cous Senegalese family. Clinical symptoms began at 1 year. Parents noticed falls and difficulties in getting up from the floor. Weakness and fatigue progressed and worsening with physical exercise was noted. Potosis and ophthalmoplegia were absent. Patient 2. Is a 19 year Spanish boy from a consanguineous family. Symptoms began when he was 7 years old with progressive and steady proximal weakness and fatigue particularly in the pelvic girdle. Potosis and ophthalmoplegia were absent. Examination: Both patients revealed a myopathic EMG pattern. Patient 1 showed a 35% decrement with repetitive stimulation in proximal muscles. Neither patients showed a decrement in the intrinsic hand muscle. CK was normal. Biopsy findings were unremarkable. Both patients had good response with anti-cholinesterase and 3-4 DAP drugs on long term follow up. Genetic studies: homocystinuria diagnoses in GFPT1 gene were identified in both patients: Patient 1: c.1534C > T (p.R512W). Patient 2 c.1472T > C (p.M49IT). Comments: (1) The identification of GFPT1 gene mutation widens the spectrum of congenital myasthenia syndrome (CMS). (2) Patients affected by a limb girdle muscle weakness and fatigue with myogenic EMG pattern and normal CK should be assessed using repetitive stimulation and genetic testing for GFPT1gene with potential consequences for treatment.

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P5.21

Novel mutation in the AChR alpha subunit C-loop dictates fast-channel kinetics by hindering channel opening triggered by agonists binding

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To characterize the molecular basis of a congenital myasthenic syndrome (CMS). Deciphering the molecular basis of a CMS is required for correct diagnosis and appropriate therapy. After agonist binding, the extracellular AChR C-loop caps the binding site and initiates structural transitions ultimately resulting in opening the AChR-channel. No AChR-C-loop mutations have been detected to date. Mutation analysis; EM; expression studies in HEK cells; single-channel recordings from mutant AChRs expressed in HEK cells; thermodynamic mutant cycle analysis. A 40-year-old woman with severe myasthenic symptoms since birth and 66% EMG decrement is heterozygous for Gly74Cys in the main immunogenic region, and Val188Met in the C-loop, of the AChR α-subunit. Both mutations are absent in 200 normal controls. Endplate ultrastructure was normal. zG74C expresses at 14% and zV188M at 90% of wild-type; thus zV188M determines the phenotype. Patch-clamp analysis reveals zV188M-AChR is a fast-channel mutation: the major component of burst open-durations is only 20% of wild-type mainly due to an 80-fold decrease of the channel opening rate. Replacement of zVal188 with Gly, Ala, Thr, or Leu results in fast-channel kinetics without correlation with size of the substituting residue. Because a previous study revealed the nearby zTyr190 in C-loop is crucial for coupling agonist binding to channel gating (J Gen Physiol 2005;126:23–39), we used mutant cycle analysis to determine whether zVal188 is energetically linked to zTyr190. This revealed that zVal188 couples zTyr190 with free energies of 3.7 kcal/mol. Brief openings by zVal188Met-AChR are due to decreased opening rate of the AChR channel which stems from interference with the structural transition that couples agonist binding to channel opening. The findings predict a beneficial response to cholinergic therapy and the patient responded well to pyridostigmine.

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INFLAMMATORY MYOPATHIES: POSTER PRESENTATIONS

P5.22

Granulomatous myositis and inclusion bodies myositis in a patient with hepatitis C

