Congenital myasthenic syndromes (CMS) show great genetic heterogeneity. Diagnosis is difficult and management often challenging leading to severe and even life-threatening complications, but may respond to a number of available drugs. We describe a case of a girl born with congenital talipes that was hospitalized at 21 days due to fever and dyspnea and soon required intensive care therapy. EMG showed myogenic changes but muscle biopsy had only minor abnormalities. Repetitive stimulation revealed significant decrement. Motor weakness partially improved with pyridostigmin but tracheostomy and gastrostomy were necessary at 4 months. Volume-controlled ventilation with high volumes was required due to diaphragmatic failure. Outpatient management was possible only after 8 months, Multi-fiber enteral nutrition, atropine and urecholine improved gastroesophageal reflux and secondary complications of pyridostigmin. Garches brace prevented spinal collapse and allowed verticalization, sitting position and head support. At 3 years she started integrated management at Garches daily hospital unit that offers nursing, medical follow-up, physical motor and respiratory therapy, speech-swallowing and occupational therapy and adapted school facilities. Systematic percussionnaire pulmonary and IPPV therapy was done in the mornings, before school. After identification of a mutation in CHRNNE gene, 3, 4 DAP was added at 3 years, with significant motor and respiratory response (able to stand up, no need of ventilation during the day). She learnt to drive an electric wheelchair. She had feet surgery at 4 years. Ephedrin was added and had significant effect in fatigue and strength (first steps with aid, lift arms, respiratory improvement). She was able to chew and swallow semi-solids. She was able to regularly assist school. This case shows the interest of a medical-scholar multidisciplinary approach in severe CMS and the positive response of polypharmaceutical treatment.

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P5.15
Clinical and serological features of very late-onset Myasthenia Gravis in Argentina: A multicentre retrospective cohort study
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Myasthenia Gravis (MG) has been considered a disease that affects predominantly young people, but diagnosis in the elderly, late onset MG (LOMG) and very late onset MG (VLOMG) is increasing. The aim of the study is to present our experience with MG patients older than 75 years (VLOMG) in our country. We analyzed the clinical records of patients with onset of MG at ≥75 years of age in five neuromuscular diseases centers in Argentina. We looked for clinical distribution of muscle weakness, results of serological test, thymus pathology and response to treatment. Disease severity at presentation was classified according to MGFA status and assessment to outcome was based on the MGFA post-interventional status criteria (PIS). 58 patients with VLOMG, median age at onset was 80.54 (±4.09) years, 30 were females and 28 males. 60.3% were positive for AChR antibodies (AChR-MG) and 39.7% were negative. Eleven patients presented the Ocular form of the disease and 47 generalized MG. Seropositivity was 45.5% and 63.8%, respectively. At diagnosis 56.9% had ocular symptoms only (MGFA I), at peak the more frequent status was MGFA Iib (55.2%) and only two patients had respiratory crisis. Six patients died. The thymus was normal, by CT scan or MRI, in 84.5% of the cases and 2 patients had thymoma. 44 were treated with steroids, 7 with azathioprine and 3 patients needed additional immunosuppression. At last follow up, 38 had a PIS of improved or better, and 36 reach minimal manifestation status. We describe the first group of LOMG in our country. Females and males were equally affected, 60.3% were AChR-MG, thymus pathology were uncommon and a good response to treatment according to PIS was seen.

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P5.16
Congenital outcome in congenital myasthenic syndromes
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Congenital myasthenic syndromes (CMS) are rare genetic diseases leading to the dysfunction of the neuromuscular transmission. As for autoimmune myasthenia, symptoms are usually fluctuant, and phase of acute worsening after years of stability are not uncommon. Different empiric observations have raised the suspicion that puberty or pregnancy may cause acute worsening of the patient’s condition. In addition, the risk for children, related to genetic transmission or teratogenicity of the treatments, is not known. To better understand the possible interactions between pregnancy and CMS, we retrospectively studied the gynaecological and obstetrical story of 23 French adult women with CMS. We reviewed a total of 17 full-term pregnancies in 8 patients. Six patients (75%) experienced a worsening of symptoms during at least one of their pregnancies. One woman with a COLQ mutation had a severe crisis, which started during the first month of pregnancy and caused respiratory failure during the post-partum period. The patient completely recovered after treatment by ephedrine. One woman with a CHRNNE mutation experienced a worsening of her bulbar trouble during the second trimester of pregnancy. Symptoms remained unchanged after three years of follow-up. Worsening of the muscle weakness was less severe in the other 4 patients, and lasted from 1 to 9 months after delivery. Only one baby was affected by CMS due to CHRNNE mutation. Two babies presented malformations: one, born from a mother with COLQ mutation, presented ureterocele and the second one, born from a mother CHRND mutation, had an atrial flutter at birth in the context of a right pulmonary artery agenesis. No hypothyrosis was noticed. This study demonstrates that pregnancy constitutes a high risk period for women with CMS, and that they should be closely followed up in a centre specialized in neuromuscular disorders.

