LATE DIAGNOSIS OF A TYPE II/III MUCOLIPIDOSES TREATED WITH GH REPLACEMENT THERAPY

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Introduction

Mucolipidoses II/III (ML) are rare autosomal recessive lysosomal storage disorders (incidence: 1/325,000 live births).

They have overlapping clinical phenotypes with mucopolysaccharidosis disorders and include:

- **growth retardation**
- **facial dysmorphism**
- **skeletal abnormalities**
- **respiratory and heart diseases**
- **hepatosplenomegaly**
- **abdominal hernias**

There is no specific treatment and the management has been limited to supportive care.

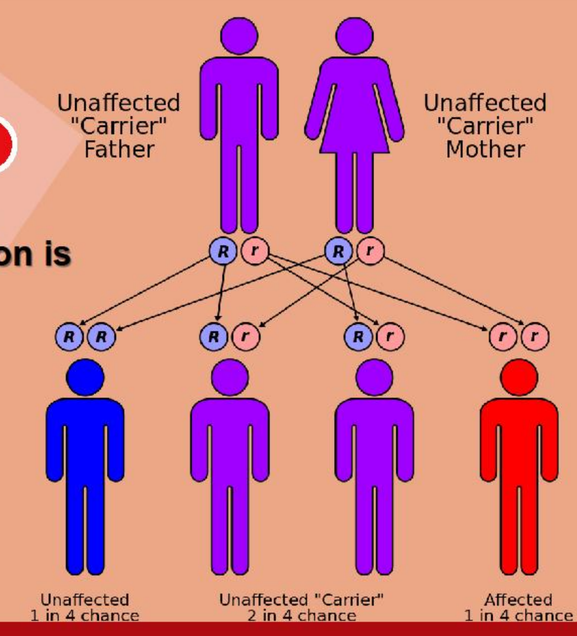
Homozygous mutations in GNPTAB and GNPTG are classically associated with mucolipidosis II (ML II) alpha/beta and mucolipidosis III (ML III) alpha/beta/gamma, which are rare lysosomal storage disorders characterized by multiple pathologies.

The range of:

inter- and intrafamilial variability

organ manifestation is wide

the variability of age at onset



Case report

- A.M., aged 18 y, boy of an apparently healthy couple
- first evaluation at 11y6m - short stature (-4 SD)

- coarse facial features (fig 1,2)
- joint stiffness
  - pain initially in the shoulders, hips, and fingers
- thoracic deformity
  - kyphosis
  - clubfeet
  - deformed long bones (fig. 3)
- cardiac involvement
  - insufficiency of the aortic valve
- no signs of pubertal onset.

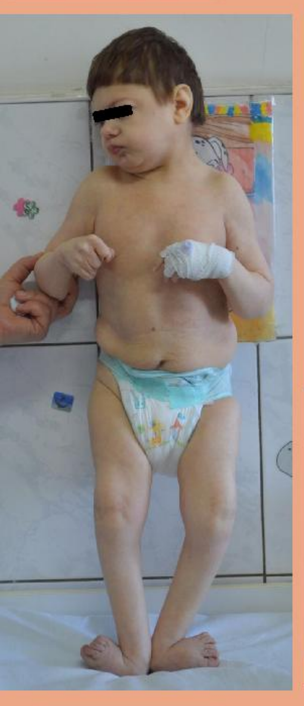


Fig 1.

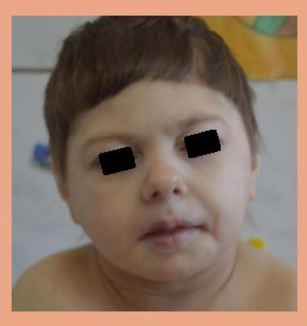


Fig 2.

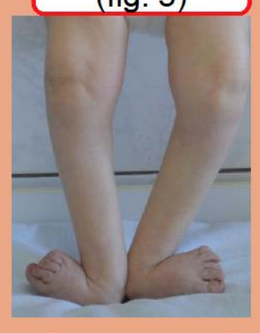


Fig 3.

DXA Results Summary:

Region	Area (cm²)	BMC (g)	BMD (g/cm²)	T-Score	PR (%)	Z-Score	AM (%)
L1	9.10	4.45	0.490	-4.7	49		
L2	8.67	4.38	0.505	-5.4	46		
L3	8.73	4.47	0.512	-5.4	46		
L4	9.44	4.38	0.464	-6.2	41		
Total	35.93	17.68	0.492	-5.4	45	-4.9	48

WHO Classification: Osteopenia
Fracture Risk: High

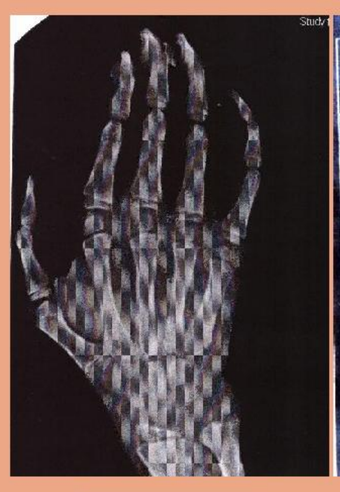


Fig 4.

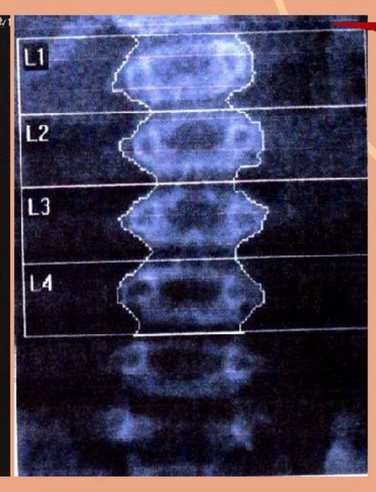


Fig 5. Bone mineral density. Generalized osteopenia

Somatotropic axis investigations		
Low IGF-1	=62.4 ng/mL,	(N=220-972)
GH =0.42 ng/mL,		
GH without stimulation at the arginine test: GH=2.75 ng/ml		
Wrist radiography - delayed bone age of 11 years 6 months (fig. 4)		

GROWTH HORMONE DEFICIENCY

Since there were not known contraindications, GH replacement therapy was started at age 11y 6m with an initial dose of 0.035mg/kg/day and biannual reassessments were performed.

Results

After 4 years of treatment the medium growth rate was 0.42 cm/month and no side effects were reported.

At the last evaluation the enzymes alpha-iduronidase, iduronate-2-sulfatase, arylsulfatase B, beta-galactosidase could be assessed and were higher in plasma → MLII or III.

Discussions

❖Corroborating the clinical phenotype, biological data and evolution, this case can be included in MLIII.

❖We haven't found in the literature any case of MLIII treated with GH replacement therapy. In our case the treatment was effective and improved the patient's quality of life.

❖Later in the disease course management will be focused on relief of general bone pain associated with osteoporosis, which has responded in a few individuals to scheduled intermittent IV administration of the bisphosphonate – pamidronate.

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