2 Siblings with Short Stature

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Case Presentation

- Two siblings, born of 3rd degree consanguineous marriage.
- Presented with short stature and severe failure to thrive.
- No history of hypoglycemia
- No history of parents or any other relatives with similar complaint

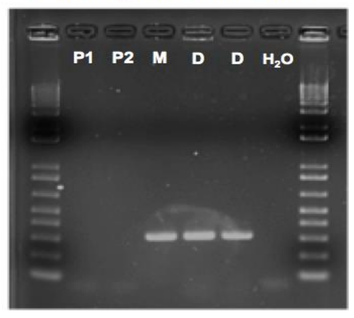
DESCRIPTION	SIBLING 1	SIBLING 2
AGE	2 year 7 month old	1 year 5 months
REFERRAL FOR	FTT, SHORT STATURE	FTT, SHORT STATURE
CONSANGUINITY	3RD DEGREE	3RD DEGREE
BIRTH ORDER	1ST	2ND
BIRTH	TERM , LCSC	TERM, LSCS
BIRTH WEIGHT	3.1 KG	3 kg
NEONATAL SEIZURES	NO	NO
NEONATAL JAUNDICE	NO	NO
HYPOGLYCEMIA	NO	NO

DESCRIPTION	SIBLING 1	SIBLING 2
LENGTH/HEIGHT	65 cm < 3rd centile	57 cm < 3rd centile
WEIGHT	6 kg < 3rd centile	4.6 kg < 3rd centile
HEAD CIRCUMFERENCE	45 cm	44 cm
MID PARENTAL HEIGHT	153.45 cm	153.45 cm
MIDFACIAL HYPOPLASIA	YES	YES
DEPRESSED NASAL BRIDGE	YES	YES
PROMINENT EARS	YES	YES
MICROGNATHIA	YES	YES

INVESTIGATION	SIBLING 1	SIBLING 2
S. Creatinine	0.66 mg/dl	0.69 mg/dl
Sodium	134 mmol/lt	135 mmol/lt
Potassium	4.87	4.23 mmol/lt
Chloride	108 mmol/lt	105 mmol/lt
CBP	WNL	WNL
LFT	WNL	WNL
RBS	77 mg/dl	69 mg/dl
TSH	9.35 mciu/ml	5.5 mciu/ml
2D Echo	Normal	Normal
Vit D	50 ng/ml	
Serum GH	**61.85 ng/ml**	**50 ng/ml**
IGF-1	**< 25 ng/ml**	**< 25 ng/ml**

Genetic Analysis was sought and had the following findings

PCR amplification: Exon 7



P1: proband
P2: proband
M: Mom
D: Dad

Results:

- Could not amplify GHR exon 7 in P1 and P2
- Could amplify GHR exon 7 in parents
- Most likely homozygous deletion of exon 7 in probands
- Need to confirm deletion using RNA

Diagnosis – IGF-1 deficiency. Advised therapy with recombinant IGF-1

DISCUSSION

- *First reported by Prof Zvi Laron in 1959 in 3 siblings with severe short stature, born to a consanguineous Jewish family.*
- *Characterized by clinical features of growth hormone (GH) deficiency and biochemical findings suggestive of GH resistance.*
- *An overall prevalence of 1-9/1000000.*
- *Short stature (height SDS between -4 to -10SD) is associated with typical facies, obesity, acromicra, high basal GH, and low IGF-1. Patients with Laron syndrome are unresponsive to exogenous GH therapy.*
- *rIGF-1 in a dose of 75 ug/kg/day s.c BD or Single dose*
- *Prolonged treatment improves linear growth, growth of hands, feet, chin, and nose as well as onset of puberty*
- *Side effects include water and electrolyte retention and calciuria.*
- *Limb lengthening – Difficult due to thin bones and weak muscles*
- *rIGF-1 in India- Not available.*
- *Normal longevity and live up to 70 years in studies by Laron and Ecuadorian study.*
- *Signs of early aging such as skin wrinkling and joint pain as well as obesity and poor muscle strength in adulthood.*
- *Sleep apnea has also been noted related to obesity and a small oropharynx.*
- *Similar case has been reported by Baumbach et al. with a G236 splice mutation in Exon 7 in a Bahamanian cohort*

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