A CASE OF FAMILIAL SILVER-RUSSELL SYNDROME

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BACKGROUND

- Silver-Russell syndrome (SRS) is a heterogeneous condition characterized by intrauterine growth restriction, relative macrocephaly at birth, postnatal growth retardation, body asymmetry, feeding difficulties/ low body mass index and dysmorphic craniofacial features [1].
- SRS is caused by loss of methylation at the H19/IGF2-imprinting control region ICR1 on chromosome 11p15 or maternal uniparental disomy of chromosome 7 (upd(7)mat) in approximately 50% and 10%, respectively. Most cases are sporadic [3].
- We present a family with clinical SRS, suggestive of a dominant mode of inheritance.

CASE PRESENTATION OF PATIENT 1

- Patient 1 was born as a child of non-consanguineous parents (maternal height: 153 cm, paternal height: 169 cm) in the 39th week of gestation with a birth weight of 1.96 kg, birth length of 45 cm (SDS -2.72) and relative macrocephaly.
- At the age of 2.5 years, he was referred because of poor postnatal growth without catch-up growth and severe short stature (height: SDS -4.28).
- Clinical examination showed a triangular face, prominent forehead and low-set ears.
- IGF-1 and IGFBP-3 levels and growth hormone stimulation test were normal.

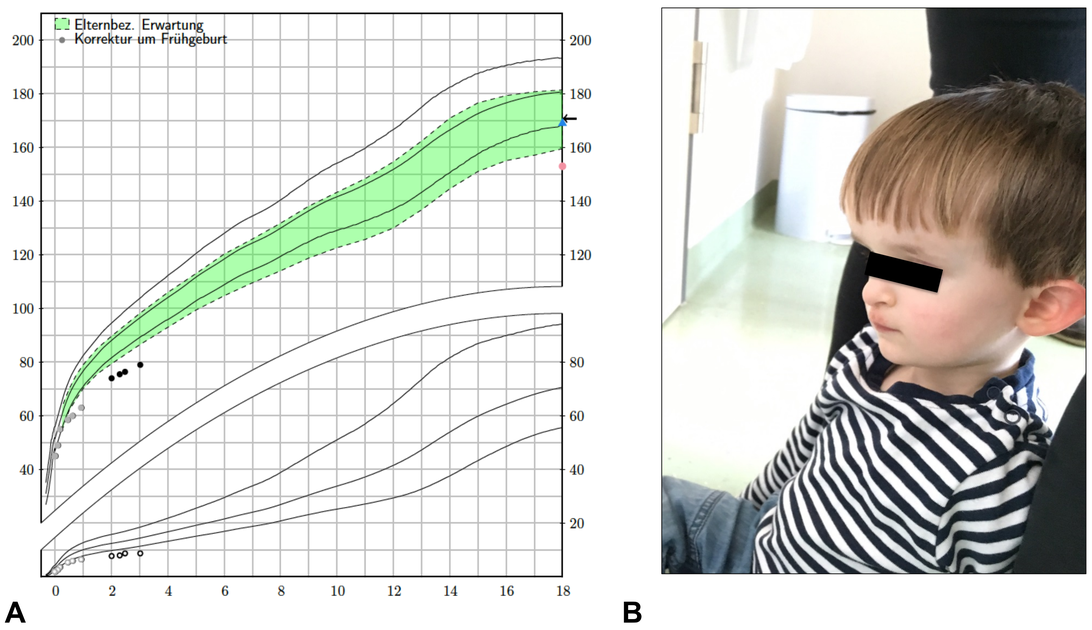

Figure 1: (A) *The patient's growth and weight curve, including expected range for parental target height (green area), parent's height (red square, blue triangle), genetic target height (black bar).* ***(B)*** *Picture of patient 1 with triangular shaped face, frontal bossing and micrognathia.*

CASE PRESENTATION OF PATIENT 2

- Patient 2 is the maternal half-brother of patient 1 (paternal height: 183 cm).
- At birth, he was small for gestational age (weight: 2.0 kg, length: 46 cm).
- At time of referral at 5.4 years, he had short stature (height: SDS -2.48) and low weight (BMI: SDS -2.80).
- Clinically, he had mild dysmorphic craniofacial features and clinodactyly V.

