

Introduction

Congenital hyperinsulinemic hypoglycemia of infancy (CHHI) associates with mutations in known genes in approximately 60% of cases. CHHI and mutations in HNF4A gene are reported in 0.5 to 2.4% in large series. A case of CHHI with renal Fanconi syndrome (FS) and hepatopathy is presented

Clinical Description

Male newborn, gestational age: 38 weeks, weight: 4250 grams +2.7 SD, length: 55 cm +3.29 SD, developed hypoglycemia during the first day of life.

Laboratory tests on hypoglycemia revealed high insulin and C peptide (6.1mU/L and 2.7ng/mL respectively) with low beta-hydroxybutyrate (10.2mcmol/L). Glucose perfusions up to 17 mg/kg/min were needed. After CHHI diagnosis, diazoxide (8mg/kg/day) was started normalizing glucose needs. Reduction of diazoxide was required because of hyperglycemias and it was stopped at three months of age because of glycemias up to 300 mg/dl, later treatment involved adapted diet alone.

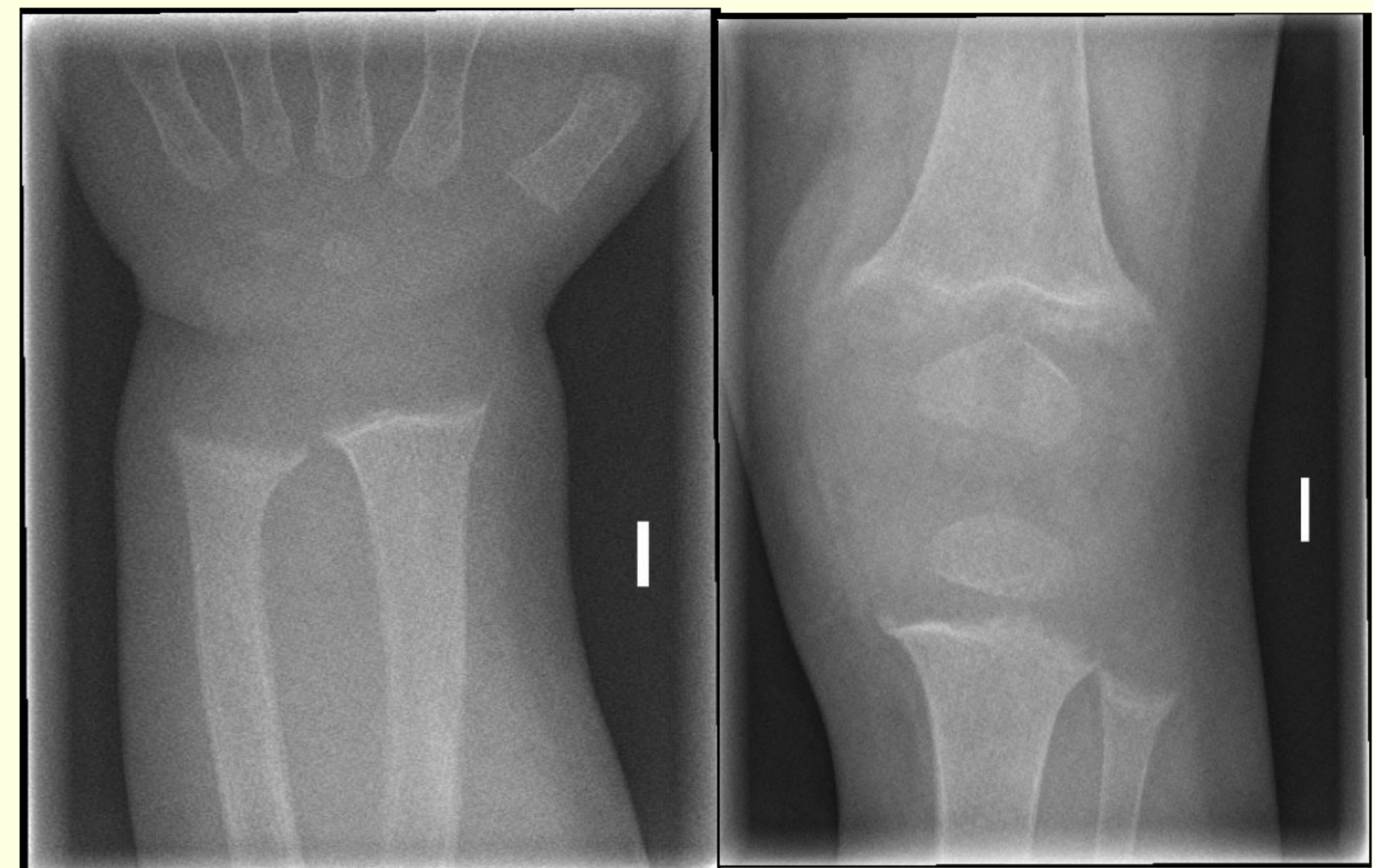
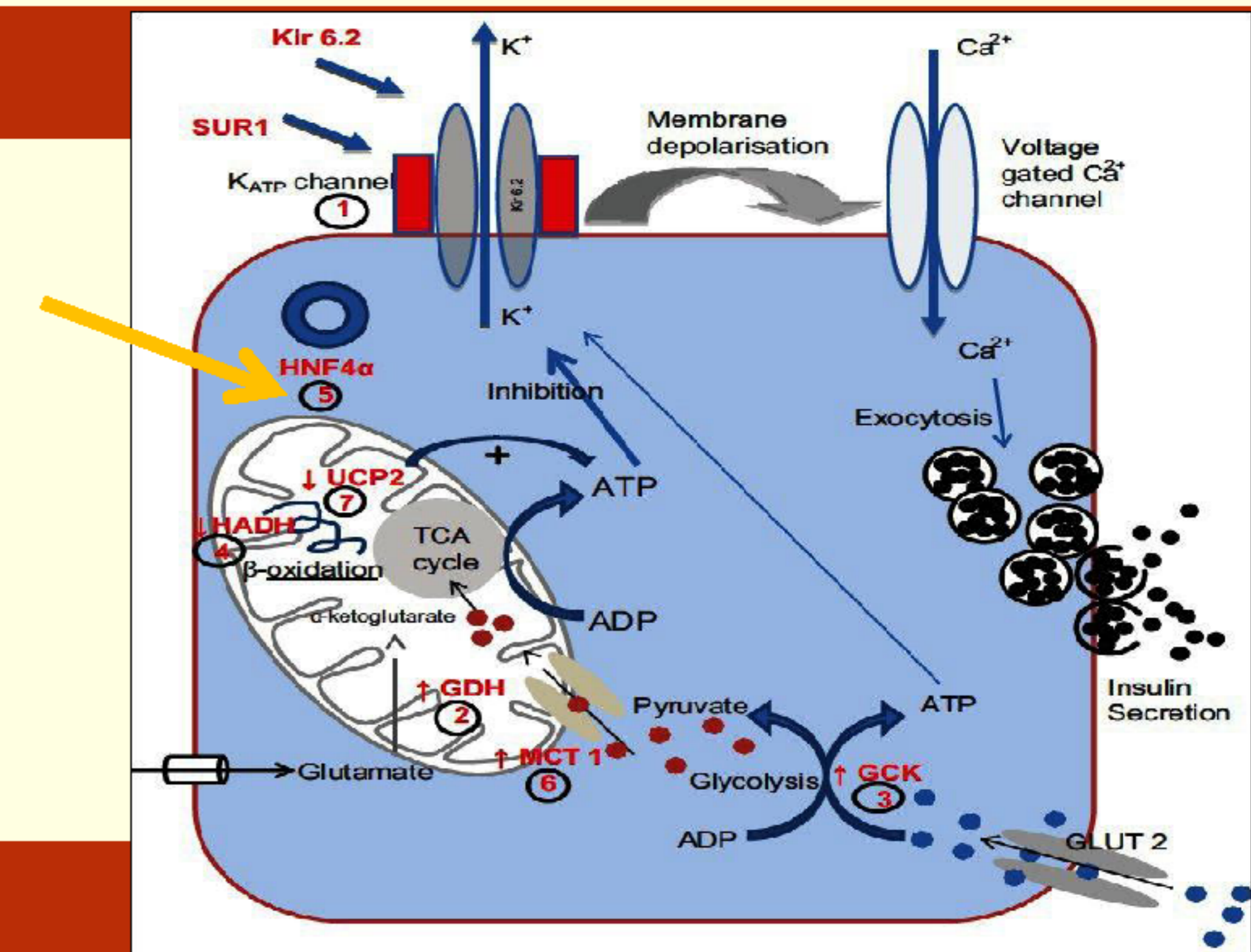
Six months old: he had failure to thrive and later presented stunting and hepatomegaly, with persistent hypertransaminasemia and glucosuria. Viral and autoimmunity tests were negative.

An increase of alkaline phosphatase (800-900IU/L), low vitamin D and phosphate (3-3.2 mg/dL) were observed. At sixteen months he presented signs of rickets and FS was diagnosed.

Genetic tests: Positive HNF4A heterozygous mutation (exon 2, c.187C>T). Negative ABCC8 and KCNJ11.

