Short stature in Protein Arginine Methyltransferase 7 (PRMT7) Mutations: first evidences of growth response to GH treatment

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INTRODUCTION

Protein arginine methyltransferase 7 (**PRMT7**) is a member of a family of enzymes that catalyzes the transfer of methyl groups from S-adenosyl-L-methionine to nitrogen atoms on arginine residues involved in multiple biological processes, such as signal transduction, mRNA splicing, transcriptional control, DNA repair and protein translocation.

Currently, **12 patients** with **homozygous/compound heterozygous mutations in PRMT7** gene have been described defining the human disorder known as **SBIDDS syndrome** (OMIM #617157).

AIM

Short stature is a pathognomonic feature of SBIDDSs, observed in all patients reported to date, although **growth hormone deficiency (GHD) has never been described before.**

We report the **endocrine manifestations** and **rGH (recombinant growth hormone) response** of two female dizygotic twin sisters (Twin A and Twin B), born small for gestational age, with novel biallelic variants in PRMT7 and features consistent with a diagnosis of SBIDDSs

Whole exome sequencing analyses showed the same **compound heterozygous mutation in PRMT7 gene** (p.Cys407Tyr of maternal origin; c.1323+2T>G of paternal origin) in both twins.

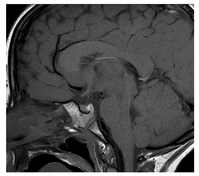
CASE REPORTS

Due to severe short stature and growth impairment endocrine investigations to rule out GHD were performed:

Twin A

peak GH at arginine test: 4.61 µg/L;
peak GH at glucagon test: 5.14 µg/L; → **GHD 0.025 mg/kg/day**
IGF-I 47 ng/mL, -2.19 SDS.

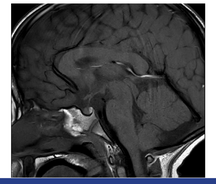
MRI
normal hypothalamic-pituitary region
corpus callosum thickening

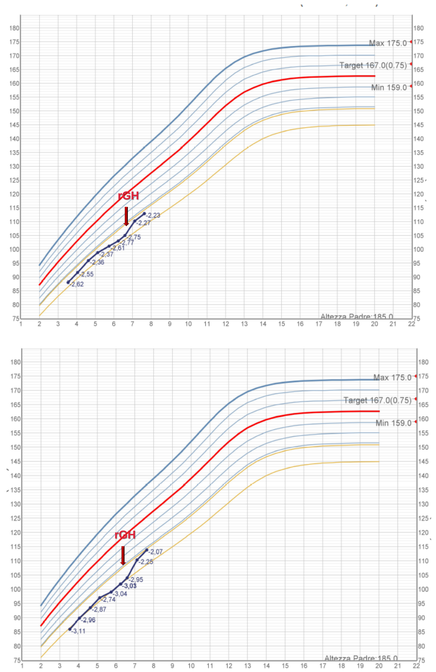


Twin B

peak GH at arginine test: 11.8 µg/L;
IGF-I 52 ng/mL, -2.05 SDS. → **SGA 0.035 mg/kg/day**

MRI
dysmorphic features of corpus callosum
and cerebellar vermis
pars intermedia cyst





Twin A	baseline	12 months
Chronological age (years)	6.6	7.6
Bone Age (years)	6.3	6.7
MPH[1] (SDS)	+0.67	-
HT[2] (cm)	105	112.3
HT[2] (SDS)	-2.75	-2.23
GV[3] (cm/year)	3.8	7.5
GV[3] (SDS)	-2.51	+2.06
IGF-I (SDS)	-2.19	0.66

Twin B	baseline	12 months
Chronological age (years)	6.6	7.6
Bone Age (years)	6.7	7.9
MPH[1] (SDS)	+0.67	-
HT[2] (cm)	104	113.8
HT[2] (SDS)	-2.95	-2.07
GV[3] (cm/year)	4.3	9.5
GV[3] (SDS)	-2.03	+4.1
IGF-I (SDS)	-2.05	0.1

[1]MPH: Mid-parental Height; [2]HT: Height; [3]GV: Growth Velocity

CONCLUSIONS

Our findings provide further clinical data and expand the knowledge of endocrine manifestations associated with PRMT7 homozygote/compound heterozygote mutations including GHD.

Considering short-term good response to rGH, further studies are needed to confirm long-term outcomes at adult height and establish whether **SBIDDSs** could be considered among those **syndromes treatable with rGH.**

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