Long-term follow-up of three patients with isolated growth hormone deficiency type IA with sustained growth response to rhGH

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Background. Isolated growth hormone deficiency type IA (IGHD IA) is described in families with homozygous *GH1* deletions that arise from unequal recombination and crossing over within the GH gene cluster during meiosis. Patients with IGHD IA show early and severe growth failure and tend to develop resistance to recombinant human growth hormone (rhGH) treatment [1].

Aims. To present a follow-up of three patients with IGHD IA treated with rhGH.

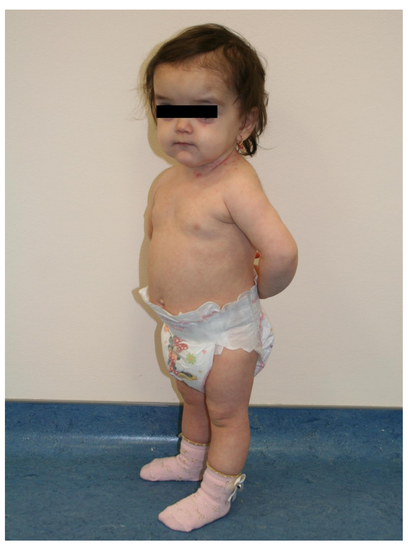
Methods. *GH1* gene was analyzed by PCR.

Results. Three female patients were included in the study. All patients were of Avars origin and were born from consanguineous marriages. Two girls were second cousins.

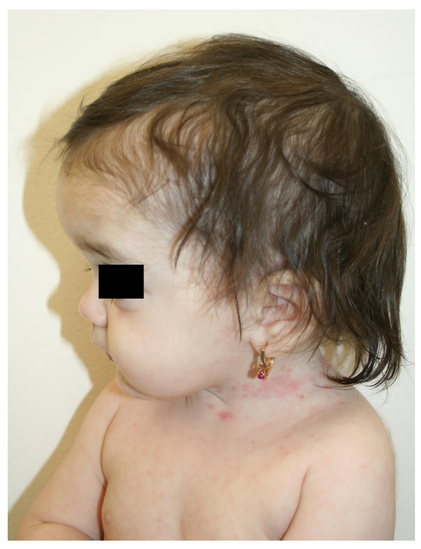
Table 1

	Birth weight, g/SD	Birth length, cm/SD	Height at presen-tation	IGF-I level before treatment, ng/ml
Case 1	3400/ -0.11	51/ +0.62	-6.4 SD (1.9 yr)	<3.0
Case 2	3200/ -0.58	52/ +1,18	-4.9 SD (1.0 yr)	<3.0
Case 3	3760/ +0.7	48/ -1.07	-7.3 SD (1.6 yr)	<3.0

The patients had typical features of congenital GHD: frontal bossing, doll face, acromicria and truncal obesity. Low height velocity was detected at the age of 3-6 months.



Case 1



Case 1

IGF-I level was undetectable (less than 3 ng/ml); TSH, fT4, prolactin and cortisol levels were normal.

DNA analysis revealed homozygous deletion of *GH1* gene in all three patients. Diagnosis of IGHD IA was established.

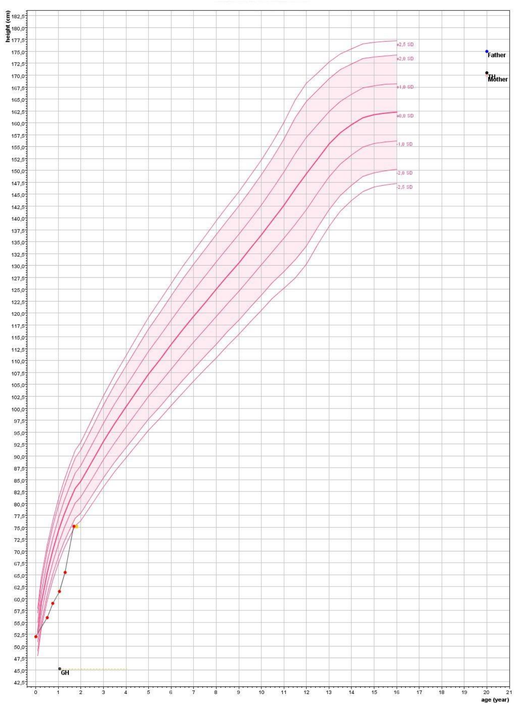
rhGH therapy (Rastan, Russia) was started at dose 0.033 mg/kg per day.

