The hypocortisolism and hypopigmentation are due to inadequate stimulation of MC2R and MC1Rs by POMC-derived peptides in the adrenal gland and skin, respectively.

A CASE OF EARLY-ONSET OBESITY WITH A NEW MUTATION AT THE PROOPIOMELANOCORTIN GENE

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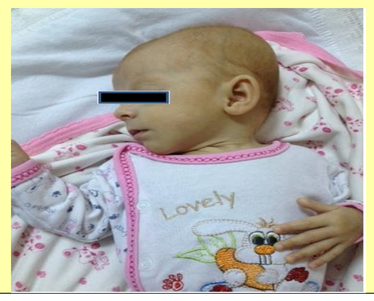
INTRODUCTION

Proopiomelanocortin (POMC) is a 241-amino acid polypeptide encoded by the POMC gene located at 2p23.3. Complete mutation in the gene is associated with the classical triad of early-onset obesity, adrenal insufficiency, and red hair. A new POMC gene mutation was detected in our patient who presented with the hypoglycemia symptom in the second month of life. With this case, our information on the new mutation to phenotype relationship, leptin-melanocortin pathway, POMC-derived peptides and energy balance will be discussed.

CASE REPORT

The female patient aged 2.5 months was brought to another healthcare center with restlessness, cyanosis, cross eye and spasms .
Her blood glucose was measured as 31 mg/dl and was therefore referred with the initial diagnosis of metabolic disease.
Born at 39 weeks with a birth weight of 3000 g, the patient had no problems during the prenatal/natal period.
Her mother and father were not relatives.

At age 2.5 months
Body weight: 3700 g (3 p)
Height: 51 cm (<3p)
Head Circumference: 35 cm (<3p)
Eyebrows and hair were red,
External female appearance

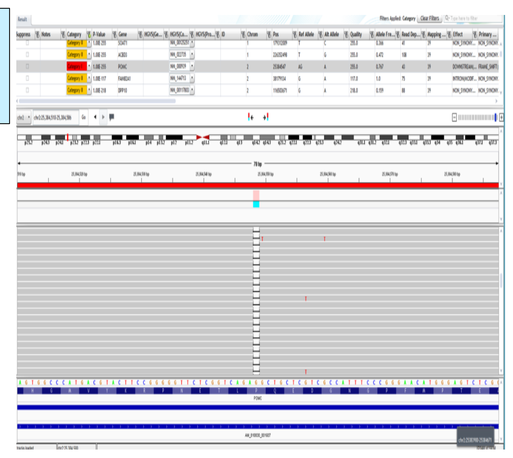


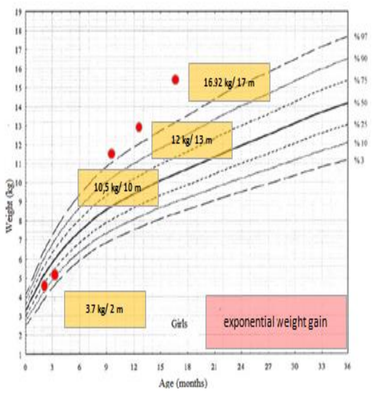
Laboratory results (During Hypoglycemia (35 mg/dl))
Blood Ketone: Negative
Urinary Ketone:Negative
Blood Gas pH: 7.39, HCO3: 18.6 mmol/l
Insulin: 0.11 mIU/ml C peptide: <0.1 ng/ml
ACTH: <5 pg/ml, Cortisol: <0.2 µg/dl
Growth Hormone: 14.8 ng/ml
Lactate: 21.4 mg/dl
Ammonium: 131 µg/dl (19-60)
Urine and blood aminoacids: normal
Urinary organic acid profile: normal
Tandem MS: normal

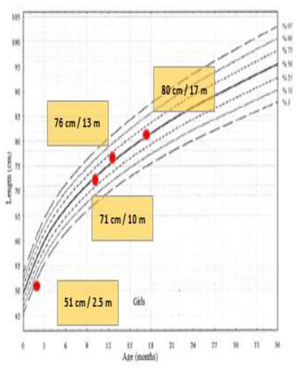
Laboratory results:
Hb: 9.5 g/dl, Hct: 30.6%, MCV: 83 fL,
WBC: 12.200/mm³, Platelet: 516 000/mm3
Glucose: 20 mg/dl
BUN: 9 mg/dl, Creatinine: 0.19 mg/dl
Uric acid: 2.6 mg/dl
ALT: 23 U/l, AST: 123 U/l (<36)
Creatinine Kinase: 419 IU/L (34-204)
Calcium: 9.8 mg/dl (8.4-10.2), Phosphor: 5.7 mg/dl (2.7-4.5)
Alkaline phosphatase: 524 U/l
Sodium: 132 mEq/l (135-143), Potassium: 4.8 mEq/l (3.1-5.5)
TSH: 1.73 mIU/ml sT4: 1.09 ng/dl, Prolactin: 18.49 ng/ml
FSH: <3 mIU/ml, LH: <0.07 mIU/ml, E2: 29.44 pg

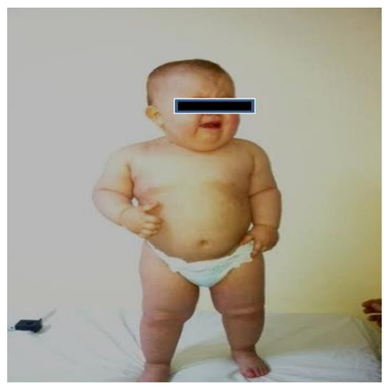
Hydrocortisone treatment→normal glucose levels

69 aminoacid (prolin) homozygous frameshiftmutation: delG209 at the POMC gene









Last visit (At 21 months):
Body weight: 21 kg (>97 p)
Height: 85 cm (50-75 p)
Eyebrows and hair were red
The final steroid treatment dose was 8.9 mg/m2/day.

POMC dervived peptides are bound to five different melanocortin receptors with varying affinity and specificity.
The hypocortisolism and hypopigmentation are due to inadequate stimulation of MC2R and MC1Rs by POMC-derived peptides in the adrenal gland and skin, respectively.

Agouti-related peptide (Ag-RP) is co-expressed with Neuropeptide-Y (NPY). This peptide increases appetite and decreases energy use and metabolism. This system is inhibited by leptin and stimulated by ghrelin.

In POMC deficiency, the appetite-stimulating effect of agouti-related peptide (Ag-RP) is not balanced by the appetite-suppressing effect of POMC.

CONCLUSION

In conclusion, our patient had classic findings of POMC deficiency. However, our options in the treatment of obesity seem to be very limited at the current state of our knowledge.

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