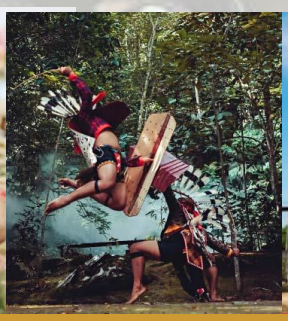
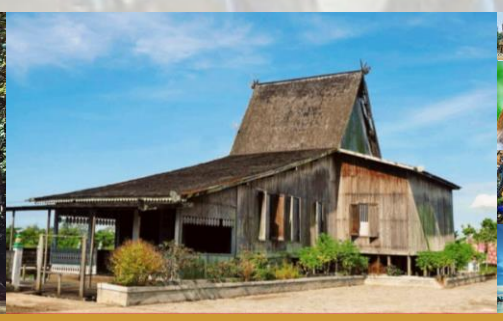
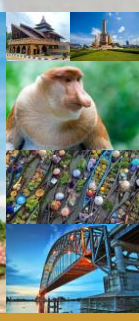
AOMC

The 20th Scientific Meeting

Indonesia
June 9th – 11th, 2022

Program & Abstract Book

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WELCOMING MESSAGE FROM CHAIRMAN OF 20TH SCIENTIFIC MEETING AOMC

Dear friends and colleagues,

On behalf of the organizing committee, we are very pleased to host the 20th Annual Scientific Meeting of Asian and Oceanian Myology Center (AOMC) in Jakarta, Indonesia in conjunction with The National Scientific Meeting of the Indonesian Neurological Association (PIN PERDOSSI 2022). Being inaugurated in January 2001 in Tokyo, AOMC has promoted the basic and clinical scientific research in the neuromuscular field, provided a scientific forum to update on the advance and innovations in the neuromuscular field, provided educational opportunities, and encouraged multidisciplinary collaborations in the neuromuscular field.

Understanding not only the activity of the neuron, neuromuscular junction, and muscle but also the related disorders are some of the worldly-wise and revolutionary health topics to discuss extensively. We intend to make significant progress to find novelties regarding neuromuscular disease including basic science, clinical characteristics, pathophysiology, diagnostic approach, to comprehensive management within the multidisciplinary team through exhausted discussion between chairs, speakers, and participants. Finally, I appreciate you all for your gracious presence. I hope you find this scientific meeting beneficial to provide a refinement of our knowledge and a promising future for neuromuscular disease. Welcome to the 20th Scientific Meeting of AOMC and to Indonesia!

Chairman of the 20th Annual Scientific Meeting of Asian Oceanian Myology Center

Manfaluthy Hakim

Head of Clinical Neurophysiology and Neuromuscular Disorders Study Group of Indonesian Neurological Association

WELCOMING MESSAGE FROM PRESIDENT OF AOMC

AOMC Website, 2022, June

"We are strong clinician-educators as AOMC, two decades and counting!"

Dear Friends and Colleagues,

The Asian and Oceanian Myology Center (AOMC) reached its second decade of existence as a center mainly dedicated for the education in our region. True to its aims, AOMC enhances its reach by sharing of expertise, by encouraging collaboration and by fortifying a collegial network, if only to enhance knowledge-base and updates of muscle disorders.

Since its birth in Tokyo, year 2001, we are now in our 20th annual convention (circa 2022), and ably hosted by our Indonesian expert counterparts. To be attuned, we experienced virtual and hybrid platforms of learning for the past two years, challenges amidst, notwithstanding. It has been a tradition in AOMC that hosting of annual conventions be done by individual countries in Asia and Oceania, empowering locales for independence, while we stay as an oversight. This model has worked effectively, in ways to co-apt AOMC conventions with annual national meetings of host country aggrupation.

Educational platforms, be it real-time, virtual or hybrid, will persevere and even be enhanced in the coming years. The 20th annual AOMC convention on 9-12June, 2022, is hosted by the team of Dr. Manfaluthy Hakim, which comes in tandem with the Indonesian Neurological Association meeting, the PIN PERDOSSI Banjarmasin, and themed, "Bridging Neurological Basic Science and Technique to Advanced Technology Services in New Habit Era." One is served a sumptuous platter of muscle disorder topics spanning from teaching courses on diagnostics, therapy and interactive case discussions.

