Jullien N et al. Clinical lessons learned in constitutional hypopituitarism from two decades of experience in a large international cohort. Clin Endocrinol (Oxf). 2020 Oct 24. doi: 10.1111/cen.14355.

CONTEXT: The international GENHYPOPIT network collects phenotypical data and screens genetic causes of non-acquired hypopituitarism.
AIMS: To describe main phenotype patterns and their evolution through life.
DESIGN: Patients were screened according to their phenotype for coding sequence variations in 8 genes: HESX1, LHX3, LHX4, PROP1, POU1F1, TBX19, OTX2 and PROKR2.
RESULTS: Among 1213 patients (1143 index cases), the age of diagnosis of hypopituitarism was congenital (24%), in childhood (28%), at puberty (32%), in adulthood (7.2%) or not available (8.8%). Noteworthy, pituitary hormonal deficiencies kept on evolving during adulthood in 49 of patients. Growth Hormone deficiency (GHD) affected 85.8% of patients and was often the first diagnosed deficiency. AdrenoCorticoTropic Hormone deficiency rarely preceded GHD, but usually followed it by over 10 years. Pituitary Magnetic Resonance Imaging (MRI) abnormalities were common (79.7%), with 39.4% pituitary stalk interruption syndrome (PSIS). The most frequently associated extrapituitary malformations were ophthalmological abnormalities (16.1%). Prevalence of identified mutations was 7.3% of index cases (84/1143) and 29.5% in familial cases (n = 146). Genetic analysis in 449 patients without extrapituitary phenotype revealed 36 PROP1, 2 POU1F1 and 17 TBX19 mutations.
CONCLUSION: This large international cohort highlights atypical phenotypic presentation of constitutional hypopituitarism, such as post pubertal presentation or adult progression of hormonal deficiencies. These results justify long-term follow-up, and the need for systematic evaluation of associated abnormalities. Genetic defects were rarely identified, mainly PROP1 mutations in pure endocrine phenotypes.