

# AN 18 MONTH OLD BOY WITH HYPOGLYCEMIC CONVULSION AND OBESITY DUE TO POMC DEFICIENCY

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## Background

Proopiomelanocortin (POMC) is the polypeptide precursor of several peptides including adrenocorticotrophic hormone (ACTH), melanocyte stimulating hormone (MSH) and  $\beta$ -endorphin. POMC deficiency is a very rare disease characterized by adrenal insufficiency, early-onset obesity, and pigmentation abnormalities.

Here we describe an 18 month old boy with central adrenal insufficiency, hypothyroidism, obesity and fair skin. Genetic analysis revealed a homozygous p.G99Afs\*59 (c.296delG) mutation in the *POMC* gene.

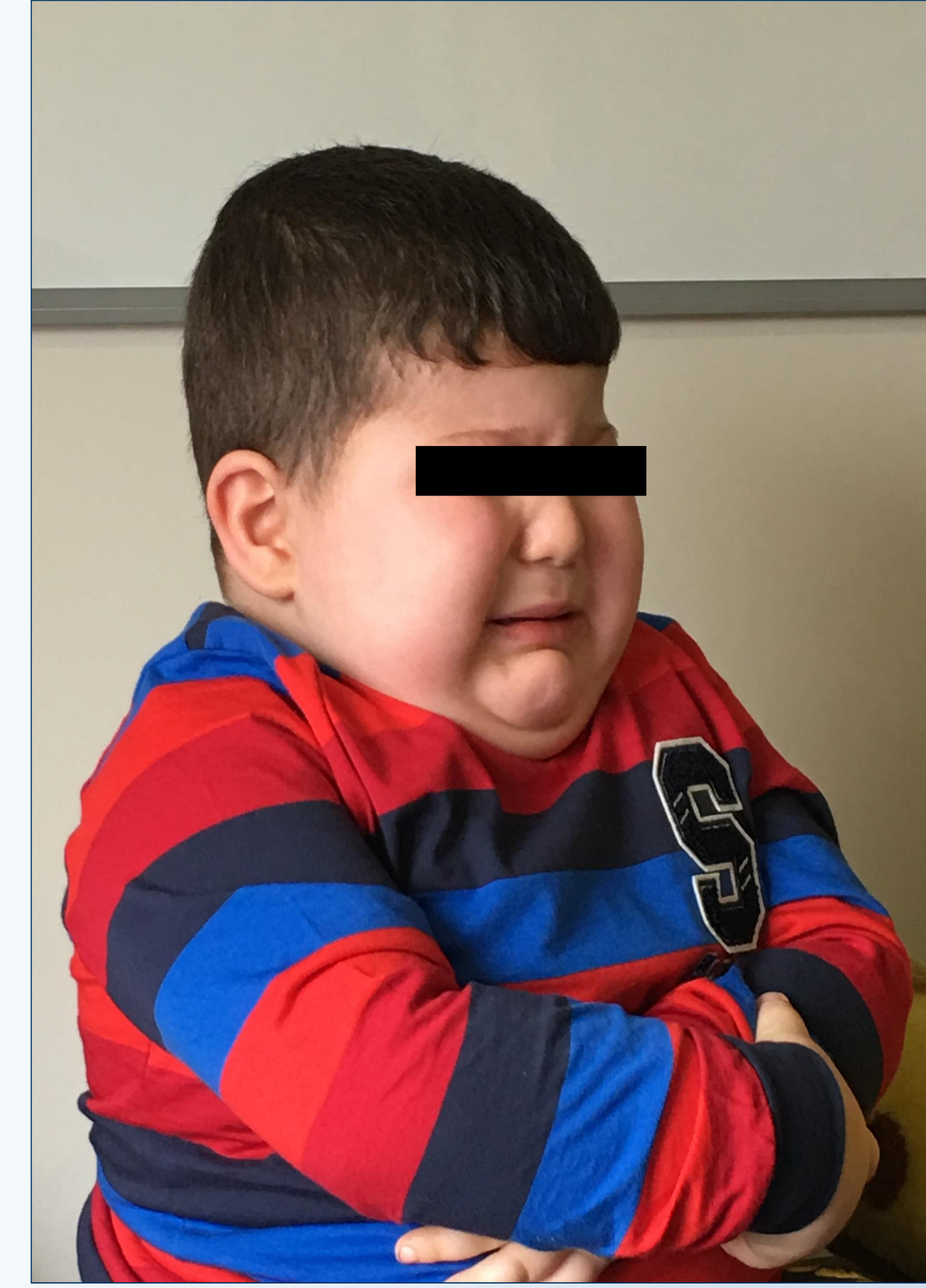
## Case Report

An 18 month old boy (Figure 1) was referred for hypoglycemia. He was born to parents from close villages at 37 weeks gestation with a birth weight of 2,500 kg. Medical history revealed neonatal intensive care hospitalization for 28 days due to respiratory distress. He had a seven year old healthy sister.

