To evaluate our center's experience and determine potential causes of delays to diagnosis as once diagnosed these patients typically have the good response to treatment. We performed a retrospective chart review of 26 patients diagnosed with juvenile myasthenia between January 1, 2010 and December 31, 2020 at Le Bonehur Children's hospital. The baseline characteristics were recorded for each patient. In our cohort, the median age at onset was 5.5 years (18mo - 16years old). We had a 2:1 female to male ratio. The median time to both neurology consultation and diagnosis was 3 months. 46% were less than 5 years of age, 31% between 5-9 years, and 23% were older than 10. 75% were African American, 18% white, and 7% Latino. Prepubertal patients had a less than 4 months' time to diagnosis on average whereas post-pubertal had 8.5 months to diagnosis on average. 56% were AChR-Ab positive, 12% were MuSK positive and 32% were seronegative. The average time to diagnosis was 18 months in MuSK patients and 3 and 2 months for AChR and seronegative patients respectively. In our cohort, post-pubertal patients had a time to diagnosis on average twice as long as compared to prepubertal patients. MuSK patients had a time to diagnosis on average 3 times as long as compared to AChR patients. Our cohort tended to present at a younger age and we had a higher percentage of MuSK patients then traditionally reported in literature, likely due to our higher African American demographic. We hypothesize that these patients' predominant bulbar symptoms clouded their clinical picture and accounted for a delay to diagnosis as they were more often referred to ENT and GI. Given general providers decreased awareness of the association with bulbar symptoms and JMG, we sought to better educate providers at our institution regarding this association.

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Paediatric myasthenia gravis: a cohort of 20 years in a referral neuromuscular center.

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Myasthenia gravis (MG) is an antibody mediated autoimmune disorder characterized by fatigable muscle weakness. MG is rare in childhood: an average annual incidence rate of 1.5–1.6 per million children has been reported in Europe. MG presents with a variable clinical phenotype ranging from isolated ocular involvement to generalized weakness with bulbar and respiratory involvement. MG is usually mediated by antibodies (Abs) that bind to the acetylcholine receptor (AChR) at the neuromuscular junction. AChR antibody negative patients may also have Abs to muscle-specific kinase (MuSK) or low-density lipoprotein receptor-related protein 4 (LRP4), Patients who remain negative to all antibody testing are defined as seronegative (SN). Our aim was to examine the demographic, clinical features, neurophysiology findings, antibody subtypes and therapeutic response in pediatric MG patients under the care of a pediatric referral neuromuscular center. This was a retrospective study, examining clinical records of all MG patients with symptom onset before the age of 18 years evaluated from January 2000 until February 2021. Twenty five patients were included with mean age at presentation of 7.6 years (0.4 to 17 years). Women patients: 19 and Men: 9. More than 50% presented at over 10 years of age. Clinical manifestations: 18 patients presented facial weakness and ptosis, the rest of the patients (7) presented with bulbar symptoms (swallowing disorders and dysphonia), associated to generalized weakness. Repetitive nerve stimulation: In 5 patients a decrement of more than 10% was observed. Antibodies: AChR: 18 patients. Musk: 4 patients. Antibody negative: 3. Four patients presented myasthenic crisis, two of them required plasmapheresis / immunoadsorption. Thymectomy: 4 patients, two went into complete remission of symptoms after surgery. Treatment: 10 patients responded well to monotherapy with pyridostigmine, the other patients (15) required combined immunosuppressive treatment. In our cohort ocular MG is the predominant phenotype, which is mostly correlated with AChR antibodies. Positive AntiMusk MGs were associated with bulbar symptoms and generalized weakness, all of which required combination therapy. Patients who presented myasthenic crisis are currently stable (mild symptoms) with combined immunosuppressive treatment.

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A case of congenital myasthenic syndrome diagnosed at adolescent period

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The congenital myasthenic syndromes are rare, inherited disorders that result from mutations in components of the neuromuscular junction. We present an adolescent boy with congenital myasthenic syndrome (CMS) due to mutation of Cholinergic Receptor Nicotinic Epsilon Subunit (*CHRNE*) gene. We present a 16-year-old boy who presented with increased fatigue and weakness since his childhood. He was born after uneventful pregnancy and delivery with nonconsanguineous marriage of his parents. There was no history of difficulty in feeding, sucking or apneic spells. The early motor developmental milestones were normal. At the age of twelve, he started getting tired quickly, had unsteady gait, was falling frequently and had difficulty climbing. Neurological examination showed ptosis and predominantly proximal muscle weakness. His serum was antibody-negative for acetylcholine receptor (AChR). Serum creatine kinase level was normal. Cranial MRI showed mild cerebral atrophy. Muscle biopsy revealed nonspecific myopathic findings. We identified a homozygous mutation of c.1192C> T (p.Gln398) in the *CHRNE* gene, and the mutation was confirmed by Sanger sequencing. He was treated with pyridostigmine and symptoms improved significantly. In CMSs, the age of disease onset, presenting symptoms, and response to treatment differ depending on the molecular mechanisms. The CMSs manifest as abnormal fatigability, permanent or fluctuating weakness of extraocular, facial, bulbar, axial, respiratory, or limb muscles, or developmental delay. These clinical profiles overlap considerably with other myopathies and can lead to diagnostic challenges. If there is a suspicion of a CMS, next generation sequencing tests may help make the correct genetic diagnosis.

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NEW GENES AND DISEASES

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The alpha2-subunit of the AP2 clathrin adaptor as the causal gene in an atypical myopathy with granulofilamentous inclusions

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Clathrin-mediated endocytosis is the best characterized process for the entry of proteins and lipids at the plasma membrane of eukaryotic cells. We have previously shown that at costameres, muscle adhesion and force transmission sites, clathrin recruited by the AP2 adaptor forms flat plaques required for actin and desmin intermediate filament organization. Here, we describe a patient presenting a progressive muscular atrophy with loss of ambulation, complete tetraplegia, ophthalmoplegia, severe scoliosis and lower limb contractures and no cardiac involvement. Electron microscopy of muscle biopsy revealed inclusions composed of filamentous material, vacuoles, honeycomb structures and thin granular material surcharge. This