What should be the diagnosis and management of short children with IGF-I deficiency, responding to growth hormone (GH) administration despite normal GH secretion?

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Introduction

Growth hormone (GH) deficiency (GHD) is currently defined as secondary insulin-like growth factor-I (IGF-I) deficiency (IGFD) [1,2]. In the patients with normal GH secretion and IGFD, significant increase of IGF-I during generation test excludes primary IGFD (PIGFD), however is not considered as a confirmation of secondary IGFD [3]. In such patients, the diagnosis of idiopathic short stature (ISS) is established. The effectiveness of GH therapy in children with ISS is still a matter of research [3-6] and ISS is an approved indication for GH therapy in some countries.

The aim of the study was to assess GH therapy effectiveness in children with IGFD, responding to short-term GH administration despite normal GH peak after falling asleep and in stimulation tests.

Patients and methods

Analysis comprised 42 children (34 boys, 8 girls), age 12.0±2.3 years (mean±SD) with short stature (patients' height below 3rd centile for age and sex) and normal GH peak (>10.0 ng/ml) both spontaneous (after falling asleep) and stimulated (assessed in 2 stimulation tests – with clonidine and with glucagon), and IGFD (IGF-I SDS for age and sex <-1.0), in whom IGF-I concentrations at least doubled and normalised during generation test, thus enabling to exclude primary IGFD.

All the patients were subjected to recombinant human GH therapy in the dose of 0.18±0,03 mg/kg/week.

First-year response to treatment: height velocity (HV) increase and IGF-I SDS increase was assessed in all of them, final height (FH) was attained in 28 patients.

The therapy effectiveness was compared with a group of 110 children (75 boys, 35 girls), age 11.2±3.3 years, with partial GHD (GH peak in 2 stimulation tests 5-10 ng/ml), treated with the same GH dose, including 42 treated up to the attainment of FH.

The following parameters were measured at diagnosis of GHD:

- height SDS before treatment (H_0SDS)
- height velocity (HV_0)
- insulin-like growth factor-I (IGF-I), expressed as IGF-I SDS for age and sex

The following indices of GH therapy effectiveness were assessed:

- first-year response to treatment:
  - height velocity in 1st year of treatment (HV_1)
  - increase of HV ($\Delta HV = HV_1 - HV_0$)
  - IGF-I SDS in 1st year of treatment and IGF-I SDS increase in 1st year of treatment (ΔIGF-I SDS)
- final height (FH), expressed as FH SDS.

Results

The data on 1st year response to GH therapy are presented in Table and in Figures 1 (an increase of HV) and 2 (an increase of IGF-I SDS). The attained FH SDS vs. $hSDS_0$ in both Groups is presented in Figure 3.
All the differences in age, therapy duration and in all the analysed indices of GH therapy effectiveness between the Groups were insignificant.

	Height SDS			Height velocity			IGF-I SDS		
	H_0SDS	FHSDS	ΔHSDS	before treatment	after 1 year of therapy	ΔHV	before treatment	after 1 year of therapy	ΔIGF-I SDS
IGFD	-2.87±0.72	-1.14±0.82	1.61±1.08	3.8±0.9	9.4±1.9	5.7±2.1	-2.19±0.78	0.34±1.07	2.54±1.15
pGHD	-2,79±0.59	-1.20±0.80	1.48±0.83	3.8±1.4	9.8±2.1	6.2±2.4	-1.76±0.88	0.52±0.87	2.28±0.90

Figure 1

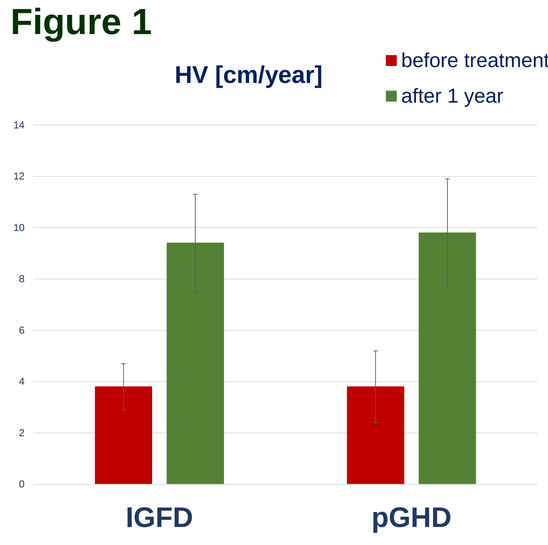


Figure 2

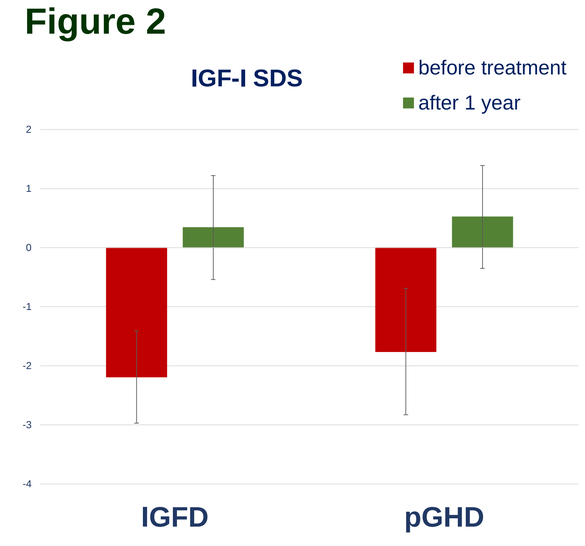
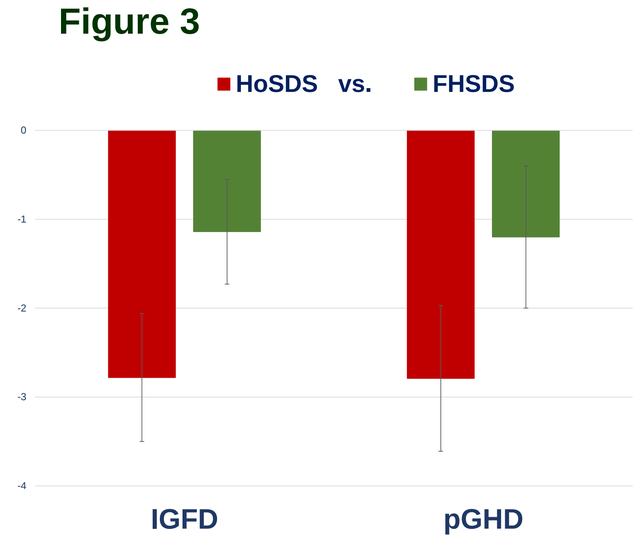


Figure 3



Conclusion

In children with short stature, normal spontaneous and stimulated GH secretion and decreased IGF-I concentration which increases significantly in generation test, IGFD is non-primary. Such patients may benefit during GH therapy similarly to children with pGHD. It seems worth considering not diagnose idiopathic short stature in them.

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