A 3-year-old boy with growth hormone deficiency and clinical features of Ritscher-Schinzel syndrome

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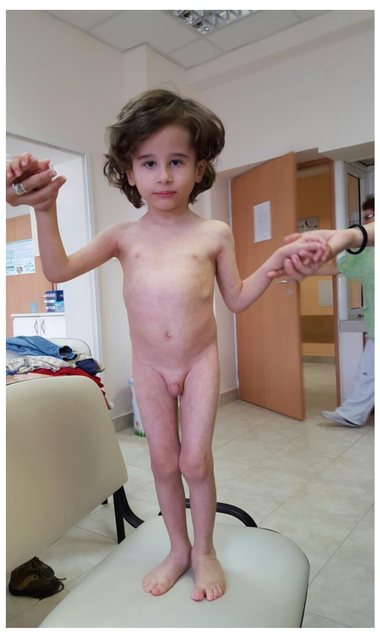
Background

Ritscher-Schinzel (cranio-cerebello-cardiac, 3C, OMIM 220210) syndrome is a very rare recently delineated disorder with:

- Dandy-Walker malformation, cerebellar vermis hypoplasia, enlarged cisterna
- congenital heart defects other than isolated PAD
- dysmorphic craniofacial features with cleft palate, ocular coloboma or 4 of the following: prominent occiput or forehead, hypertelorism, micrognathia, down-slanting palpebral fissures, depressed nasal bridge, low-set ears.

Patient presentation



- 3 y 3 m old Caucasian boy with:

- Short stature
- Underweight
- Developmental delay
- Mild facial dysmorphism
- Visual problems
- Episodes of rectal bleeding due to constipation and anal fissures
- No clinical hypoglycaemia, but registered BGLs <3 mmol/l

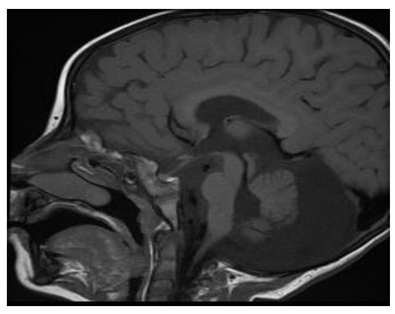
Medical history

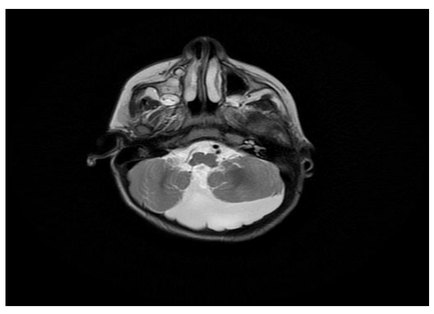
- From a 3rd complicated pregnancy via C-section at 37 w. g.
- **BW** 1750 g (-**2.98** SDS), **BL** 38см (-**5.89** SDS), **HC** 32 см (-1.50 SDS)
- After delivery:

- birth asphyxia, RDS
- PDA and ASD II
- pulmonary hypertension, umbilical hernia
- asymmetric dilatation of the lateral ventricles with a few periventricular cysts

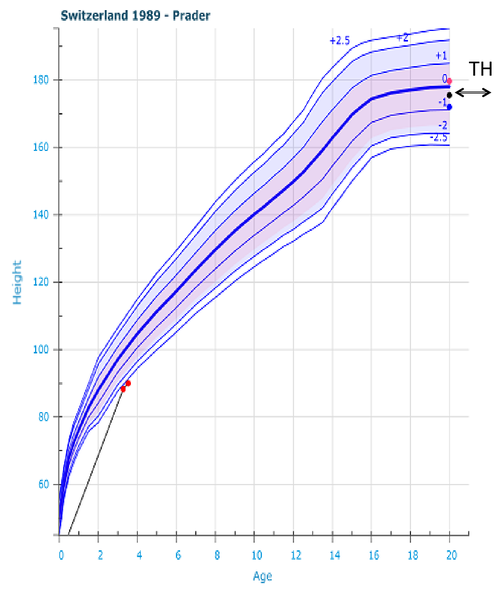
- Ventilated for 10 days, anti-failure treatment, no surgical cardiac intervention.
- At 3 m - bilateral ocular coloboma and strabismus
- Frequent respiratory and gastrointestinal infections
- Motor and speech skills delay, estimated IQ 35

Dandy-Walker variant with vermian hypoplasia and moderate non-obstructive communicating hydrocephalus





Auxology



- Height 88.3 cm **(-2.84 SDS)**
- Weight 9.9 kg (-**4.41 SDS**)
- Weight/Height **(-3.82 SDS)**
- BMI 12.86 kg/m² **(-3.67 SDS)**
- HC 47.9 cm **(-1.52 SDS)**
- SH/height 0.54 (-0.75 SDS)

- Father's height 172 cm (-0.87 SDS)
- Mother's height 166 cm (+0.23 SDS)
- Target height 175.5 cm (-0.36 SDS)

Physical examination

- unsteady gait
- craniofacial dysmorphic features with ocular coloboma
- systolic murmur
- normal male genitalia
- reduced fat mass and muscle waste
- clinodactyly

- flat feet with overpronation and cutaneous syndactyly (2nd – 3rd toes)

Laboratory/Imagining investigations

- Normal male karyotype 46,XY

Investigation	Result	RR
TSH uIU/ml	**5.03**	0.4-4.0
FT4 pmol/l	11.4	10.3-24.0
Cortisol nmol/l	376.26	118.0- 660.0
IGF-1 ng/ml	**50.8**	49 – 289

- Fasting hypoglycaemia and dyslipidemia
- GHD - two GH stimulation tests with peak GH < 5 ng/ml.
- ECG - mild LVH
- Echo-CG - small restrictive ASD II (3 mm) with mild endocardial hypertrophy and AV regurgitation 0-1 gr.

- Slightly delayed BA (2y 9 m) with mild hypoplasia of 5th distal phalanges
- Normal structure of the spine

Treatment and genetic testing

- rhGH treatment initiated – 0.035 mg/kg/d - no AEs

- mutation analysis of KIAA0196 gene[1] (8q24.13; coding for strumpellin) - – to reinforce the diagnosis

Ritscher-Schinzel syndrome

- Rare condition with < 50 cases described in the literature.
- Postnatal short stature, noted in most of the patients, could be a result of isolated growth hormone deficiency.

[1] Elliott AM, Simard LR, Coglan G et al. A Novel Mutation in KIAA0196: Identification of a Gene Involved in Ritscher-Schinzel Syndrome in a First Nations Cohort. J Med Genet 2013; 50: 819-822.

No conflict of interest

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55ESPE 853--P2
Syndromes : Mechanisms and Management
Sonya Galcheva
DOI: 10.3252/pso.eu.55ESPE.2016
Poster presented at: ESPE 2016 PARIS
PosterSessionOnline.com