Growth hormone treatment for short stature associated with TRNT1 deficiency: a case series

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Background

- TRNT1: CCA-adding transfer RNA nucleotidyl transferase
- TRNT1 enzyme deficiency is a newly reported inborn error of metabolism caused by defective post-transcriptional modification of mitochondrial and cytosolic transfer RNAs (tRNAs).
- TRNT1 mutations cause a complex mutilsystem disease leading to manifestations in most organs.
- We here described the effect of growth hormone (GH) treatment on short stature in two siblings with TRNT1 deficiency.

Case Presentation

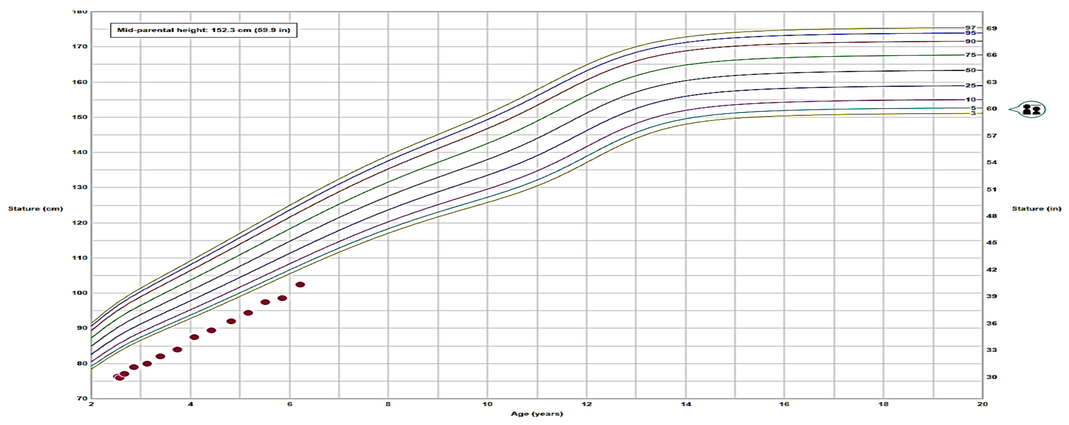
- Two siblings presented with developmental delay, anemia, elevated transaminases, recurrent infection, hearing loss, macrocephaly and severe failure to thrive.
- Both were initially diagnosed with SIFD (sideroblastic anemia, immunodeficiency, fever, developmental delay).
- They were later confirmed to have TRNT1 mutation by whole exome sequencing.

