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 interindividual 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 <3rd 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 (Cacciani) (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 + 3763_3762del/ c.4814delG. The second mutation was not previously described.

HEMATOCHEMICAL 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.

<table>
<thead>
<tr>
<th>ARGinine</th>
<th>CLONIDINE</th>
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<tbody>
<tr>
<td>GH basis</td>
<td>0.64 ng/ml</td>
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<tr>
<td>GH after 30’</td>
<td>0.80 ng/ml</td>
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<tr>
<td>GH after 60’</td>
<td>0.43 ng/ml</td>
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<tr>
<td>GH after 90’</td>
<td>3.32 ng/ml</td>
</tr>
<tr>
<td>GH after 120’</td>
<td>5.95 ng/ml</td>
</tr>
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BRAIN MRI

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

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

2) Hanson D1, Murray PG, Coulton 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