Ectopic posterior pituitary, polydactyly, midfacial hypoplasia and panhypopituitarism due to a novel heterozygous IVS11-2A>C(c.1957-2A>C) mutation in GLI2 gene

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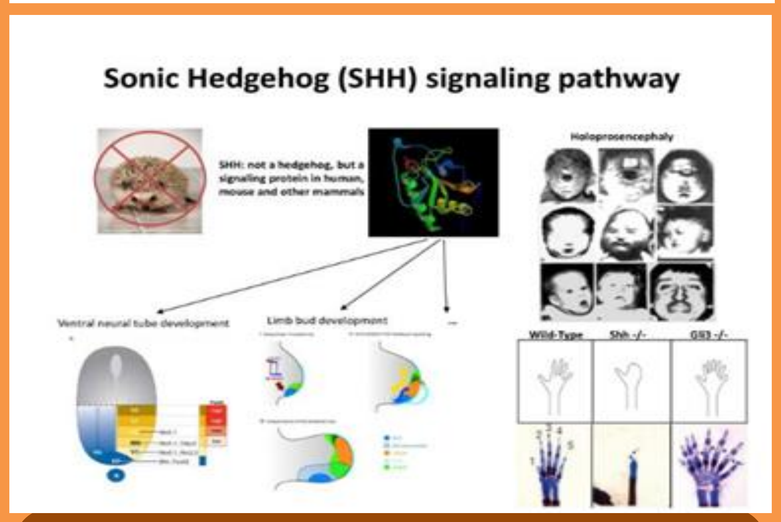
Objective

GLI2 is an activating zinc-finger transcription factor in the Sonic hedgehog (SH) signalling pathway which plays a crucial role in the development of diencephalon and distal extremities during embryogenesis. We, report a novel heterozygous IVS11-2A>C(c.1957-2A>C) mutation in GLI2 gene with an extremely distinct phenotypical expression in two siblings and their father from an unrelated family.



Conclusion

Present novel heterozygous mutation detected in the GLI2 gene suggested an extremely variable clinical phenotype in individuals with identical mutation, even in those within the same family and incomplete penetrance of GLI2 mutations.