As I step down, I am very deeply honored and privileged to be the ***third President of the AOMC****.* From this role, the collective efforts of the founders, previous Presidents, officers and members to propel the growth of AOMC, are truly acknowledged. The achievement of AOMC goals remains our priority: promote clinical scientific research and achievement of clinical practice standards; provide for scientific forum while also opening education opportunities for young investigators and; encourage multidisciplinary collaboration. In my opening remarks accepting the AOMC helm, I spoke about **Innovation, Collaboration** and **Integration.** It is my fervent hope that by passing the baton to the next President, we will eventually and collectively see through these noble aspirations.

As a penultimate note, having a 'home' for AOMC will soon be a reality, and this becomes my legacy to all of you. Taking the cudgels, Dr. Satish Vasant Khadilkar and his Indian team, have leveled this arduous task to eventually make this an 'indelible ink' for AOMC. AOMC is therefore grateful as ever, for your perseverance on this matter.

Finally, my ardent desire is for us to not only continue, but also enhance our capabilities as clinician-educators, for we indeed embody AOMC, and that has been two decades now and counting!

President of AOMC

Raymond L. Rosales

Professor and Academic Researcher, Faculty of Medicine and Surgery
Head of Neuromuscular Unit, The Neuroscience Institute
University of Santo Tomas and Hospital
Manila, Philippines

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PROGRAM OVERVIEW

DAY 1: Pre-Teaching Congress

Thursday, June 9th, 2022

08.00-09.35 (GMT+7)	**Session 1** Chairperson: Rusdy Ghazali Malueka **Diagnostic approach in muscle disease** (Raymond Rosales) **Role of electrodiagnostic studies in diagnosis of muscle disease** (Manfaluthy Hakim)
09.40-11.45 (GMT+7)	**Session 2** Chairpersons: Marcel Prasetyo & Nelly Amalia Risan **Muscle imaging in diagnosis of muscle diseases** (Yun Yuan) **Role of myositis-specific and -associated autoantibodies in inflammatory myopathy** (Akinori Uruha) **How to get representative muscle sample and the role of muscle biopsy in diagnosis of muscle diseases** (Jantima Tanboon)
13.00-14.50 (GMT+7)	**Session 3** Chairperson: Amanda Soebadi **Immunotherapy of inflammatory myopathy** (Guochun Wang)
14.55-16.15 (GMT+7)	**Session 4: Interactive Case Studies** Chairperson: Eka Susanto Panelists: Ery Kus Dwianingsih, Jantima Tanboon, Phillipa Lamont, Satish Khadilkar

PROGRAM OVERVIEW

DAY 2: Symposium Day 1 Friday, June 10th, 2022	
07.30-07.50 (GMT+7)	OPENING CEREMONY
08.00-09.15 (GMT+7)	**New Muscle Disease** Chairperson: Luh Ari Indrawati **Oculopharyngeal distal myopathy** (Zhaoxia Wang) **OBSCN, new causative gene of rhabdomyolisis** (Gianina Ravenscroft) **JAG2-related muscular dystrophy** (Peter B Kang)
09.20-10.35 (GMT+7)	**Inflammatory Myopathy** Chairperson: Ichizo Nishino **Diagnosis approach in idiopathic inflammatory myopathy** (Namita Goyal) **Clinicopathologic features of immune-mediated necrotizing myopathy** (Arada Rojana-Udomsart) **Clinicopathologic features in idiopathic inflammatory myopathy with myositis-specific autoantibodies subgroups** (Jantima Tanboon)
10.40-11.55 (GMT+7)	**Spinal Muscular Atrophy** Chairperson: Yuh-Jyh Jong **Experience in Thailand** (Oranee Sanmaneechai) **Experience in Korea** (Jong Hee Chae) **Experience in Hong Kong** (Sophelia Hoi-Shan Chan)
12.00-12.35 (GMT+7)	**Artificial Inteligence Utilization in Muscle Diseases Diagnosis** Chairperson: Raymond Rosales Speakers: Yen-Lin Chen
12.40-13.55 (GMT+7)	**Updates in Muscular Dystrophy** Chairperson: Dae-Song Kim **Updates in therapy of facioscapulohumeral muscular dystrophy** (Leo H Wang) **What's new in DMD therapy** (Yoshitsugu Aoki) **Update in limb girdle muscular dystrophy** (Luh Ari Indrawati)
14.20-15.15 (GMT+7)	**Updates in Therapy of Inflammatory Muscle Disease** Chairperson: Anna Arianne **Updates in therapy of immune-mediated necrotizing myopathy** (Wen-Chen Liang) **Therapy for inclusion body myositis** (Merilee Needham)
15.20-16.25 (GMT+7)	**Supportive Management in Muscle Disease** Chairperson: Muhammad Deryl Ivansyah **Respiratory care in muscle disease: diagnosis to management** (Yuka Ishikawa) **Orthopedic management in muscle disease** (Wildan Latief) **Improvement function for daily activity of muscle disease patients** (Luh Karunia Wahyuni)