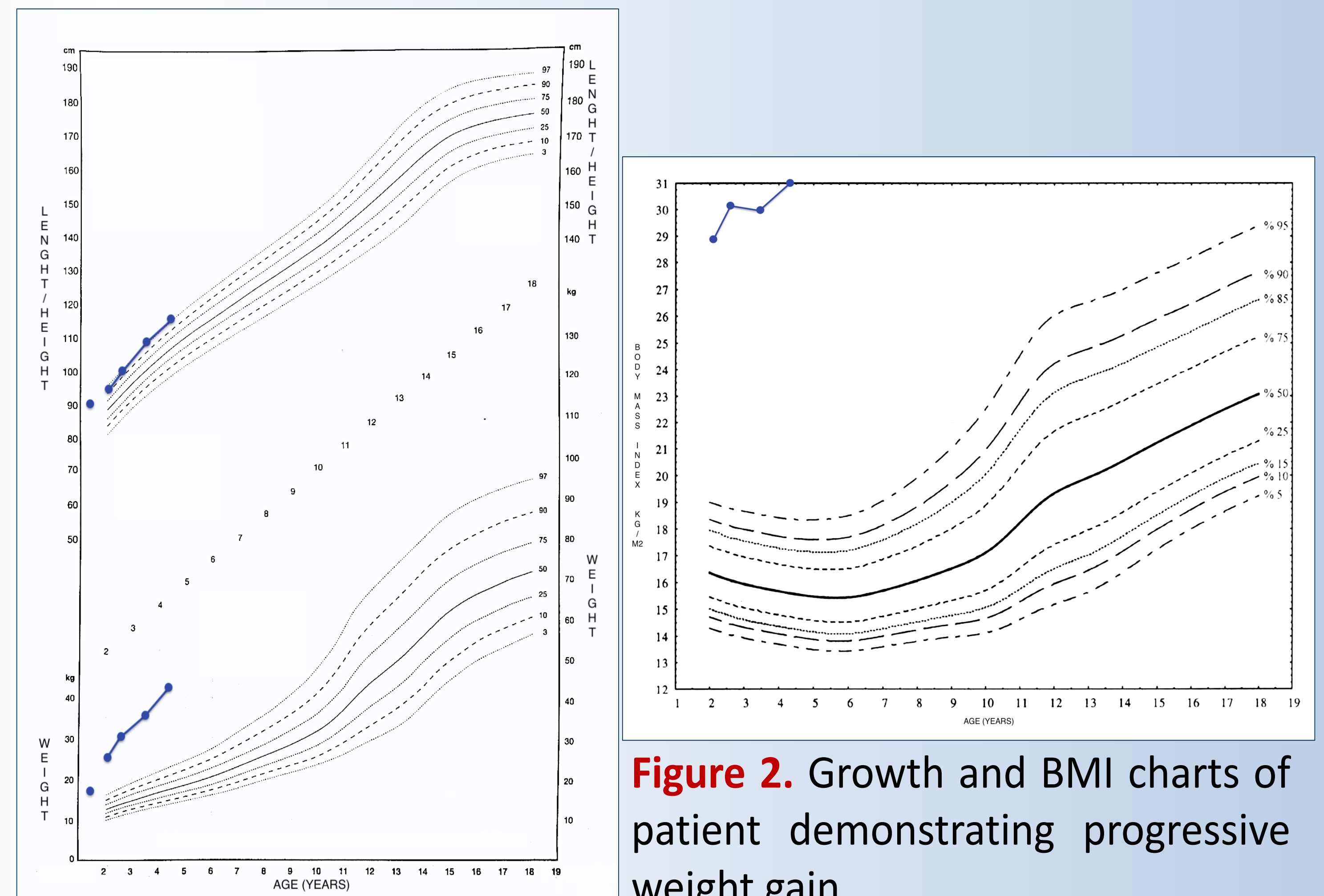
He was admitted to emergency department with seizure. The laboratory tests revealed hypoglycemia (venous glucose: 30 mg/dl), hyponatremia (130 mEq/L), hypocortisolism (cortisol: 0.619 ug/dl) as well as subclinic hypothyroidism (free T4: 0.845 ng/dL (0.93-1.7), TSH: 9.9 mIU/mL (0.5-6.5)). Morning ACTH was < 5 pg/mL, and cortisol was 0,488  $\mu$ g/dl. Magnetic resonance imaging (MRI) of the brain and pituitary gland was normal. On his initial examination height SDS was +2,28 (90,5cm), weight SDS was +3,34 (17,2kg) and BMI SDS was +2,46 (21 kg/m<sup>2</sup>) (Figure 2). He was noted to have mild developmental delay, obesity, fair skin and hepatosplenomegaly. A homozygous p.G99Afs\*59 (c.296delG) mutation in the *POMC* gene was detected (Figure 3). This mutation has already been described in Turkish patients (Krude 2000, Darcan 2009). Hydrocortisone and L-thyroxine replacement was initiated.

