Clinical evolution of a patient with isolated growth hormone deficiency type IA treated with rIGF1 for 5 years after the development of GH-antibodies

Albert Feliu Rovira (Presenting), Esther Latorre Martínez, Inés Porcar Cardona, Joaquín Escribano Subías. **University Hospital Sant Joan de Reus, Reus, Spain**

INTRODUCTION and OBJECTIVE

The main causes of isolated growth hormone deficiency are shown below.

Isolated growth hormone deficiency (IGHD)

IGHD ETIOLOGY → Organic (20%) / Genetic (10%) / Idiopathic (70%)

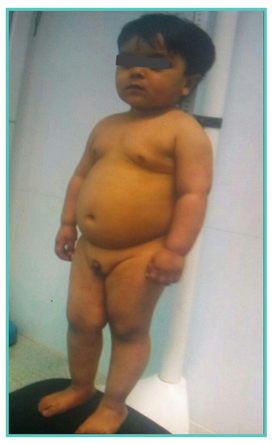
Type	Endogenous GH	Heritage pattern	Genes implicated (chromosome)	Other characteristics
IA	Absent	AR	GH1 (17q22-24)	- Neonatal hypoglycaemia - Parental consanguinity - Variable presence of GH antibodies at the start of the treatment
IB	Low	AR	GH1 (17q22-24) GHRH-R (7p14)	- Normal response to GH stimulation tests - Good response to exogenous GH based treatment.
II	Low	AD	GH1 (17q22-24)	
III	Low	Bound to X	BTK (Xq21.3q22)	- Hypogammaglobulinemia

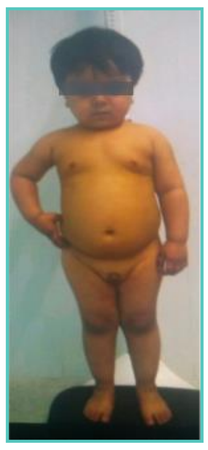
Isolated Growth Hormone deficiency type IA causes a severe growth retardation.
Their initial good response to exogenous GH is hampered by the development of anti−GH−antibodies leading to treat with IGF1 as the only therapeutic option.
Here we present the evolution of a patient with IGHD type IA treated with IGF1r for more than 5 years.

CLINICAL CASE

Personal background
5-year-old patient from Pakistan
Normal pregnancy and birth: RNAT (unknown PN and TN)
Normal psychomotor development
No pathologic background

Family background
Consaguineous parents (close cousins)
Mother height: 158 cm / Father height: 168 cm
3 brothers with a normal height. Healthy.





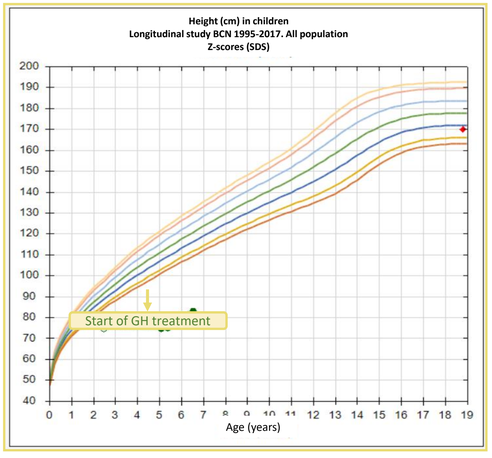
Somatometry
Height: 74.2 cm (- 8.93 SD)
Weight: 9 kg (- 4.48 SD)

Bone age	Tanner
2y 6m	Prepubertal

Physical exploration
Normal segmental proportions
Small face and wide forehead
Trunk obesity
Micropenis / Bilateral cryptorchidism
High voice

Laboratory tests	
Kariotype	46 XY
IGF-1	41.3 ng/ml (- 0.99 SD)
GH test	**Basal: 0.24 ng/ml Peak: 0.28 ng/ml**
Hormonal study	Normal

Image tests	
Testicular echography	Testes in the inguinal canal (1.5cm)
Cerebral NMR	Sella turcica Partially empty, with an anterior pituitary hypoplasia. Posterior pituitary without anomalies.



Good initial response to GH: VC: 7.74 cm/year (+1.5 SD)

After 6 months of treatment with GH, response decreases: VC 4cm/year (- 2.1 SD)

Analysis		Response of igf1 to stimulation with GH
IGF-1	< 15	
IGBP3	< 0.5	
Hormonal study	Normal	< 15 ng/dl

Genetic study

Absence of the GH1 gene in homozygosis (ENSG00000189162) by joint amplification of the GH1 and GH2 genes and digestion with BamHI, as well as the methodology of Vnenck-Jones

Study of Antibodies anti-GH

Positive by using RPA technique in dilution **1:10000**, with a 35% inhibition

Final diagnosis:

Type IA IGHD with formation of Ab anti-GH

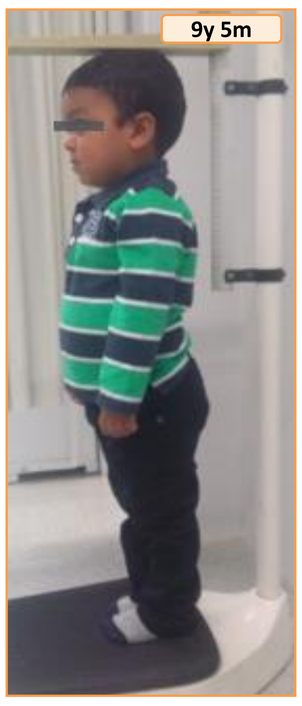
Tests performed at the start of the treatment with rIGF1 and during the follow-up:

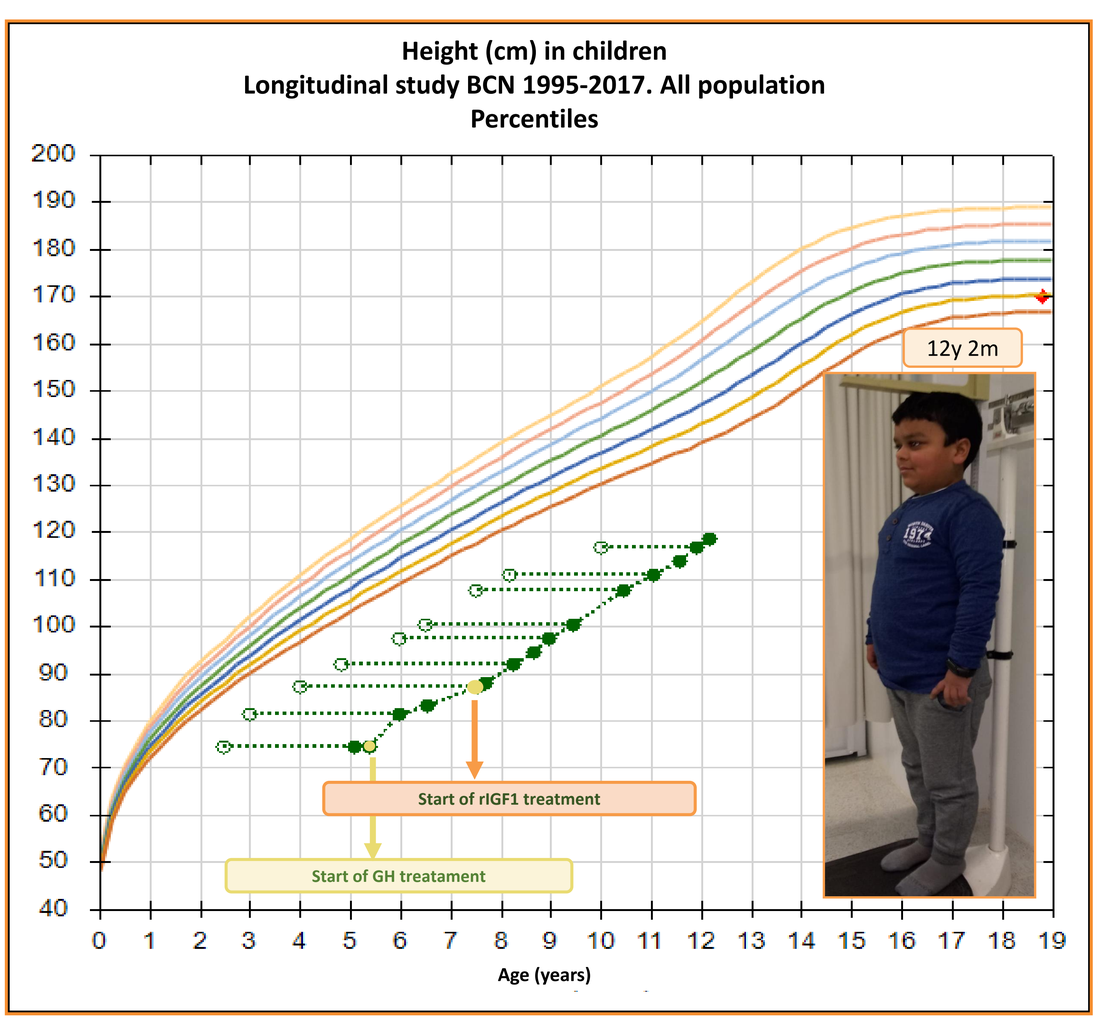
- ECG, Echocardiography
- Abdominal ultrasound
- Fundoscopy and audiometry

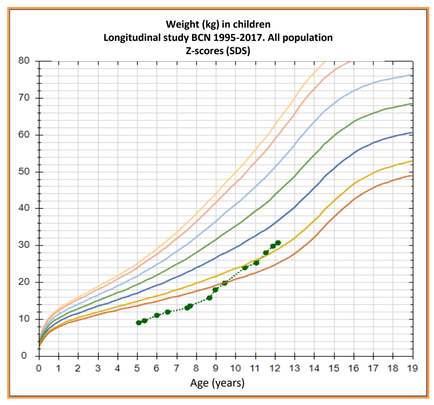
} **Normal**

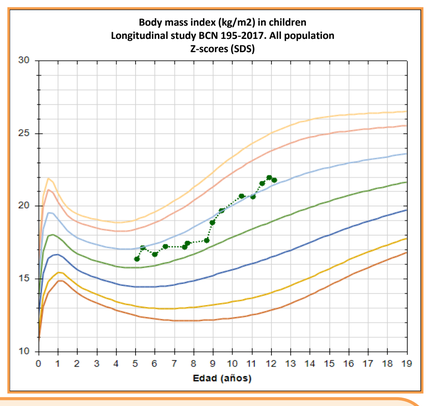
- Carotid ultrasound : Increased systemic arterial rigidity (p75)

Age	Height (SD)
5y 1m	- 8.93
5y 5m	- 9.12
5y 11m	- 8.19
6y 6m	- 8.30
7y 5m	- 8.25
8y 2m	- 7.75
8y 8m	- 7.56
8y 11m	- 7.17
9y 5m	- 7.01
10y 5m	- 6.28
11y	- 5.98
11y 6m	- 5.48
11y 10m	- 5.09
12y 2m	- 4.88









Currently the patient is 12 years old and after 5 years of treatment with rIGF1 his height is 118.6 cm (-4.88 SD) and he maintains a HV of 6.87 cm/year.
No adverse effects associated with the treatment were observed, except a significant increase in **BMI** during the first 3 years that required dietary support.

CONCLUSIONS

- Treatment with recombinant IGF-1 for 5 years has shown good results without adverse reactions, in a patient with IGHD type IA, with GH-antibodies.
- In our patient we, could detect a significant increase in BMI possibly related to the treatment that was controlled with dietary support

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Albert Feliu Rovira
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