



Endocrine Abnormalities in Phosphoglucomutase 1 Deficiency

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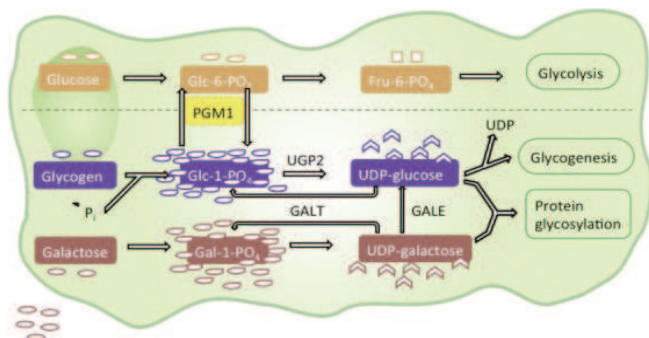
Conclusion:

- Phosphoglucomutase 1 (PGM1) Deficiency affects glycogen metabolism, as well as protein glycosylation.
- Endocrine abnormalities appear to be a consistent feature of PGM1 deficiency, resulting in hypogonadotropic hypogonadism and growth retardation.

Introduction:

- **Phosphoglucomutase 1 Deficiency** previously known as glycogenosis type XIV, is caused by mutations in the **PGM1** gene resulting in altered conversion from Glucose-1-phosphate to Glucose-6-phosphate (shown in Fig. 1).
- Because Glucose-1-phosphate is also involved in metabolic processes of the glycosylation of proteins, PGM1 deficiency can result in abnormalities of hormones and their binding proteins, which is well known in Congenital Disorders of Glycosylation (CDG).
- We present a girl with PGM1, featuring endocrine abnormalities also found in patients with CDG.

Fig. 1: PGM1-CDG



Case Report:

First consultation: age 13;7 years, with growth retardation and lack of pubertal development (Fig. 2)

Medical history: cleft soft palate, malignant hyperthermia, myopathy, hepatopathia, fasting hypoglycemia, dilated cardiomyopathy, normal intelligence

First results:

- abdominal sonography: prepubertal uterus and ovary glands
- bone age: 13 years (G+P)
- cranial MRI: normal
- echocardiography: SF 25%, LV 60 mm, MI II°
- chromosomal analysis: 46, XX

Endocrine findings:

- **Low:** E2 < 10 pg/ml (n:16,2-136,3), IGF1: 79 ng/ml (n: 188-510), IGFBP3 1,82 µg/ml (n: 2,7-10) TBG: 1,3 mg/dl (n: 2,0-3,0), transcortin: 28 µg/ml (n: 40-60)
- **Normal:** cortisol 9,4 µg/dl, FT4 1,16 ng/dl (n: 0,88-1,63), FT3 3,5 pg/ml (n: 2,0-4,2), TSH 1,75 µU/ml (n: 0,35-7,0), prolaktin 4,0 ng/ml (n: 3,6-25,8)
- **GnRH-test:** LH basal <0,1 U/l, max. 2,9 U/l
FSH basal 1,7 U/l, max. 7,6 U/l

Proceedings:

- Induction of puberty at the age of 14;8 years with standard hormone therapy
 - normal breast development
 - age of menarche 17,1 years
 - catch-up growth with pubertal growth spurt (however adult height below target height) (Fig. 2)
- PGM1 enzyme activity in skin fibroblasts: 1,3 % of controls
- PGM1 gene: heterozygous for c.988G>C (p.G330R) and 1129G>A (p.E377K)

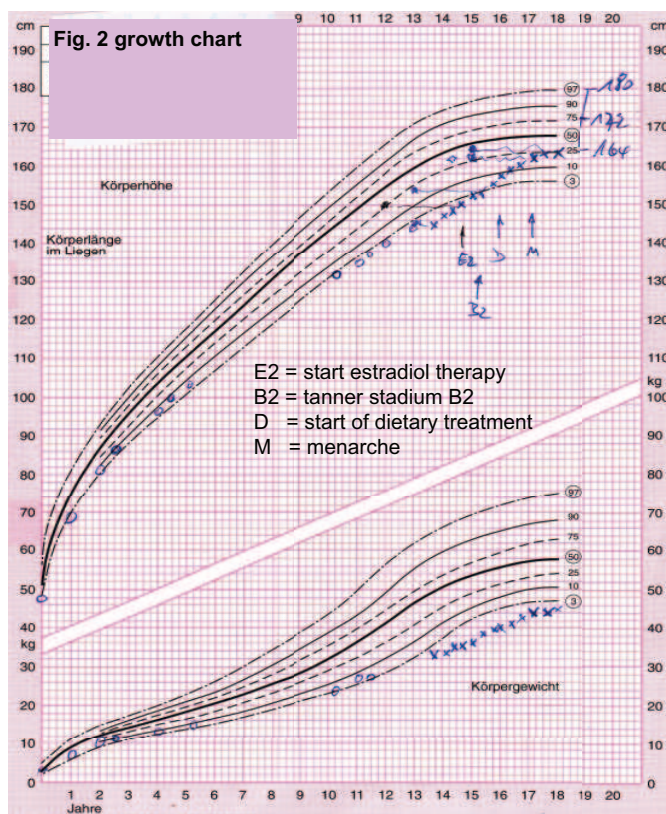


Chart 1: Comparison of endocrine findings

	PGM1-CDG	CDG (literature)
	our case/patient	literature
thyroid	euthyroid	not specified
growth	retardation	retardation approx. 80%
puberty	delayed	delayed or normal
gonadotropins	hypogonadotropic hypogonadism	hypogonadism due to inactive FSH or hypergonadotropic hypogonadism
binding globulins (TBG/ CBG)	decreased	not specified
IGF1 and IGFBP3	decreased	decreased
hypoglycemia	documented	frequently

Fig. 3: GnRH-test

