Idiopathic Hypogonadotropic Hypogonadism due to a GNRH1 Mutation

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**Background:** Idiopathic hypogonadotropic hypogonadism may be normosmic (nIHH) or it may be associated with anosmia, which is known as Kallmann syndrome (KS). First mutation GNRH1 was described in 2009 in patients with nIHH. Mutations of the human GNRH1 gene are a very rare cause of nIHH, with only six mutations so far described.

**Case:** The proband is a 11.3-year-old boy who first presented at age 1 with micropenis and cryptorchidism. His past medical history is unremarkable except for a bilateral orchiopexy surgery at the age of two years. His parents are healthy cousins. The proband’s height and weight are 149 cm (50th-75th percentile) and 84.5 kg (>95 percentile), respectively. His pubic and axillary hair are at Tanner stage 4 and 2, respectively. His testes are 1 mL bilaterally in the scrotum. His stretched penile length was 3.6 cm. Chromosome analysis revealed a 46,XY karyotype. Pelvic ultrasonography confirmed the absence of müllerian structures and the presence of both gonads with features of normal testes in the scrotum. His bone age is 11 years.

**Results:** Genetic analysis of this patient identified a homozygous deletion (c.87delA) leading to a frameshift mutation (p.G29GfsX12) in GNRH1.

**Conclusion:** We here described a frameshift GNRH1 mutation which is predicted to lead a total failure of GnRH synthesis. This mutation was previously reported by Chan et al. Comparison of phenotypes show no difference. GNRH1 mutation in IHH are indeed very rare as we found only one mutation among 30 families with identified causative mutations. These rare patients offer a unique opportunity to study the effects of human GnRH deficiency.