# GH REPLACEMENT IN 3 M SYNDROME : A SUCCESSFUL TRIAL

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## INTRODUCTION

3-M syndrome is an autosomal recessive primordial growth disorder characterized by severe prenatal and postnatal growth retardation, normal mental development, unusual facial features and skeletal abnormalities (1). Mutations in the *CUL7*, *OBSL1* and *CCDC8* genes are described (2). 3M children usually have normal GH levels with low IGF values and a modest response to GH treatment in term of improvement in the final height. These features suggest a picture of GH insensitivity even if an interindivual variation cannot be denied (1,3).

**Conflict of interest:** Authors declare no conflict of interest relatively to the topic of this poster

## CASE REPORT

Here we describe the case of an italian girl born from non-consanguineous parents, full term, small for gestational age (2120 g <3° centile Bertino' s chart, (4)) with a length of 40.5 cm (<3° centile Bertino's chart (4)). She presented postnatal growth retardation, hip dysplasia, hyperextensible joints and normal mental development. At the age of 4 years and 4 months she had a stature at -2,74 SDS, a growth rate at -2,60 SDS (Cacciari) (Figure 1,2).

## DIAGNOSIS

### *GENETICS*

Clinical suspicion of 3M syndrome was supposed and then confirmed by array-CGH analysis with the finding of *CUL7* mutation in compound heterozygosity *c. 3750delA + 3753_3762 del/ c.4814delG*. The second mutation was not previously described.

### *HEMATOCHIMICAL EXAMS*

Blood count, ferritin, blood glucose, creatinine, hepatic functionality and urinalysis were normal. Moreover thyroid function, blood cortisol level, calcium-phosphorus metabolism and 25-OH vitamin D were tested and all resulted normal except for a mild impairment of vitamin D.

### *GH STIMULATION TESTS*

GH stimulation tests with arginine and clonidine showed an insufficient peak of 5.95 ng/ml at 120' and 4.97 ng/ml at 60', respectively.

| | ARGININE | CLONIDINE |
|---|---|---|
| GH basis | 0.64 ng/ml | 1.67 ng/ml |
| GH after 30' | 0.80 ng/ml | 2.74 ng/ml |
| GH after 60' | 0.43 ng/ml | **4.97** ng/ml |
| GH after 90' | 3.32 ng/ml | 3.04 ng/ml |
| GH after 120' | **5.95** ng/ml | 1.86 ng/ml |

### *BRAIN MRI*

Not alterations in size, morphology and impregnation of pituitary gland and pedicle axis were found at brain MRI.

## THERAPY

Therefore GH deficiency was diagnosed and replacement was started with rhGH 0,33 mg/kg/die once daily.

## FOLLOW UP

After six months of therapy we report a significant catch up growth with a stature at -2,16 SDS (+0.58) and a growth velocity at 0.64 SDS (+3.24) (Figure 1,2).

