Homozygosity for Proopiomelanocortin (POMC) mutation in a Palestininan child

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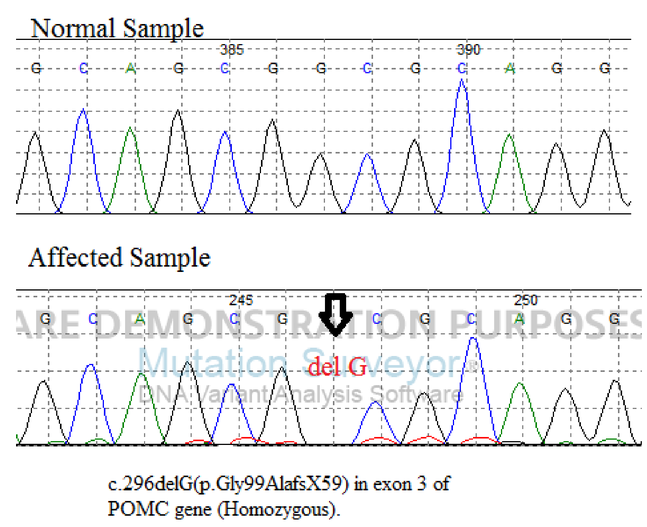
Background: Congenital Proopiomelanocortin deficiency (POMC) is a rare autosomal recessive disorder characterized by the association of adrenal insufficiency, early onset obesity, hyperphagia and altered skin & hair pigmentation. POMC is a complex propeptide encoding a range of melanocortin peptides that are released by tissue-specific proteolytic processing. These peptides have important roles in a range of functions such as skin pigmentation and the control of adrenal growth and function. In the central nervous system, POMC is most highly expressed in the arcuate nucleus of the hypothalamus, and POMC-expressing neurons are critically involved in the control of appetite and energy balance.

Here we describe a novel homozygosity mutation for POMC gene in a Palestinian family with congenital proopiomelanocortin deficiency.

Clinical presentation and Methods: A Palestinian infant, born to consanguineous parents, presented with early onset obesity, hyperphagia, adrenal insufficiency, and red hair. Cortisol level was undetectable before and after stimulation, very low ACTH level. Congenital Proopiocmelanocortin deficiency syndrome was suspected and confirmed by molecular testing.

Results: DNA sequencing of the POMC gene revealed a homozygous mutation c.296delG (p.G99AfsX59) in exon 3, while his father & mother are heterozygous. This mutation has been detected before as a compound heterozygous and as a disease causing mutation.

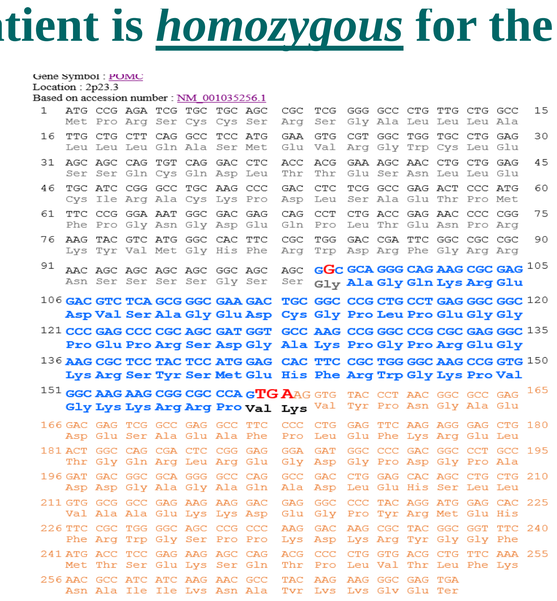
A



c.296delG(p.Gly99AlafsX59) in exon 3 of POMC gene (Homozygous).

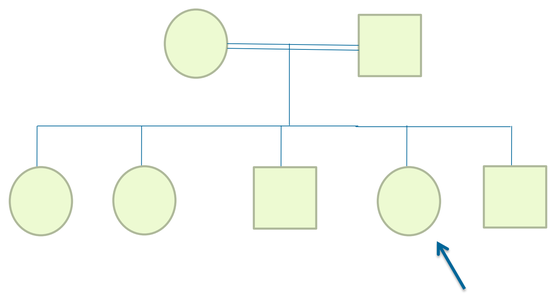
A. The patient is *homozygous* for the mutation

B



B. c.296delG mutation is a deletion mutation of G at codon 99 that leads to frame shift and premature termination of protein translation after 59 codons (p. p.G99AfsX59).

Family Pedigree:



Conclusions

- To our knowledge, this is the first description of this disease in a Palestinian family with molecular confirmation in a homozygous form, allowing accurate genetic counseling, early diagnosis of affected kindreds, early therapeutic interventions and avoiding complications.
- Molecular genetic abnormalities of POMC should always be considered in patients with early onset adrenal insufficiency and hyperphagic obesity, even in the presence of normal pigmentation.