Height and HV were measured at baseline and every 6 months during the treatment period (from 1 to 5 years). HV increased after 2-4 months of rhGH, during the first year of therapy median of growth velocity was 20 cm/year. Over 2 years of treatment (cases 1 and 3), height increased from 60.8 ± 2.5 to 93.9 ± 3.7 cm, with an increase in height SDS from −6.85 ± 0.45 to −0.18 ± 0.05. After 5-year follow-up of patient 3, Δ height SD was +7 and growth velocity was 10.2 cm/year.

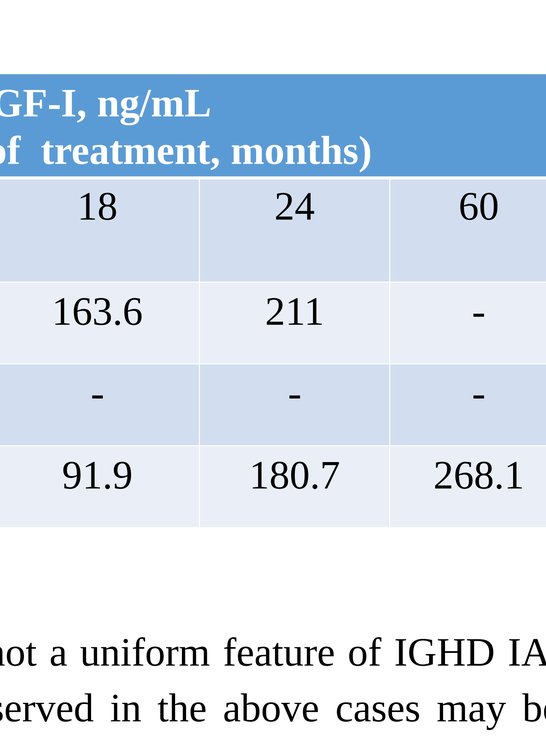
Table 2

	IGF-I, ng/mL (duration of treatment, months)				
	6	12	18	24	60
Case 1	63.7	132	163.6	211	-
Case 2	29.2	62.7	-	-	-
Case 3	21.1	133.6	91.9	180.7	268.1

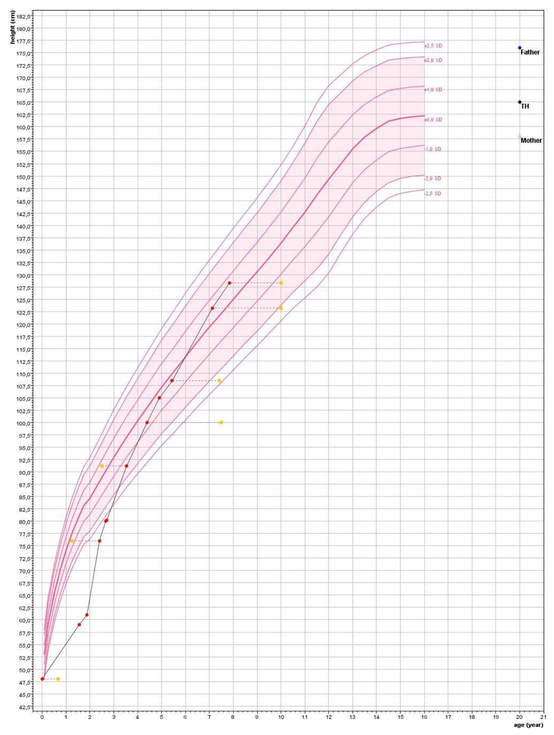
Conclusions. GH resistance is not a uniform feature of IGHD IA. The sustained GH response observed in the above cases may be related to the patients' genotypes and/or type of rhGH preparation.



Case 2 Growth Chart



Case 1 Growth Chart



Case 3 Growth Chart

References: 1. Kyriaki S. Alatzoglou et al. Isolated Growth Hormone Deficiency (GHD) in Childhood and Adolescence: Recent Advances, Endocrine Reviews – Vol.35(3)-2014, p.376–432. https://doi.org/10.1210/er.2013-1067

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