Fetal and post-natal growth are impaired in children with deletions of the *GH1* gene: description of a cohort of 14 patients.

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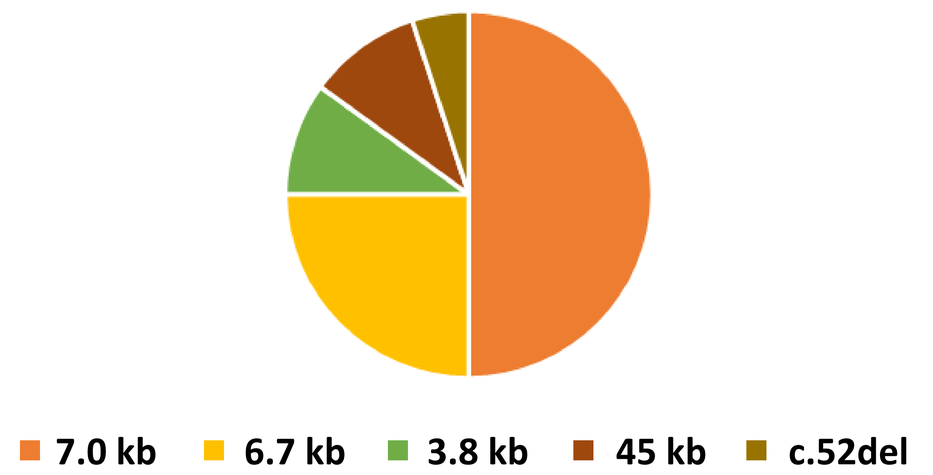
Introduction

Isolated growth hormone deficiency (IGHD) can be due to genetic mechanisms, including *GH1* mutations or deletions. IGHD type 1a is an autosomal recessive disease, mainly caused by homozygous *GH1* deletions. In this case, postnatal growth is severely impaired, associated with hypoglycemia, and extremely low levels of GH and IGF-I. Since the first description of GH1 deletions in 1970, small series of patients have been reported, with conflicting data about birth parameters and response to GH therapy.
We report the genetic and clinical data from a cohort of 14 patients with *GH1* deletions.

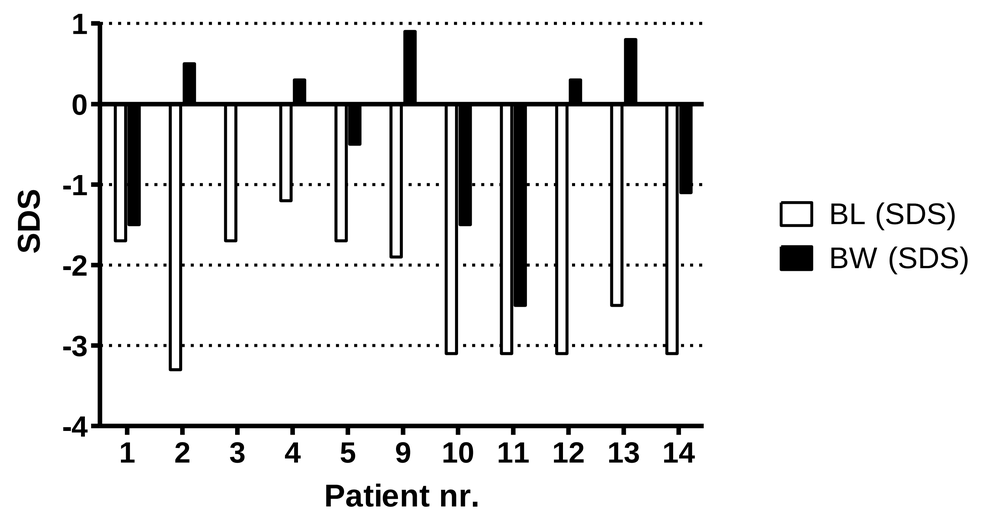
Methods

Fourteen patients (8 familial, 6 sporadic cases) were included in this study, after molecular testing in a unique molecular laboratory (Hôpital Trousseau, APHP, Paris)
GH1 deletions were detected after amplification of DNA by PCR and enzymatic digestion.
Clinical data were obtained from a standardized form at the time of molecular testing. In 2018, clinicians were asked to complete a second form in order to obtain for actualized data.
Birth parameters are expressed as SDS according to Usher and MacLean references.