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A 54-year-old man diagnosed with hepatitis C presented muscle atrophy and progressive muscle weakness in the lower limbs, resulting in difficulties in walking, with frequent falls without pain or sensitivity changes. He was treated with interferon and ribavirin, with improvement of the muscle symptoms. It was performed an electromyography and a muscle biopsy for neuromuscular disease research. Electromyography revealed a myopathic pattern. Muscle biopsy showed sarcoplasmic vacuoles and granulomas with epitheloid histiocytes, lymphocytes and occasional multinucleate giant cells of the Langerhans type within muscle parenchyma. Special histochemical stains for microorganisms detection were negative and we did not observe vasulitis using established histologic criteria. The presence of granulomas is a histological finding described in the group of granulomatous myositis. The sarcoplasmic vacuoles that represent autophagic vacuoles in the electron microscopy exam are described in the group of inclusion body myositis. The classical group of inflammatory myopathies is formed by dermatomyositis, polymyositis and inclusion body myositis, although these group includes a broad spectrum of others immunological conditions such as granulomatous myositis. This entity is characterized by the presence of granulomas in the skeletal muscle and has been reported in collagen diseases, sarcoidosis, inflammatory bowel disease, myasthenia gravis and infectious diseases, including hepatitis C. Here we describe a patient with hepatitis C associated with granulomatous myositis and inclusion body myositis in the same muscle biopsy. To our knowledge, this association (hepatitis C; granulomatous myositis and inclusion body myositis) has not been reported in the literature.

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P5.23

Autoantibodies in sporadic Inclusion Body Myositis (sIBM): A population control study

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There is debate as to whether sIBM is a primary autoimmune muscle disease or a late-onset degenerative myopathy with inflammatory features. The reported occurrence of systemic autoantibodies (AAAb) in 43% of sIBM cases in a previous study by Koffman et al. (1998) was considered to support the autoimmune hypothesis. However, the significance of this finding is uncertain as AAb frequencies were not compared with population control frequencies. In the present study the frequencies of myositis- associated AAb (antinuclear antibody (ANA), extractable nuclear antigen (ENA) and its subgroups, Thyroid peroxidase (TPO), and IgA-anti-tissue transglutaminase) were compared in a group of 54 patients with biopsy-proven sIBM and a control group of 198 sera from the Busselton Population Health Survey. Patient and control sera were tested in the
same laboratory using identical techniques. Seropositivity for one or more AAb was found in 50% of sIBM patients vs 11.6% of controls ($p < 0.001$). The most frequent AAb was ANA (37% vs 11% in controls; $p < 0.001$). Screening for ENA by ELISA was positive in 27% vs 5% of controls ($p < 0.001$). Among the subgroups of ENA, anti-SSA/Ro-52 was most frequent (sIBM 17% vs controls 0%), while anti-Jo1 was not found in any sIBM sera. In a subgroup of 47 sIBM cases a more extensive screen for myositis-specific and myositis-associated AAb (including EJ, OJ, PL-12, PL-7, SRP, Jo-1, PM-Scl 75 and 100, Ku, and Mi-2) was carried out using the Euroimmuno-EL 3 immunoblot. Six patients were positive for anti-PM-Scl 75, two for anti-OJ and one for both anti-SRP and anti-PM-Scl 75. Our findings confirm that there is a high incidence of AAb in patients with sIBM and support the view that altered immune function may play a role in the pathogenesis of the disease.

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P5.24

Immune-mediated Necrotizing Myopathy Associated with Statins: Presentation of two cases and review of the literature

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Necrotizing myopathy is a rare form of statin myopathy. In these patients, discontinuation of the drug does not translate into recovery even after several months and necrosis without inflammation is found in muscle biopsy. This entity responds to steroid and immunotherapy. The other known causes of necrotizing inflammatory myopathy include overlap syndromes, particularly in the setting of signal recognition particle (SRP) antibodies and also paraneoplastic myopathies. We report a male and a female patients aged 58 and 78 years old, who were on statin treatment for a period of 4 and 5 years, respectively. They developed muscle weakness with a limb girdle distribution and respiratory and neck weakness in the female patient who were more affected. CK were highly elevated and EMG showed myopathic potentials with denervation at rest. Muscle biopsy showed necrosis without inflammation Both patients met the following criteria for immune-mediated necrotizing myopathy: (1) proximal muscle weakness occurring during or after treatment with statins (2) elevated serum creatine kinase (CK) (3) persistence of weakness and elevated CK despite discontinuation of the statin; (4) improvement with immunosuppressive agents; and (5) muscle biopsy showing necrotizing myopathy without significant inflammation. The man were treated with steroids with complete recovery in four months, and the female, who were more severely ill, did not respond to therapy. We present two patients with immune-mediated necrotizing myopathy associated to statins. These are a rare subgroup of patients with an immune-mediated necrotizing myopathy that does not improve after discontinuation of the drug and requires aggressive treatment with immunosuppressive agents. Awareness and early recognition of this disease is very important because responds to immunotherapy.