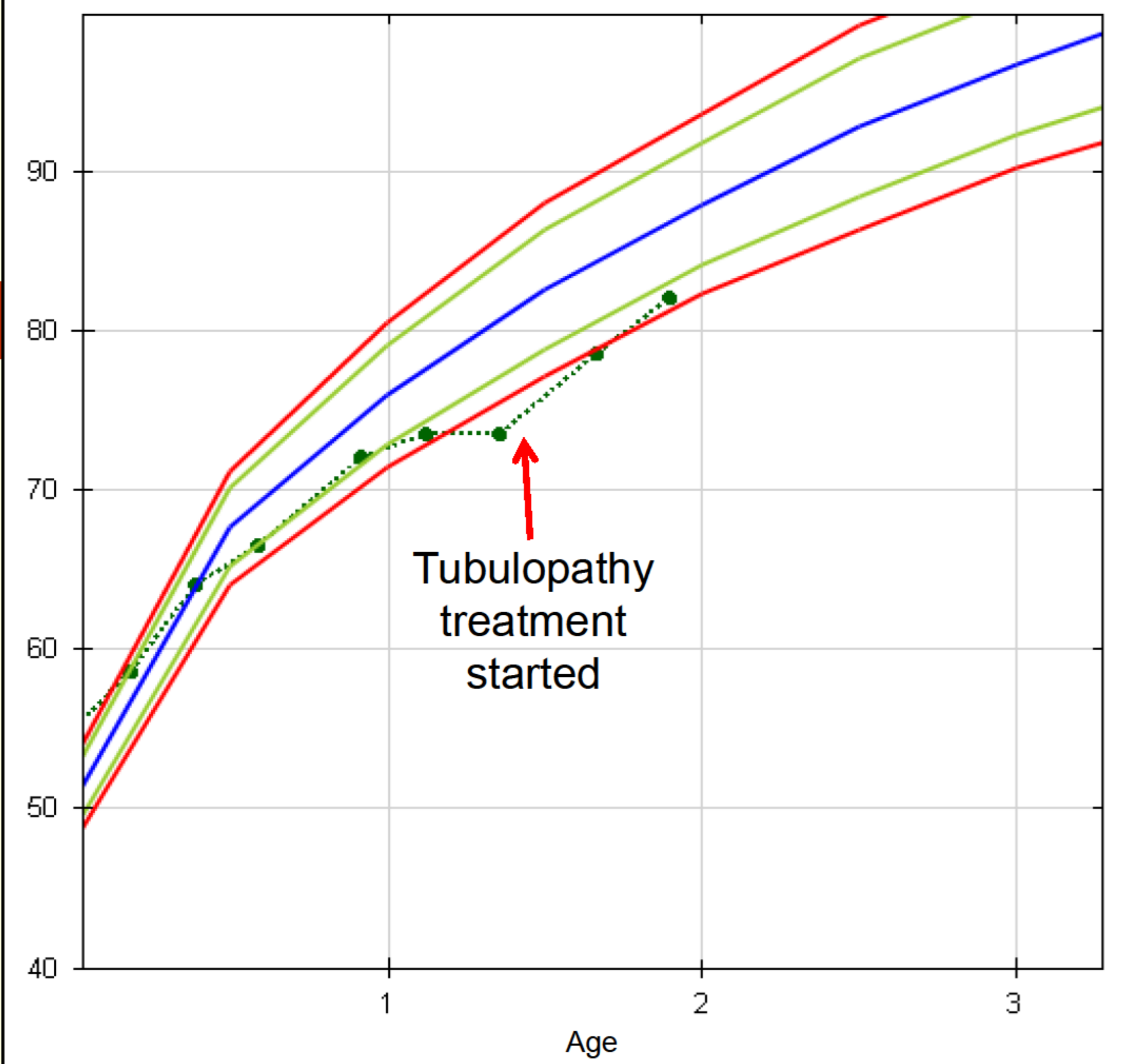
28 months old: he is receiving treatment for the tubulopathy and recovering satisfactorily from his height and weight deficits. No relatives are phenotypically affected.

HNF4A gene in the pancreatic beta cell



X-rays at age 16 months

Height (cm) for Age (years)
Spanish Longitudinal Study 1978/ 2000



Discussion

This mutation was first reported in 2010; it is linked to CHHI, FS and frequently, macrosomia and subsequent DM. Seven cases have been reported, only one had hypertransaminasemia and liver glycogen accumulation. No other mutations causing this phenotype have been described.

Conclusions

Mutations in HNF4A must be suspected in patients with CHHI, macrosomia and diazoxide hyperresponse. During follow-up, awareness about the possibility of associated diseases is needed, like in this exceptional case.

Bibliography:

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- 3.-Hamilton AJ, Bingham C, McDonald TJ, et al. The HNF4A R76W mutation causes atypical dominant Fanconi syndrome in addition to a β cell phenotype. J Med Genet 2014;51:165–169.