Genetic aspects

The cohort included :
- 12 patients with homozygous deletions
- 1 patient with a compound heterozygous deletion
- 1 patient with a deletion and a nonsense mutation on the remaining allele

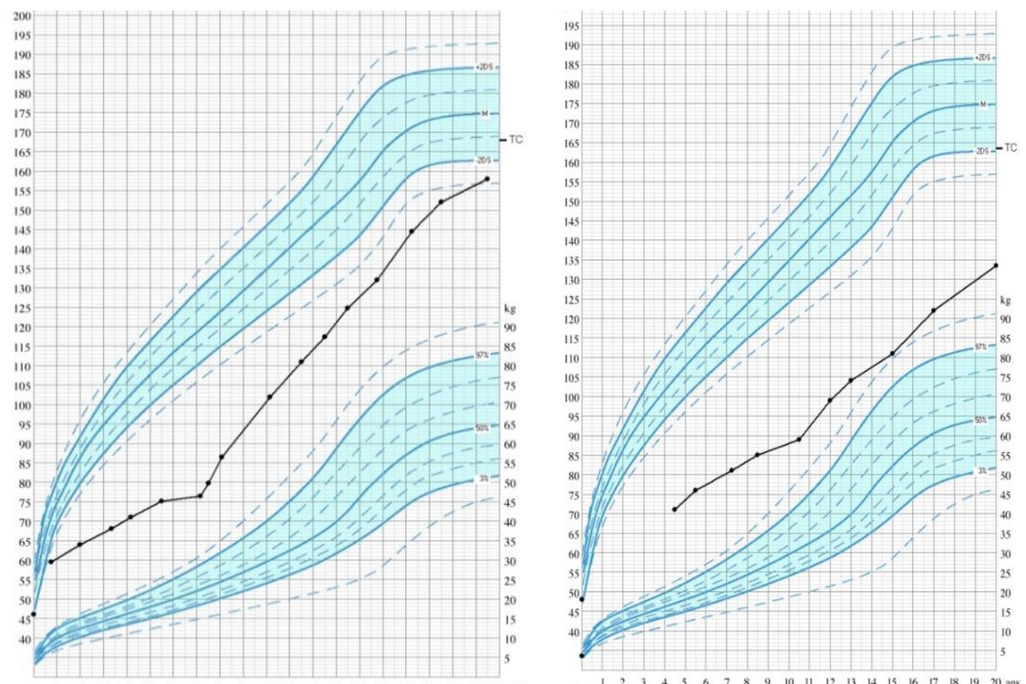


Results

Mean birth length (BL) was reduced (-2.4 +/- 0.7 SDS) whereas **birth weight (BW) was normal** (-0.4 +/- 1.1 SDS). 6/11 patients presented with a birth length < -2 SDS. Head circumference at birth was normal.
Median age at diagnosis was 3.1 years, with a mean height at diagnosis at -7.1 SDS +/- 1.9 SDS

12/14 patients were treated with GH. Median age at start of GH therapy was 3.3 years. A growth catch-up was observed for 7 patients, 2 patients did not respond to GH and one patient present a partial response with incomplete catch-up (no data for 2 patients)
GH antibodies were detected in 3 patients. For one patient, IGF-I therapy was given, with a moderate effect on growth velocity.

Final height (FH) was available for 6 patients. **Mean FH was -3.26 +/- 1.8 SDS**, and only 2 patients had a FH above -2 SDS.



Discussion/Conclusion

IGHD type 1a due to *GH1* deletions is associated with reduced birth length, with normal birth weight and head circumference. Despite IGF-I secretion being independent from GH during fetal life, our data are in favor of a role of growth hormone in stimulating fetal growth. Response to GH therapy is variable, which might be due to GH antibodies

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