High prevalence of PROP1 defects in Lithuania: phenotypic findings in an ethnically homogenous cohort of patients with multiple pituitary hormone deficiency

Abstract

CONTEXT: PROP1 gene mutations cause multiple pituitary hormone deficiency (MPHD).

OBJECTIVE: We sought to expand experience with PROP1 mutation carriers by studying a large cohort of Lithuanian patients.

PATIENTS AND METHODS: Sixty-seven MPHD patients were tested for PROP1 defects. Perinatal and postnatal data were obtained from medical records. Hormonal investigations, pituitary imaging, and GH therapy were provided in a single center in Kaunas, Lithuania.
RESULTS: A biallelic PROP1 gene mutation was found in 47 subjects (70.1%), of which 46 were homozygous for 296delGA. Positive finding rate among MPHD and population prevalence of PROP1 defects in Lithuania (15.8 per million) were the highest reported to date. Patients' birth lengths/weights were normal. Testicular retention was noted in 31% of boys. Median height SD scores declined over years 1-5: -1.56, -2.34, -3.43, -3.52, and -3.70. Mid-parental height predicted severity of growth retardation at diagnosis (r² = 0.30; P = .0001). Deficiencies of GH, TSH, ACTH, and FSH/LH were diagnosed in 44/44, 44/44, 19/44, and 22/44 subjects at median age of 5.5, 5.6, 13.1, and 15.0 years, respectively. Pituitary height ranged from 16.6 mm (+20.2 SD) to 1.4 mm (-15.5 SD) and declined with age (r² = 0.27, P = .001). GH replacement (dose 0.027 mg/kg/d) led to height velocities 12.2; 9.1; 6.9; 6.8; 6.7; 5.6; and 5.7 cm/y (medians) at years 1-7 and final height SD scores (17 patients) -0.98 ± 1.77 (-1.04 ± 1.41 below target height; P = .008 vs 0).

CONCLUSIONS: High prevalence of PROP1 defects in Lithuania is due to 296delGA mutation, suggesting a founder effect.


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