the *GNAS*.

Materials and methods

28 patients from 27 families with PHP

Hormone resistance
- PTH, Ca, P
- TSH. fT4
- IGF-1
- FSH/LH

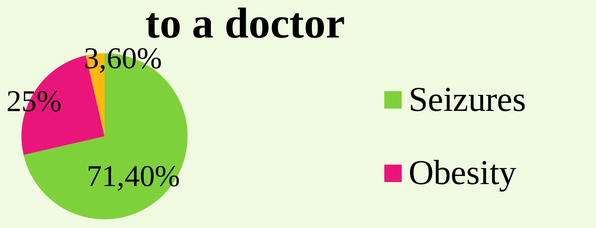
AHO-features
- brachydactyly,
- short stature,
- obesity
- round face
- subcutaneous ossifications
- mental retardation

Molecular analysis
GNAS gene sequencing for patients with AHO-features

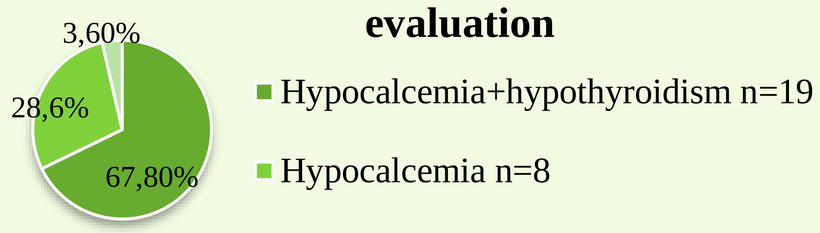
Compications
Cataract
Fahr's syndrome
Nephrocalcinosis

Results

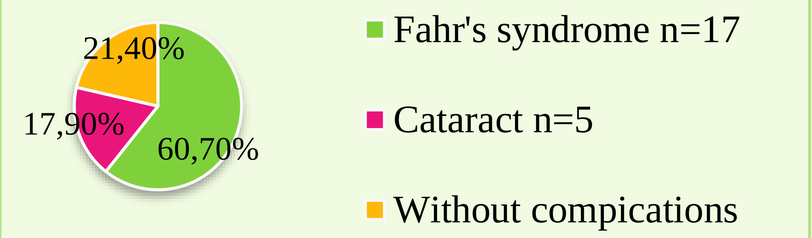
The reason for the first visit to a doctor



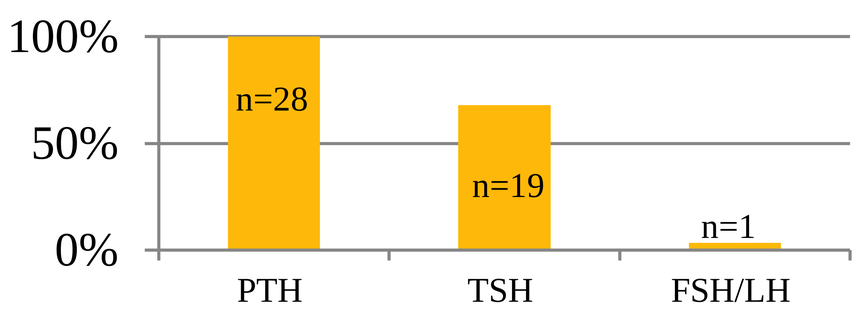
Laboratory findings at the first evaluation



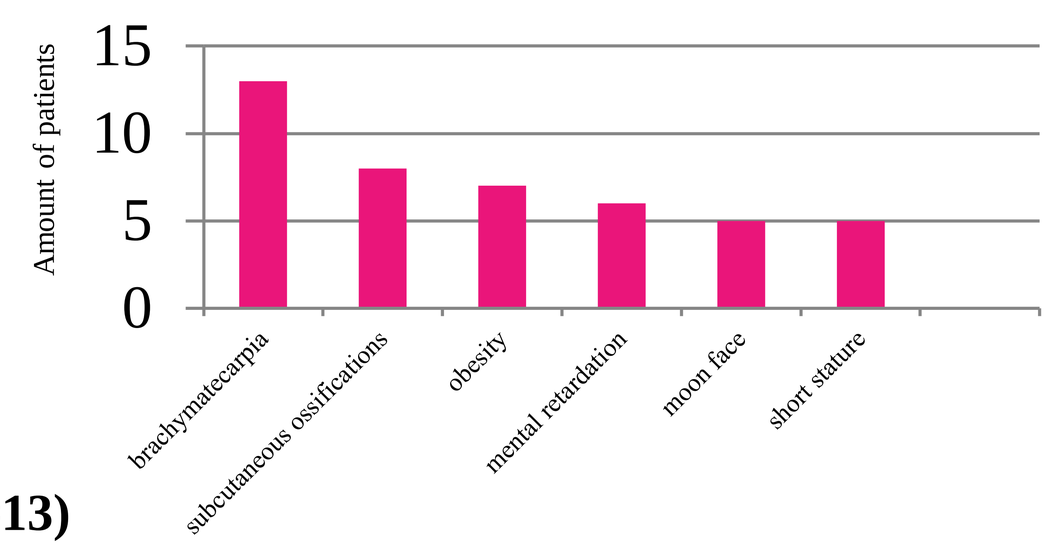
Complications



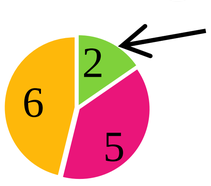
Hormone resistance



Patients with AHO-features n=13



Genetic findings in patients with AHO-phenotype (n=13)



Sister and brother, mother – without any AHO-signs and HR

- Maternally inherited GNAS mutation
- De novo GNAS mutations
- No GNAS mutations

Conclusion

Obesity or hypothyroidism can precedes hypocalcaemia in PHP. Evaluation of serum Ca is important for all patients with seizures to avoid misdiagnosing. Absence of *GNAS* mutation in patients with AHO indicates overlap between PHPIa and PHPIb. Further investigations including MS-MLPA assay are planned to explore potential phenotype-genotype correlations in PTH.

The authors have nothing to disclose

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