GROWPATI study: Growth and puberty description pattern in a well-characterized cohort of patients with growth retardation due to severe primary IGF-1 deficiency

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INTRODUCTION

Severe primary insulin-growth factor-1 (IGF1) deficiency (SPIGF1D) is a rare cause of growth delay.

Diagnostic criteria include age- and sex-dependent low basal IGF1 levels (<2.5th percentile), height ≤ -3SDS, absence of growth hormone (GH) deficiency and of any secondary causes of growth failure.

AIM

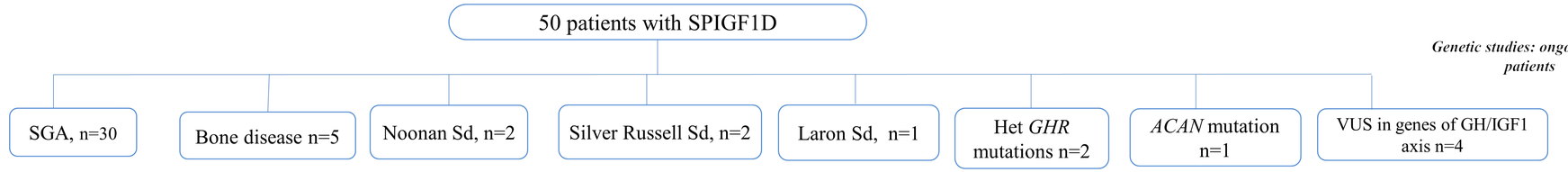
- Report the growth pattern and pubertal status
- Identify the molecular causes of SPIGF1D
- Describe the growth response after 1-year of recombinant human IGF1 (rhIGF1) treatment in a young patient with *ACAN* mutation

METHODS

- Thirty patients (M/F:17/13, n=30) with SPIGF1D (*historical study cohort*) out of 2546 patients referred for growth failure to Paediatric Endocrinology Department of Necker Children's University Hospital, in Paris between 2004-2009 (*Teissier et al, EJE, 2014*).
- Twenty patients with SPIGF1D (*new cohort, n=20*) among patients referred with growth retardation between 2016-2020.
- Data were collected retrospectively concerning puberty and growth pattern
- Molecular studies are on going, based on a candidate gene approach or next-generation sequencing gene panel

RESULTS

Clinical and molecular characteristics of SPIGF1D patients

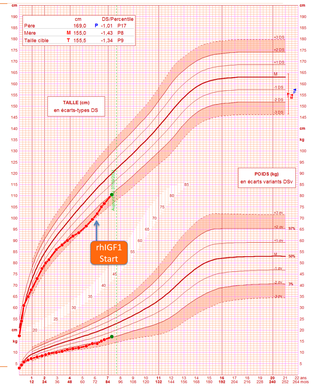


Puberty pattern

- Pubertal onset: mean age for Tanner 2: 12.5 years (M, n=11) 12 years (F, n=8). Mean age of menarche was 13.6 years with regular menses.
- Two boys had advanced evolutive central puberty, treated by GnRH agonist.

Case report: A young patient with ACAN mutation treated with rhIGF1

Medical history:
A 5-year old girl was reffered to our clinic for growth failure.
Born after a full term uneventful pregnancy, with SGA (BH: 47.5cm (4.5th p, BW: 3070g (14th p).
Endocrine investigations showed SPIGF1D.
Molecular studies by NGS gene panel identified an heterozygous missense (p.Arg279Gln) mutation in the *ACAN* gene
rhIGF1 started (0.04 mg/kg twice daily) at age of 6y (height: 104.5cm, -3SDS and after 1 year of treatment (0.12 mg/kg twice daily) very good response was documented, without any reported adverse effects.



CONCLUSIONS

- **Genetic analysis reflect the heterogeneous spectrum of the disease**
- **rhIGF1 is indicated if criteria for treatment in the approved indication are fulfilled and should not be delayed**
- **Long-term follow-up and genetic investigations are necessary for providing more insights in the SPIGF1D management**

CONTACT INFORMATION

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