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

1- Department of Endocrinology, St. Spiridon Emergency Hospital, University of Medicine and Pharmacy “Grigore T Popa” Iasi  
2 - Department of genetics, University of Medicine and Pharmacy “Grigore T Popa” Iasi

Iulia Crumpei1, Alina Belceanu1, Elena Braha1, Cristina Rusu1, Ioana Armasu1, Adina Manolache1, Zmau George1, Cristina Preda1, Carmen Vulpoi1

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 infranomial variability
- organ manifestation is wide
- the variability of age at onset
- Affected 1. Carrier
- Unaffected Carrier

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
- thoracic deformity
- pain initially in the shoulders, hips, and fingers
- kyphosis
- clubfeet
- deformed long bones (fig. 3)
- cardiac involvement
- insufficiency of the aortic valve
- no signs of puberty onset

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.

References: