in 3 prior cases, but limited clinical data were presented. We present detailed clinical features of a family with two siblings having a distal myopathy with rimmed vacuoles (DMRV), and genetic variants in SQSTM1 and TIA1. Methods: Clinicopathologic study of a family with DMRV to describe clinical features, laboratory and neurophysiology studies, neuroimaging, and genetic sequencing. Results: Two siblings with variants in SQSTM1 and TIA1 developed myopathy in their early 60's, with early involvement of ankle dorsiflexors and finger extensors. A decade after onset, patients remain ambulatory and have not developed cardiac or respiratory complications. MRI of the legs showed selective involvement of adductor magnus, vastus lateralis, and in lower legs the anterior compartment and medial gastrocnemius. Muscle pathology demonstrated rimmed vacuoles, disrupted myofibrillar architecture, and mislocalised TDP43. Two unaffected family members had one genetic variant but not both. Conclusions: We describe a fourth family with co-occurrence of TIA1 and SQSTM1 genetic variants and describe their detailed phenotype. Future study should address the mechanism of the interaction between these two variants.

# **P.075**

## Inflammatory Myositis associated with Myasthenia Gravis with and without thymic pathology: case series and literature review

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doi: 10.1017/cjn.2018.177

**Background:** The association of myasthenia gravis (MG) and inflammatory myositis (IM) is rare and often only one of the diseases is diagnosed. **Methods:** In this study, we reviewed medical records of patients seen at NMDU from 2004 to 2017 who had diagnosis of concurrent MG and IM. The data is presented descriptively. **Results:** We identified 7 patients with MG-IM overlap. Clinical features, laboratory and pathology data of the patients are summarized in Table 1. **Conclusions:** This is one of the largest case series with MG-IM overlap. It is very important to recognize such association and the different pattern of muscle involvement because therapies may be adjusted to treat both conditions. In patients with thymic pathology, conventional disease modifying agents, IVIG and glucocorticoid in addition to thymoma resection appear to be effective. In patients with refractory MG and myositis who were AChR negative, rituximab may be effective.

# **P.076**

## Safety of Eteplirsen, a phosphorodiamidate morpholino oligomer, in Duchenne Muscular Dystrophy patients amenable to Exon 51 skipping

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#### doi: 10.1017/cjn.2018.178

**Background:** Duchenne muscular dystrophy (DMD) is an Xlinked disorder affecting 1:3500-5000 live male births, causing a lifelimiting form of muscular dystrophy. Whole exon deletions disrupting the reading frame result in near-absence of sarcolemmal dystrophin, essential for muscle function. Eteplirsen is a phosphorodiamidate

morpholino oligomer (PMO) designed to induce production of internally-truncated dystrophin in certain patients. Methods: As of June 2016, 150 patients (4-19 years of age) with DMD received eteplirsen in 7 clinical trials. 143 patients received ≥1 intravenous infusion of eteplirsen (range: 0.5 - 50 mg/kg). 81 (54%) received treatment for  $\geq 1$  year (Range: 1-4+ years). **Results:** Common (>15%) adverse events (AEs) were cough, headache, vomiting, back pain, extremity pain, contusion, nasopharyngitis, upper respiratory tract infection, nasal congestion, arthralgia and rash. Non-serious facial flushing, erythema and mild transient temperature elevation occurred with eteplirsen. 10 (6.7%) patients experienced severe AEs; 12 (8%) patients experienced serious AEs. All serious and all but 1 severe AEs were considered unrelated to eteplirsen by the treating physicians. Serial echocardiograms in 12 treated patients demonstrated no functional decline over 4+ years. Conclusions: Eteplirsen's tolerability will continue to be assessed in ongoing clinical trials.

An updated data summary will be presented.

# **P.077**

## Utility of a next generation sequencing in the diagnosis of Congenital Myasthenic Syndromes

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doi: 10.1017/cjn.2018.179

Background: Congenital Myasthenic Syndromes (CMS) are heterogeneous disorders caused by genetically determined structural or functional differences in proteins involved with the neuromuscular junctions. Clinical and molecular genetics studies of CMS patients have revealed significant locus heterogeneity; there are 21 known genes related to CMS, but other genes may mimic the phenotype, justifying the use of a multi-gene panel for genetic testing Methods: Our group developed custom sequence capture probes designed to flank 27 different genes associated with CMS, including enrichment for all coding exons as well the flanking intronic regions. We enrolled 20 patients from the paediatric and adult neuromuscular clinic with a clinical phenotype of CMS. Using custom analytical, we assessed the sequence variants and exon-level CNVs for each patient. Results: Thirteen male and seven female patients with median age of 12.25 years (range 1.5-39y) were assessed. We identified missense and CNVs in 17 patients, including established pathogenic mutations confirming the diagnosis in 5 patients Conclusions: The use of Next Generation Sequence with CNV for CMS can help determine the underlying causes of most CMS disorders and allow appropriate medical treatment, refined genetic counseling, and improved understanding of prognosis, justifying the implementation in the standard clinical screening of CMS.