Congenital central hypothyroidism due to a homozygous mutation in the *TSHB* gene- just think about it!

M. Flury[1], N. Di Donato[2], A. Naeke[1], G. Hahn[3], A. Hübner[1]
[1]University Childrens`Hospital Carl Gustav Carus Dresden, [2]Institute of Clinical Genetics and [3]Department of Pediatric Radiology, University Hospital Dresden, Technical University Dresden, Germany

Backround

Congenital primary hypothyreoidism occurs in about 1 of 3600 life births and is usually detected with newborn screening. Early levothyroxine treatment is the prerequisite for normal psychomotor development of affected children. However, patients suffering from congenital central hypothyroidism are missed by the screening procedure, which may lead to delayed diagnosis and therapy. In very rare cases central hypothyroidism is caused by isolated TSH deficiency due to mutations in the *TSHB* gene.

Case presentation

Anamnesis

- **Poor condition, severe RSV infection** at the age of 5 months
- **Feeding problems and weight loss, exclusively breastfeeding**
- **Clinical features: floppy infant, umbilical hernia, meteorism, constipation, icterus prolongatus, short stature**
- **Developmental delay:** Bayley scales of infant development at age 14 months:
  - developmental age of 9-10 months
  - absent speech
  - normal hearing
- **Pregnancy and birth:** fourth child of healthy, non-consanguineous parents, 40 weeks of gestation, birth weight 3145g, length 50 cm, head circumference 38 cm, pH 7,26
- **Social aspects:** a 4 months stay in a rehabilitation centre with his mother, physiotherapy is ongoing

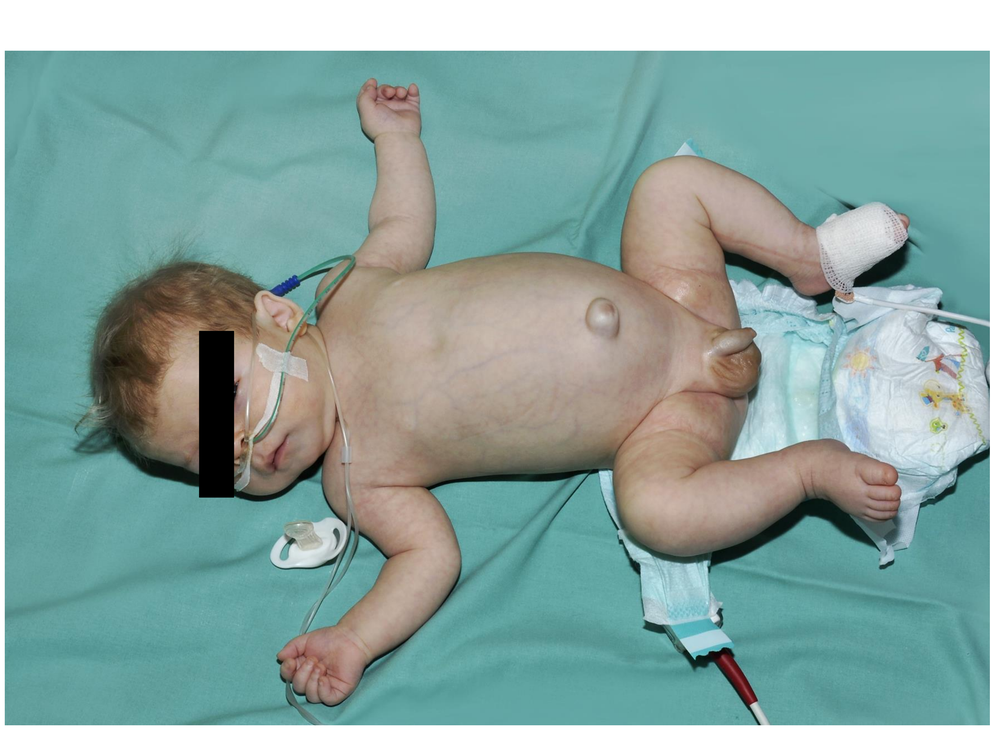

fig. 1 severe illness and floppy infant, umbilical hernia at the age of 5 months

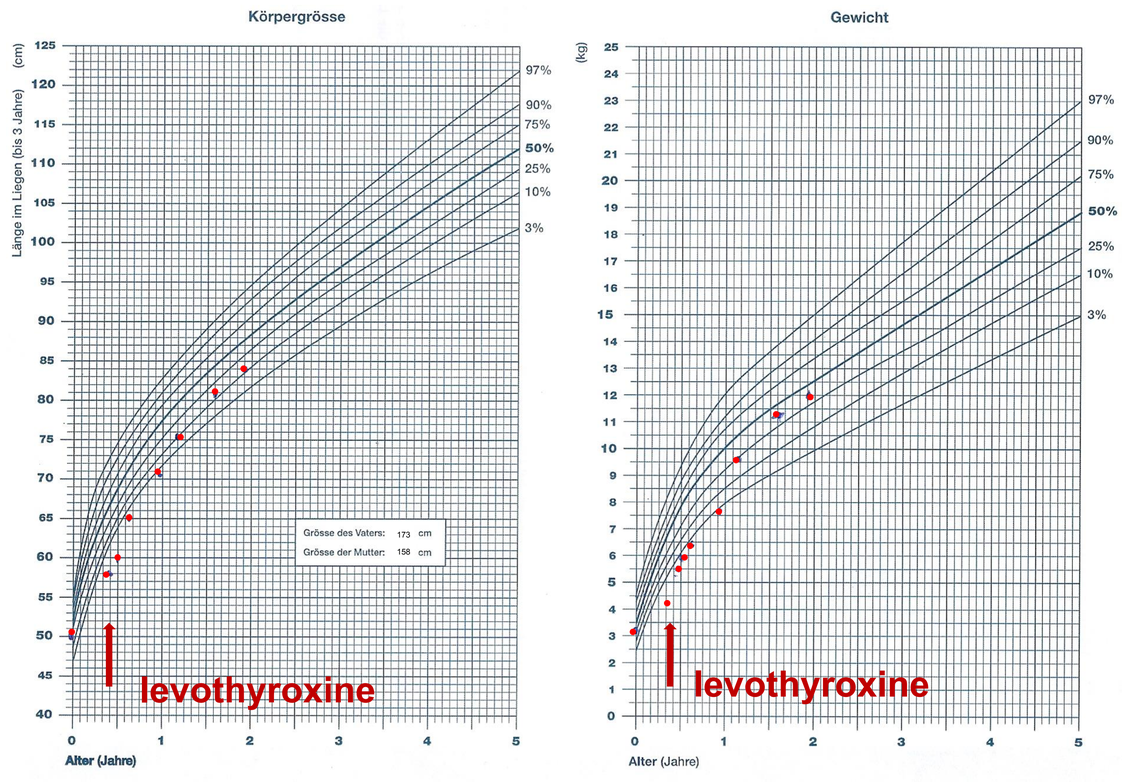

fig. 2 body height and weight gain from birth until 2 years of age

Results

Diagnostics

- **Newborn screening**: TSH < 0.1 mU/l (NR: <15.0 mU/l)
- **Analyses**:TSH 0.17 mU/l, fT4 and T3 immeasurable
- **Sequencing: *TSHß* gene:** homozygous mutation c.373delT; p.Cys125Valfs*10 (formerly named C105V or 313ΔT)

Therapy

Oral levothyroxine 75 µg per day

Conclusion

Central hypothyroidism is still a clinical challenge, as it is not detected in newborn screening in Europe while only measuring TSH. Paediatric endocrinologists should therefore advice their paediatric colleagues about this syndrome and its clinical picture. *TSHB* gene mutations (OMIM 188540) should be considered in cases with very low TSH with preservation of other pituitary axes and normal pituitary MRI.

Kontakt: monika.flury@uniklinikum-dresden.de, Telefon: 0351-458-2345

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