

The cost of treatment is covered by health insurance and is continued in health centers, at home of patients and in the inclusive school departments. Patients with neuromuscular diseases from other (mostly rural) areas are also allowed to rehabilitate in these institutions.

#### P-12

### **Becker patients with isolated deletion of exon 48 in dystrophin gene present with a mild phenotype and seem to escape cardiomyopathy**

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Duchenne and Becker muscular dystrophies have similar signs and symptoms and are caused by different mutations in the same gene. The two conditions differ in their severity, age of onset, and rate of progression. The signs and symptoms of Becker muscular dystrophy are usually milder and exhibit a large range of variation. In most cases, muscle weakness becomes apparent later in childhood or adolescence and progresses at a much slower rate. Individuals can remain ambulatory into their 40s. Despite the milder skeletal muscle involvement, heart failure from dilated cardiomyopathy (DCM) is a common cause of morbidity and the most common cause of death, in the mid-40s. Two hot-spots BMD mutations have been described, at the 5' end of the dystrophin gene, comprising exons 2 to 11 and at the 44-45 exon level. The most part of BMD patients present a deletion of the exons 45-48 or 45-49. We present cardiologic data – retrospectively evaluated – from 16 Becker patients, aged from 7 to 52 years, sharing a deletion involving exon 48 alone. The mean age of the follow-up was 6,6 years (range 1-13,9). Cardiac function was evaluated, at 6-month intervals, by standard and dynamic Ecg, Mono and 2D-echocardiography, echocolor-doppler-cardiography. The following cardiologic parameters were considered: Heart Rate, PQ interval, PQ segment, QT interval, Cardiomyopathic Index, T wave anomalies, presence of ectopic ventricular beats, ventricle diameters, left ventricular free wall and septum thickness, ejection fraction, fiber shortening, integrated back scattering. Data collected at the last control, compared with those at the time of the first control, show that no sign or symptom of cardiomyopathy is evident in these patients, suggesting that BMD patients sharing deletions limited to exon 48, seem to escape dystrophinopathic cardiomyopathy for a long time. The possible causes of such a condition are discussed.

#### P-13

### **Non-muscle myosin II-C is abundantly expressed in skeletal muscle and associated with Z-lines**

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Non-muscle myosin II (NMHC II) is an ubiquitously expressed protein present in all vertebrate cells. There are three known isoforms of NMHC II, namely NMHC II-A, II-B and II-C,

that have a central role in cell adhesion and differentiation. NMHC II-A and B have been demonstrated to be present in human skeletal muscle and to localize to Z-lines. NMHC II-C mRNA and protein has been found widespread in human and mouse organs but its localization and function in human skeletal muscle have not been investigated. We performed single-labeling immunofluorescence, which showed that NMHC II-C is abundantly expressed in human skeletal muscle, with a transverse banding pattern of distribution. By double-labeling immunofluorescence with either slow myosin heavy chain, desmin,  $\alpha$ -actin or  $\alpha$ -actinin, we localized NMHC II-C overlying the Z-lines and in perinuclear regions. The abundance of this protein in association with Z-lines suggests that NMHC II-C might play a role in regulating muscle contractility or in maintaining integrity of the myofibrillar machinery. Further studies need to be performed to establish the exact role of NMHC II-C in normal and diseased skeletal muscle.

#### P-14

### **Multiple acyl-coa dehydrogenase deficiency: a possibly treatable condition**

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Multiple Acyl CoA Dehydrogenase Deficiency (MADD), also known as glutaric aciduria type II, is an autosomal recessively inherited disorder of fatty acid metabolism which affects all the fatty-acid acyl-CoA dehydrogenase enzyme system. The disorder is usually due to defects in the genes of either alpha- or beta-subunit of electron transfer flavoprotein (ETF; MIM# 231680, ETFB; MIM# 130410) or ETF dehydrogenase (ETFDH; MIM#231675).

Molecular defects in the ETFDH gene were found to be responsible for a specific sub-group of patients affected with a variant of the disease responsive to riboflavin (vitamin B2), a precursor of flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN) required in biological oxidation-reduction reactions. These patients are usually young adult presenting with proximal muscle weakness, exercise intolerance, elevated serum CK, cyclical vomiting and episodes of acute encephalopathy, generally precipitated by an infection.

Herein, we report on a patient suffering from a riboflavin-responsive MADD with no evidence of molecular defects in the ETFA, ETFB and ETFDH genes.

The patient was treated with riboflavin at the dosage of 100 mg/day associated with a low-fatty acid diet. After six months, clinical examination showed global improvement in motor functions.

Our report remarks that not all the cases of riboflavin-responsive MADD are due to ETFDH mutations, suggesting a genetic heterogeneity in this disease. As flavin binding is essential for the normal function of the Acyl CoA dehydrogenases, this riboflavin-responsive disease could be caused by some yet unidentified disorder of mitochondrial flavin metabolism and transport or flavoprotein homeostasis.

Anyway, in these cases, treatment with riboflavin can be alike effective. Therefore, early diagnosis is important to achieve the best treatment response.