Late diagnosis of adrenal insufficiency caused by novel compound heterozygous mutations in *POMC*

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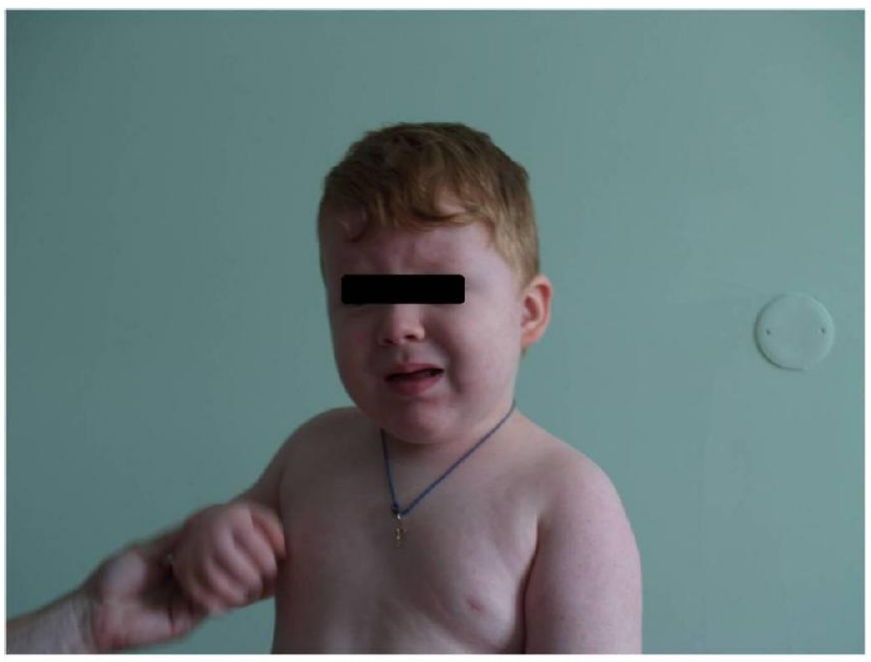
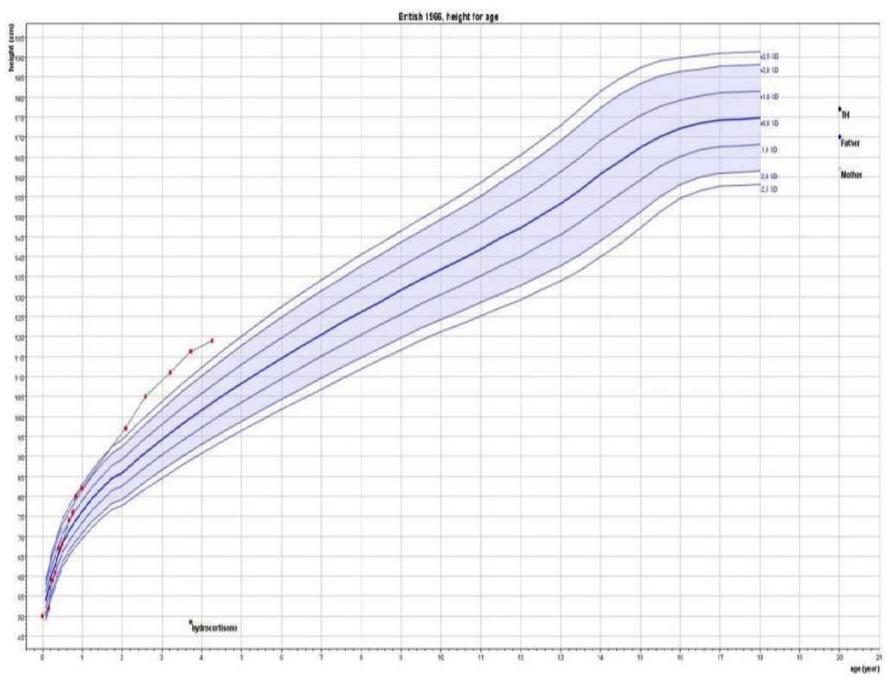
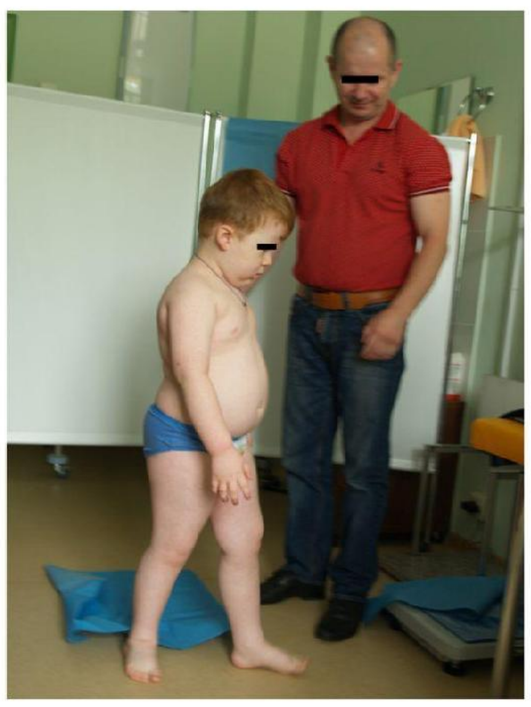
Introduction. Proopiomelanocortin (POMC) deficiency is characterised clinically by adrenal insufficiency, obesity and red hair. As a rule, such patients present early in life with severe hypoglycemia, which leads to initiation of glucocorticoid therapy. We describe here a case of POMC deficiency, where adrenal insufficiency was not diagnosed until the fourth year of life.

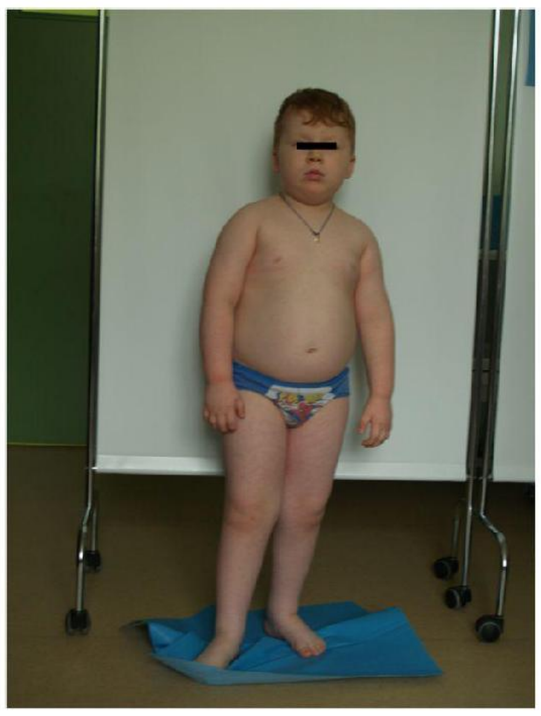
Objective. To present a case of late diagnosis of POMC deficiency and characterise novel mutations in *POMC* gene.



Case report. The boy initially presented with prolonged neonatal jaundice. By the end of his first year the growth acceleration was evident. There were two episodes of severe hypoglycemia (glucose level 1,7 mmol/L) at ages of 1.5 and 3 years. In addition, there were recurrent episodes of cholestasis with bilirubin level 101 mcmol/L, ALAT 276 U/l, ASAT 444 U/l. At presentation at 3.6 years his height was at 4.1 SD, the BMI at 3.0 SD. He had red hair and light skin. Plasma ACTH and serum cortisol were undetectable. Replacement with hydrocortisone was initiated.







Sequencing of *POMC* gene revealed two novel heterozygous mutations: p.W84X and c.-11C>A. The latter mutation is predicted to create an alternative initiation codon, which results in a frameshift.

Conclusion: A case of late diagnosis of POMC deficiency is presented. It is not yet clear whether c.-11C>A mutation is compatible with partial inframe POMC translation, which could explain less severe adrenal insufficiency in infancy.

References: Severe early-onset obesity, adrenal insufficiency and red hair pigmentation caused by POMC mutations in humans, Heiko Krude, Heike Biebermann, Werner Luck, Rüdiger Horn, Georg Brabant & Annette Grüters, Nature genetics volume, 19 june 1998

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