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P5.25

Inflammatory myopathies – Characteristics of a population

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The inflammatory muscle diseases represent a group of rare autoimmune diseases of unknown etiology which can have an acute, subacute or chronic presentation. Polymyositis (PM), Dermatomyositis (DM) and Inclusion Body Myositis (IBM) are the largest group of acquired and potentially treatable inflammatory myopathies. Clinically these entities share the presence of symmetric proximal muscle weakness caused by muscle inflammation and necrosis, heralded by elevated serum muscle enzymes. Frequently there are extramuscular manifestations associated and the presence of myositis-specific auto-antibodies. Diagnosis is based on clinical findings, confirmed by laboratory examinations. The aim of the present study was to make a review of the demographic characteristics, main clinical features, laboratory findings (with emphasis on the importance of immunologic profile) and therapeutic strategies in patients with PM, DM and IBM in a Rheumatology Department. The population of this study was constituted by 32 patients diagnosed, submitted to medical therapy and followed in our center in a 5 year-period (January 2006 to December 2010). We diagnosed and managed 32 patients with inflammatory myopathies in this period; 25 females and 7 males. PM represented 57% of the cases, followed by DM (37%) and IBM (6%). The mean age at time of diagnosis was 48.3 years. CK and aldolase were, with one exception, elevated. 75% of the patients presented antinuclear antibodies, more frequently with a specificity anti-Jo-1 and anti-SSa. The most frequent presenting clinical was muscular weakness (65%) and 31 patients presented it at the time of diagnosis. Involvement of other organs besides muscle occurred in half of the patients, and the most frequently involved organ was the lung. 8 patients were successfully treated only with glucocorticoids with no recurrence of the symptoms; the others needed iv immunoglobulin or immunosuppressive therapy. We registered 4 deaths.

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P5.26

Myopathy associated with HIV, a review of 50 muscle biopsies

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Different myopathies may be observed in HIV-infected patients. The most frequent are mitochondrial myopathies due to nucleoside analogs toxicity, and HIV-associated myositis like sporadic inclusion body myositis (sIBM) or polymyositis, which seem to be due to viral replication. More rarely described are myositis related to opportunistic infections in case of severe immunodeficiency or some sporadic late onset nemaline myopathies (SLONM). Nevertheless, the frequency and evolution of these different HIV associated myopathies are not precisely known. Our aim was thus to describe these myopathies from our reference center for neuromuscular disorders. On the database of the Department of pathology of our center, we crossed key words HIV and muscle biopsy for the period 2005-2010. For each muscle biopsy, morphological (hematoin cosin staining), mitochondrial (Gomori trichrome, succinic dehydrogenase and cytochrome oxidase staining) and immunological (HLA1 staining) analyses were performed. Between 2005 and 2010, 2880 muscle biopsies were performed. Fifty biopsies (1.7%) were realised in 45 HIV infected patients. Mean age at the first muscle biopsy was 50.1 years [39–61.2] with a 2.46 male/female sex ratio. Among the 50 biopsies, 43 were abnormal corresponding to 84.4% of HIV infected patients. Among patients with abnormal biopsies, the most frequent myopathy was polymyositis (65.4%), followed by mitochondrial abnormalities (47.7%). Only 3 cases (7.9%) of sIBM were observed. One case of necrotizing myopathy, 1 case of fasciitis and 1 case of cortisone myopathy were also described. No myositis due to opportunistic infection nor SLONM were observed. These retrospective study confirms that polymyositis is the most frequent HIV associated myopathy, fol-

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