Patients

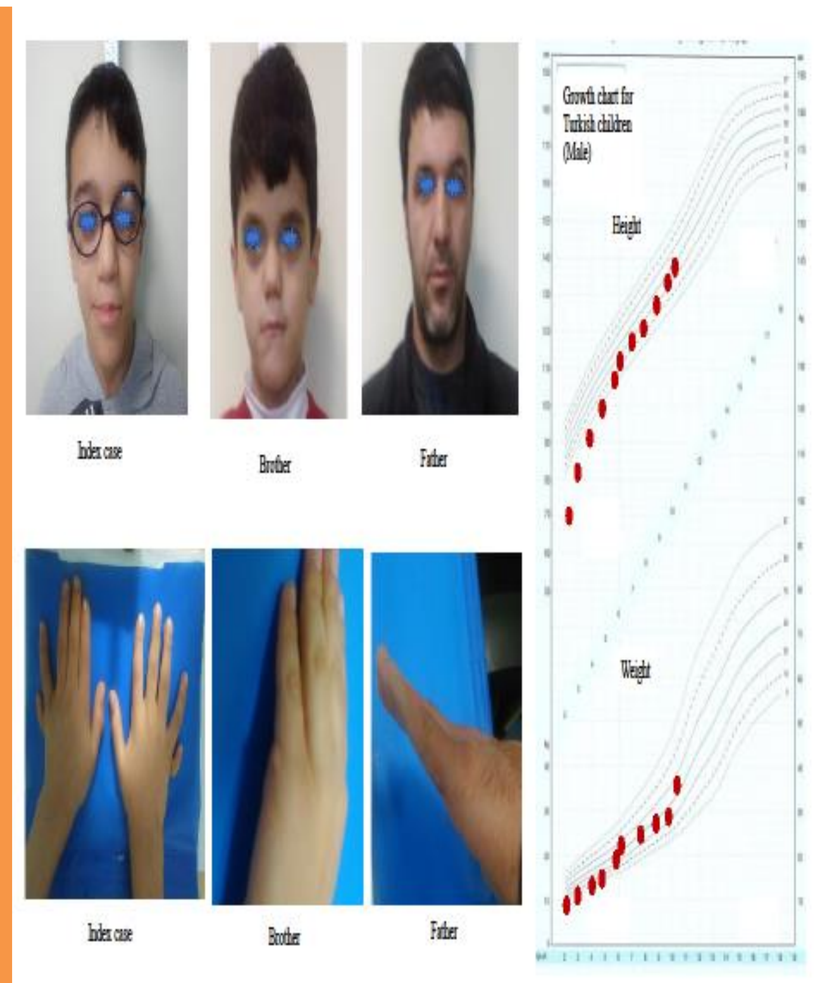


Figure 1. Facial dysmorphism and polydactyly in index case, his brother and father (a-f). Good response to rhGH therapy in index case (g).

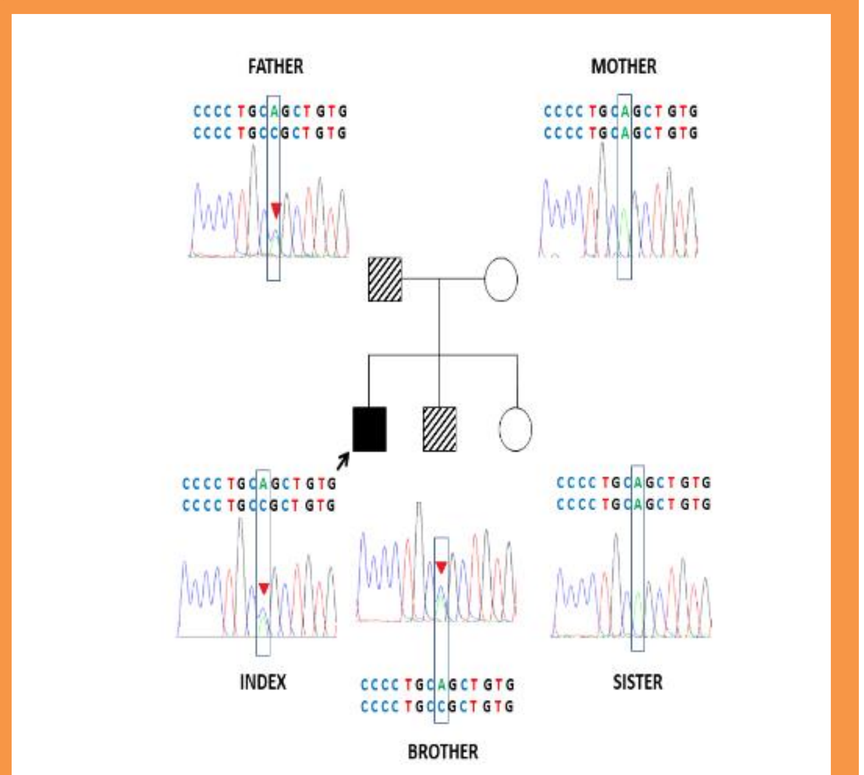


Figure 2.Family pedigree and electropherogram of heterozygous IVS11-2A>C(c.1957-2A>C) mutation in GLI2 gene

A male who was born to non-consanguineous parents after a 40 weeks gestation and birth weight was 3700 gr. He had postaxial polydactyly, mid-facial hypoplasia, high palatal arch, micropenis and bilateral cryptorchidism. He developed cholestasis and hypoglycaemia episodes during follow up. Critical blood samples revealed a diagnosis of congenital panhypopituitarism. He had severe anterior pituitary hypoplasia, absent pituitary stalk and ectopic posterior pituitary with no any other midline structural abnormality. Na-L-T4, hydrocortisone and GH replacement therapies were commenced. The response to the GH replacement was excellent (Figure 1). At his most recent follow up visit his height was 133.5 cm (-0,46), weight was 28.7kg (-0.51 SD) and body mass index was 16.1 kg/m2 (-0.4 SD). He had moderate developmental delay. One of his brother, father and paternal grandfather had polydactyly and/or atypical facial appearance with no any hormonal disorders.

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