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P5.17
Congenital Myasthenic Syndromes with COLQ mutations: Long term follow-up
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P5.17
Congenital Myasthenic Syndromes with COLQ mutations: Long term follow-up
Congenital myasthenic syndromes (CMS) are clinically and genetically heterogeneous inherited disorders characterized by impaired neuromuscular transmission. Mutations in the acetylcholinesterase (AChE) collagen-like tail subunit gene (ColQ) cause recessive forms of synaptic CMS with end plate AChE deficiency. We report the time course of clinical manifestations in 15 COLQ-mutated patients followed from 1987 to 2010. All patients suffered from a muscle weakness with onset at birth or in childhood. Ocular and bulbar signs were found in 60% of the patients and delayed pupillary light response in 20% of our patients. EMG study demonstrated a decrement on repetitive nerve stimulation and repetitive compound muscle action potential in all patients. Clinical symptoms strongly fluctuated daily, weekly, monthly or even yearly. Severe relapses were characterized by a general motor weakness associated with pain which resolved spontaneously after a few months whereas the relapses with these symptoms and bulbar signs could last up to several years. Genetic analyses identified 16 different mutations including 9 novel ones. There was no genotype-phenotype correlation. Our study confirms the predominance of ocuobulbar signs and the frequency of respiratory distress in COLQ-related CMS. At the end of the follow up of 23 years, interesting findings were (i) the spontaneous reversibility of severe relapses, some of them lasting for up to 5 years (ii) the good prognosis of COLQ-related CMS, since at the end of the follow-up 80% of patients were ambulant and 87% of patients had no respiratory trouble (iii) the efficacy of Ephedrine and, to a lesser extend, of 3-4 DAP. The triggering factors of relapses were esterase inhibitors, effort, puberty, pregnancy and delivery highlighting the importance of hormonal factors in CMS. In conclusion, patients diagnosed with unknown congenital myopathy should undergo an electrophysiological study of neuromuscular junction to identify ColQ-related CMS.

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P5.18
Human anti-MuSK IgG4 autoantibodies cause myasthenia gravis in immunodeficient mice
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Myasthenia gravis (MG) is a paralytic disorder with autoantibodies against components of the neuromuscular junction (NMJ). The most prevalent form is caused by antibodies against the acetylcholine receptor (AChR), but some patients instead have antibodies against muscle-specific kinase (MuSK). A protein essential for AChR clustering, MuSK MG antibodies are generally IgG4 subclass, contrasting most autoimmune diseases including AChR MG, which are IgG1/3-mediated. IgG4 antibodies are considered anti-inflammatory, but in some autoimmune diseases a direct pathogenic role of IgG4 autoantibodies has been suggested. Interestingly, anti-MuSK IgG4 titers correlate with disease severity, suggesting specific myasthenogenic activity of these specific antibodies. However, direct evidence is lacking. We show that injection of purified IgG4 from MuSK MG patients into immunodeficient mice causes severe myasthenic weakness, demonstrated and quantified with in vivo neuromuscular tests and electromyography. The MuSK IgG4 bound to mouse NMJs and caused reduced density and fragmented area of AChRs. Electrophysiological analyses revealed reduction of postsynaptic ACh sensitivity and exaggerated depression of presynaptic ACh release during intense synaptic activity. Neither IgG1-3 from the same MuSK MG patients, nor IgG4 from healthy controls induced any of these effects. We thus demonstrate that human anti-MuSK IgG4 autoantibody alone is directly myasthenogenic in this MuSK MG model, and elucidate the underlying electrophysiological abnormalities it causes at the NMJ.

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P5.19
A study on emotion recognition in patients with myasthenia
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The investigation of nonverbal communication in clinical populations can illuminate brain-behavior relationships underlying emotional expression, as well as provide about social an interpersonal functioning. Assessment of facial expression is an important aspect of the clinical neurological examination, both as an indicator of a mood disorder and as a sign of neurological damage. To the date there are studies about some psychosocial aspects of myasthenia, such as quality of life, anxiety or about neuropsychological aspects like a memory. However, there is not a study which has assessed facial emotion recognition accuracy. To assess the facial emotion recognition accuracy (fear, surprise, sadness, happiness, anger and disgust) and reaction time of patients with myasthenia. 35 patients with myasthenia and 36 healthy controls were tested for the ability to differ between emotional facial expressions. They were matched for age, sex and education’s level. This ability was evaluated using the computer based program called the feel test. The data showed that healthy controls scored significantly higher (p < 0.05) than patients affected by myasthenia in the following variables: total feel-score, fear, surprise and showed significantly lower reaction time. There was no significant correlation between scores and duration of the disease, neither with the degree of myasthenia. However, people with myasthenia showed a significant negative correlation between age and scores of recognition in all emotions and a positive correlation between age and reaction time. The findings imply that the ability of facial affect recognition is reduced in persons with myasthenia.

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P5.20
Limb Girdle Congenital Myasthenia Syndrome associated with mutations in GFTP1 gene. Report of two patients
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Recently a new form of congenital myasthenia has been associated with mutations in the gene encoding glutamine-fructuosa-6-phosphate transaminase (GFTP1). Patients usually present weakness in a limb girdle distribution and fatigue. Ocular and facial muscles are spared. Decremental response in repetitive stimulation is common and most patients benefit from anticholinesterase drugs. Many patients have tubular aggregates in conventional muscle biopsies. Hereby we report two patients affected with this condition. Patient 1: Is a 7 year old black girl born from a consanguin-