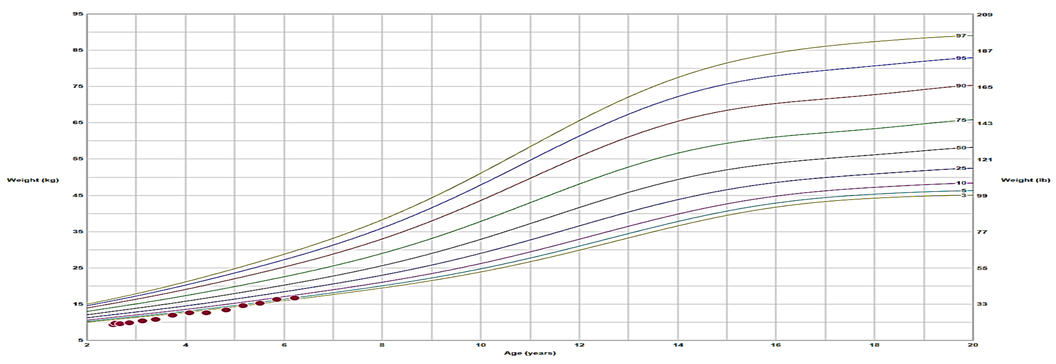
Patient 1

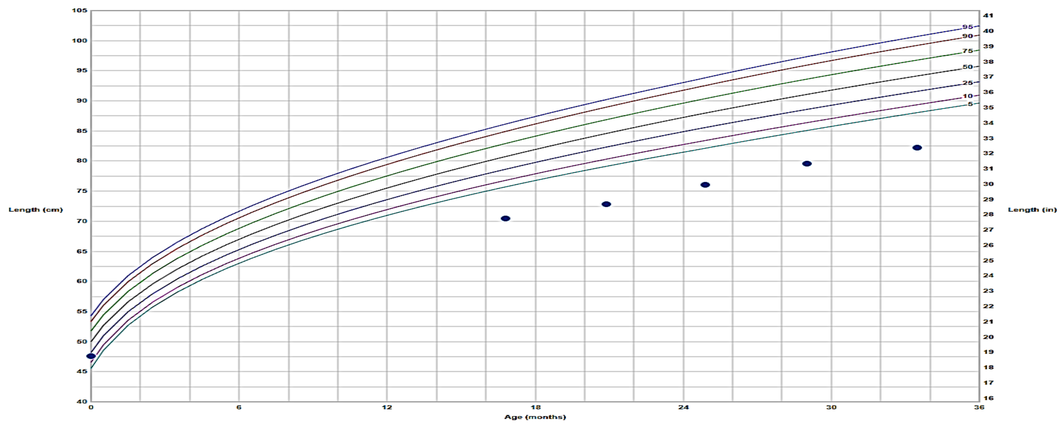
- 6 years old female initially presented to endocrine clinic at 18 months of age for severe short stature and episodes of hypoglycemia.
- Lab evaluation was only remarkable for low IGFI. Other pituitary evaluation and hypoglycemia workup were unrevealing.
- She was started on GH treatment at 18 months of age. Her hypoglycemia resolved and growth velocity is also improving.
- As of now, she has been on GH treatment for 3.5 years. Her height SDS has increased from pretreat - 4.22 to current - 3.22.

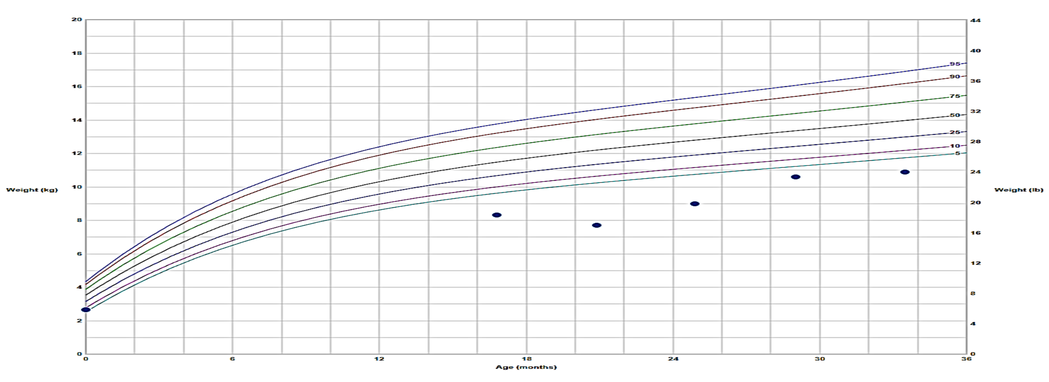
Patient 2

- The younger male sibling of patient 1. He has more severe phenotypes than patient 1
- He presented to endocrine clinic at 14 months of age also for severe short stature evaluation.
- Lab evaluation revealed low IGF I without other pituitary deficiency.
- He was started on GH treatment at 15 months of age. At 20 months of age, he became very ill due to recurrent infection and severe anemia. As a result, his GH treatment was on hold up to now.









Discussion

- TRNT1 mutations cause a spectrum of disease ranging from a childhood-onset complex disease with manifestations in most organs to an adult-onset isolated retinitis pigmentosa presentation. The severity of the signs and symptoms vary widely.
- The clinical manifestations in children can include cyclical, aseptic febrile episodes, sideroblastic anaemia, B lymphocyte immunodeficiency, retinitis pigmentosa, hepatosplenomegaly, exocrine pancreatic insufficiency and renal tubulopathy, sensorineural deafness, cerebellar atrophy, brittle hair, partial villous atrophy and nephrocalcinosis.
- About 20 cases have been reported in the literature so far.
- This is the first report of growth hormone treatment on short stature in the patients with TRNT1 deficiency. So far, the result of patient 1 appears to be encouraging although more long term data are needed.
- Reference:

"TRNT1 deficiency: clinical, biochemical and molecular genetic features. Orphanet Journal of Rare Diseases (2016) 11:90.

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