P-10
Malignancies associated with idiopathic inflammatory myopathies: a 35-years retrospective study
R. Neri, V. Iacopetti, S. Barsotti, A. d’Ascanio, A. Tavoni, M. Mosca, G. Iacopetti, S. Bombardieri
Internal Medicine, AOU Pisa, UO Reumatologia, Italy; Internal Medicine, AOU Pisa, UO Immunollogery Clinic, Pisa, Italy

An increased incidence of malignancy in patients with poly/dermatomyositis (PM/DM) has been reported; several points remain unclear: incidence and the predictive factors for the presence of cancer and its prognosis.

Aim of the study was to evaluate the frequency of malignancy among myositis patients diagnosed in our Unit in a 35 years follow-up (from 1975 to 2010). We compared epidemiological, clinical, serological and survival data of the patients with cancer associated myositis (CAM) with the findings of primary myositis, trying to define predictive factors for malignancies development.

162 primary PM/DM patients were enrolled by our Rheumatology Unit. Diagnosis of PM/DM was based on Bohan and Peter criteria (1975). Myositis was considered tumor-associated if diagnosed within 2 years before or after the diagnosis of cancer. Concerning the comparison of CAM and primary myositis, we analyzed: age, sex, systemic symptoms (Raynaud’s phenomenon, dysphagia, dyspnea, fever, arthritis, dysphonia), creatine kinase (CK) levels at onset, autoantibodies, number of deaths, survival rates.

Out of 162 patients with myositis, cancer was present in 18/72 DM patients (25%) and in 9/90 PM patients (10%). In 10 cases the malignancy and myositis appeared simultaneously; in 6 cases the tumor was diagnosed before and in 11 after the onset of myositis; cancer types more frequent were breast and ovarian carcinoma. Patients with CAM were older than those without cancer (59 yr vs. 51yr) p < 0.01. There was a female predominance in primary myositis group (M/F = 30/51 in PM and 13/41 in DM) and in CAM-DM (6/12) while CAM-PM patients were equally shared. Dysphagia was more frequent in CAM than in primary myositis patients (37% vs. 17.5%) p < 0.035; in the CAM subgroup was more present in DM than PM (44% vs. 14%) p < 0.006. Prevalence of other extramuscular features was similar in the 2 subgroups.

In patients with CAM, CK medium levels were lower than in primary myositis (3013 U/L vs. 2412 U/L); positive ENA were significantly more present in primary myositis group (20% vs. 7%). AntiJO1 antibodies were detectable in 6% of PM/DM patients but not in cancer group.

22/135 (16%) with primary myositis and 15/27 patients with CAM (55%) died; in this second group deaths were in the first two years from diagnosis and in 13/15 patients were caused by cancer.

The survival rate of primary PM/DM at 5 years was significantly higher (87% and 74%) compared to the CAM patients, where survival at 2 years was 56% for PM and 44% for DM.

The risk of cancer is significantly higher in older female patients with DM. Some clinical and serological features can be considered predictive risk factors for malignancy, although without statistical significance: dysphagia, lower CK levels, lower prevalence of anti-ENA antibodies.

The overall survival rates were considerably worse in CAM: early discovery of malignancy is crucial and examinations for detections of an underlying malignancy are important in the management of patients with PM/DM.

P-11
Rehabilitation of patients with neuromuscular diseases in the region of the Bay of Kotor (Montenegro)
R. Ognjenovic, K. Tomcuk
Hospital “Vaso Cuckovic” Risan, Montenegro

The aim of this paper is to demonstrate the ability of professional teams from medical institutions in Bay of Kotor (Montenegro) to carry out the rehabilitation of patients with neuromuscular diseases in the optimal way.

A multi-year clinical course with adequate rehabilitation of two patients with neuromuscular disease is presented. In the first case, the course of the disease with rehabilitation of a boy diagnosed with Duchenne muscular dystrophy followed from his fifth to eleventh year of life is presented.

Another patient (with spinal muscular atrophy type 3) was followed for 3 years.

Muscular dystrophy, as a group of muscle diseases characterized by progressive weakness and atrophy of the muscles responsible for body movements, fortunately, is not a common disease in the region of the Bay of Kotor.

In first case an initial muscle weakness was noticed at age 3. Diagnostics(high levels of serum creatine phosphokinase,genetical testing which confirmed the deletion of dystrophin gene,EMG, biopsy, and a confirmation that the mother is the carrier) was made in his fifth year.

Abnormality was noticed during running, jumping and standing up (with Gowers maneuver). Other development of weakness in lower extremeties, joint contractures, scoliosis. Until the age of 10 the patient had been sent out annually to a stationary physical therapy professionally led with education of the mother. He also took aed doses of prednisolone intermittently. Since year 11 he was wheelchair-bound.

A patient with Kugelberg Welander spinal muscular atrophy (SMA) type 3 noticed the first symptoms (fatigue of gaiter muscles during walking) in age 12. After the diagnostics the only possible treatment was started -physical therapy (in hospital and at home).He still walks independently. Other neuromuscular diseases are sporadic and very rarely seen in our region.

In neuromuscular diseases maximizing the use of rehabilitation procedures with all medical supplies is necessary, so that the patient would be able to move independently for longer.

To the satisfaction of professional teams (pediatricians, neurologists,physiatrists, orthopedists, physical therapists and medical technicians) in Montenegro, rehabilitation of patients with neuromuscular diseases in recent years is being organized better than before, despite bad socio-economic conditions. It has implemented in the special institutions located on the coast.
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
A. Taglia, E. Viggiano, M.G. Di Gregorio, P. Ambrosio, A. Palladino, G. Negro, L. Politian
Cardiology and Medical Genetics, Second Naples University, Naples, Italy

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 cardiological 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 cardiological 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
C. Terracciano, E. Lena, A. Botta1, G. Bernardi, R. Massa
Department of Neurosciences and 1 Department of Biopathology, “Tor Vergata” University, Rome, Italy

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, α-actin or α-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
A. Todeschini, M.S. Cotelli, V. Vielmi, M. Rimoldi1, V. Gregorelli, M. Rizzato1, B. Castellotti1, A. Padovani, M. Filosto
Clinical Neurology, Section for Neuromuscular Diseases and Neuropathies, University Hospital “Spedali Civili”, Brescia, Italy; 1Neurological Institute “C. Besta”, Milano, Italy

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 (ETFA; 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.