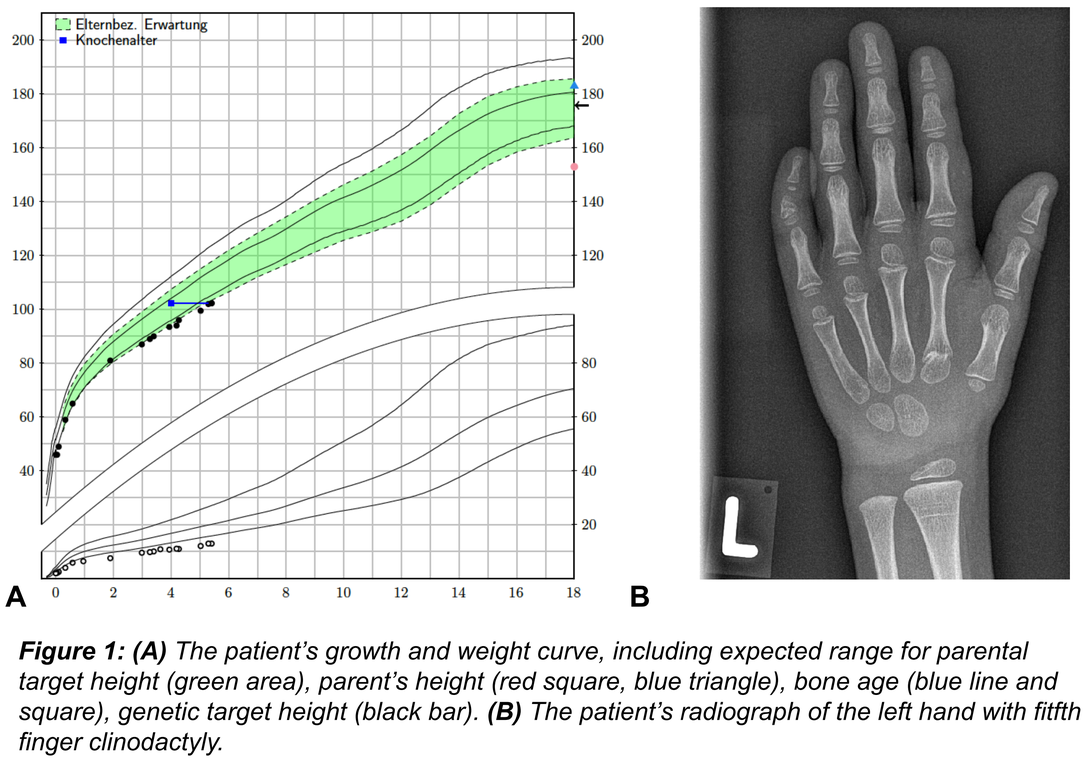

Figure 1: (A) *The patient's growth and weight curve, including expected range for parental target height (green area), parent's height (red square, blue triangle), bone age (blue line and square), genetic target height (black bar).* ***(B)*** *The patient's radiograph of the left hand with fitfth finger clinodactyly.*

CLINICAL SCORING SYSTEM

Netchine-Harbison clinical scoring system	Patient 1	Patient 2
1. Small for gestational age, birth length and/or weight ≤ -2 SDS	✓	✓
2. Postnatal growth retardation (height ≤ -2 SDS)	✓	✓
3. Relative macrocephaly at birth	✓	
4. Body asymmetry		
5. Feeding difficulties and/or body mass index ≤ -2 SDS in toddlers		✓
6. Protruding forehead at the age of 1-3 years	✓	✓

Table 1: *Classification of patient 1 and patient 2 according to the clinical scoring system by Azzi S et al. [2]. Subjects are considered to have likely SRS if they met at least four criteria.*

FAMILY TREE

- The mother of patient 1 and patient 2 was born as child of tall parents (maternal height: 178 cm, paternal height: 193 cm). She reached a final height of 153 cm.
- She has clinodactyly V and subtle SRS-like features.

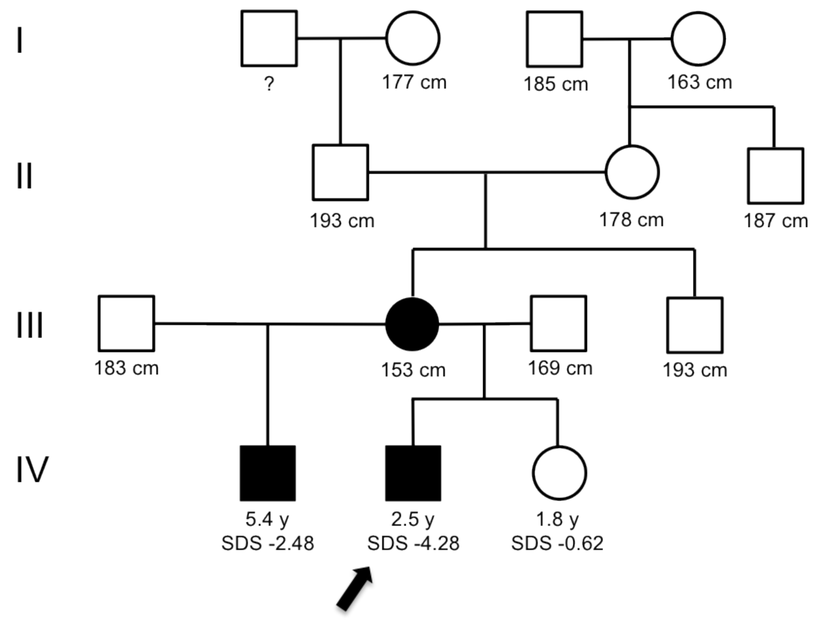

Figure 3: *Family tree. Black symbols indicate short stature. Height SDS or height in cm are given below the pedigree symbols.*

GENETIC ANALYSES

- Methylation analyses of ICR1 on chromosome 11p15 and investigation for maternal uniparental disomy of chromosome 7 (upd(7)mat) as well as array CGH were normal.
- Additional genetic analyses are currently being carried out to identify the underlying etiology of the familial SRS.

CONCLUSION

- The molecular cause of a significant number of patients with characteristic clinical features of SRS is still unknown.
- We present a multigenerational family with three affected members with clinical SRS suggestive of a dominant mode of inheritance of unknown genetic etiology.

REFERENCES

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