## Conclusions

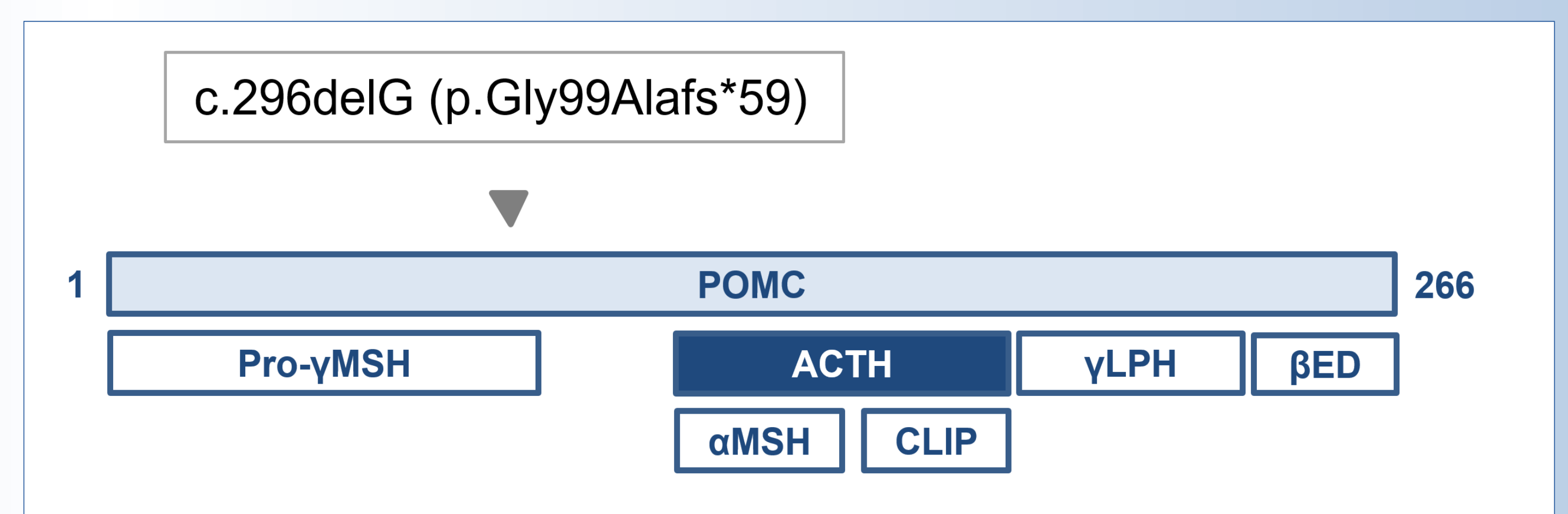
Central adrenal insufficiency is rare in children. In our patient, p.G99Afs\*59 mutation of the *POMC* gene results in ACTH deficiency subsequently leading to impaired adrenal steroidogenesis, dysregulation of food intake and early-onset obesity, increased linear growth, and melanocyte dysfunction. Early identification of these patients may enable early management of adrenal failure and its associated morbidities as well as severe obesity by novel therapeutic approaches.



**Figure 1.** Facial appearance of the patient with POMC deficiency at 3 years of age.



**Figure 2.** Growth and BMI charts of patient demonstrating progressive weight gain.



**Figure 3.** Chromatogram showing the homozygous c.296delG change in *POMC* gene that results in a glycine residue being replaced by an alanine residue which subsequently causes a stop codon and a truncated protein after 59 aminoacids (upper). This mutation causes disruption of POMC and prevents cleavage of POMC into key peptides such as ACTH and  $\alpha$  MSH.

## References

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