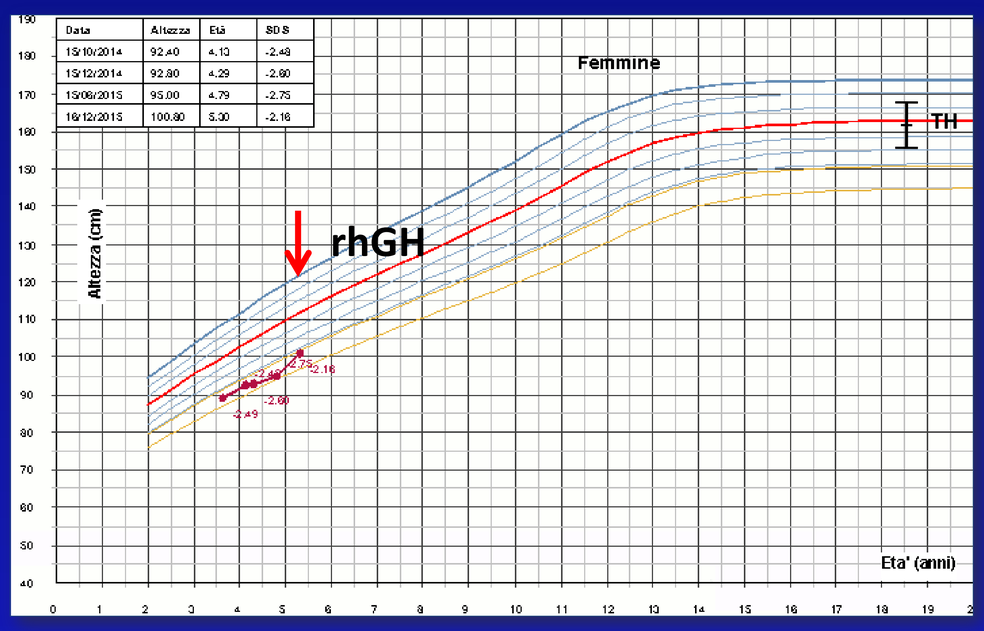


Figure 1. Statural growth curve before and after 6 months of therapy with rhGH

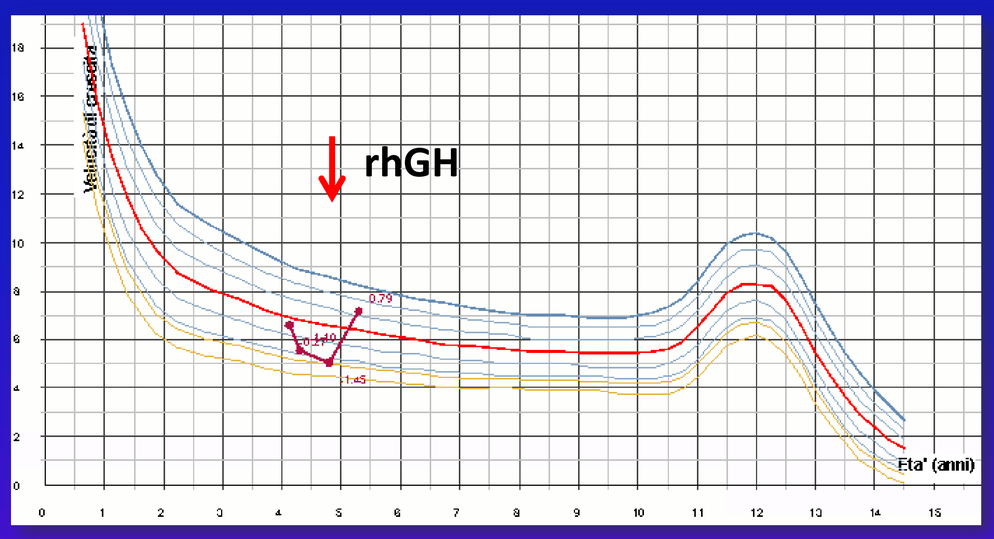


Figure 2. Growth velocity curve before and after 6 months of therapy with rhGH

## CONCLUSIONS

Even if a longer follow up is necessary to confirm this finding, current data support the possibility of an interindividual variation in response to rhGH in 3M syndrome and suggest the recommendation of a trial with GH replacement in these patients.

## REFERENCES

1) Clayton PE[1], Hanson D, Magee L, Murray PG, Saunders E, Abu-Amero SN, Moore GE, Black GC *Exploring the spectrum of 3-M syndrome, a primordial short stature disorder of disrupted ubiquitination*. Clin Endocrinol (Oxf). 2012; 77(3):335-42
2) Hanson D[1], Murray PG, Coulson T, Sud A, Omokanye A et al. *Mutations in CUL7, OBSL1 and CCDC8 in 3-M syndrome lead to disordered growth factor signalling*. J Mol Endocrinol. 2012 Oct 30;49(3):267-75
3) Meazza C[1], Lausch E, Pagani S, Bozzola E, Calcaterra V, Superti-Furga A, Silengo M, Bozzola M. *3-M syndrome associated with growth hormone deficiency: 18 year follow-up of a patient.* Ital J Pediatr. 2013 Mar 21;39:21
4) Bertino E, Spada E, Occhi L, Coscia A, Giuliani F, Gagliardi L, Gilli G, Bona G, Fabris C, De Curtis M, Milani S. *Neonatal Anthropometric Charts: The Italian neonatal study compared with other European studies.* JPGN. 2010; 51: 353-361

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