PROGRAM OVERVIEW

	DAY 3: Symposium Day 2 **Saturday, June 11th, 2022**
09.15-10.30 (GMT+7)	**Motor Neuron Disease** Chairperson: Indra Sari Kusuma Harahap **Update in diagnosis modalities and its pitfal in motor neuron diseases** (Kazumoto Shibuya) **Updates in ALS: promising therapy** (Seung Hyun Kim) **Update in therapy of spinal muscular atrophy** (Hisahide Nisiho)
10.35-11.50 (GMT+7)	**Peripheral Nerve Disease** Chairperson: Umapathi N. Thirugnanam **Updates in diagnosis of Guillain Barre syndrome and new therapy modalities** (Nortina Shahrizaila) **Genetic study of large on small fiber neuropathy in HIV sensory neuropathy** (Ahmad Yanuar Safri) **Autoimmune nodopathies** (Norito Kokubun)
11.15-13.00 (GMT+7)	**COVID 19-related Neuromuscular Diseases** Chairperson: Sara Khan **COVID 19-related inflammatory myopathy** (Khean-Jin Goh) **Myasthenia gravis in COVID-19** (Fitri Octaviana) **SARS CoV2 vaccination-related neuromuscular disorders** (Shahriar Nafissi)
13.25-14.40 (GMT+7)	**Neuromuscular Junction Disease** Chairperson: Atchayaram Nalini **Updates in Congenital Myasthenic Syndrome** (Kinji Ohno) **Therapy of Myasthenia Gravis in special population** (Charungthai Dejthevaporn) **Updates in immunotherapy in MG: how to manage refractory MG** (Chongbo Zhao)
14.45-16.00 (GMT+7)	**Clinicopathology Conference** Chairperson: Josiah Chai Panelists: Chanin Limwongse, Eka Susanto, Ichizo Nishino, Kum Thong Wong
16.00 (GMT+7)	CLOSING CEREMONY

e-POSTERS ABSTRACT

CPF 010

Dermatomyositis

Citra Mega Kharisma[1], Aida Fithrie[2]
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Introduction: Myopathy is characterized by symmetrical weakness, more severe in the proximal muscles and no sensory disturbances. Dermatomyositis is a myopathy characterized by inflammation attacks the skeletal muscles and skin that manifests as various rashes. Dermatomyositis can occur in children and adults and more common in women.

Case Presentation: A 36-year-old woman presented with weakness in four limbs experienced since 4 months slowly. The patient has difficulty when doing activities such as getting up from sitting on the floor to standing position. The patient also complained of myalgia. One month before experienced weakness, the patient complained of the appearance of blackish rashes on the skin. Previous allergy history was denied. Physical examination revealed lower motor neuron type tetraparesis and rashes were found on the face, neck, abdomen and limbs. There is an elevation of muscle enzyme levels by 8x upper limit normal, diffuse myogenic lesions on electroneurophysiology and ANA test results (-). The patient was given corticosteroid and physiotherapy. The patient was also consulted to the dermatovenereology and diagnosed with post-inflammatory hyperpigmentation and given desoximethasone cream. No muscle biopsy was performed in this patient.

Discussion: Dermatomyositis is generally found in the age 40 to 60 years. Dermatomyositis manifests as a symmetrical proximal muscle weakness with acute or subacute onset with pathognomonic skin lesions. If a patient is suspected of dermatomyositis, it can be confirmed by muscle enzyme levels, immunological markers, electroneurophysiology and muscle biopsy. The goal of therapy for dermatomyositis is to increase muscle strength, repair skin rashes and improving quality of life. In dermatomyositis, monitoring the risk of malignancy is an important step.

Conclusion: Dermatomyositis is diagnosed based on the history, clinical manifestation, laboratory, electroneurophysiology and muscle biopsy. Management consists of corticosteroids, immunosuppressants, immunomodulators, physical rehabilitation and management of skin rashes.

Keywords: dermatomyositis, inflammation, myopathy

CPF 021

ADSSL1 Myopathy: Diagnostic Challenges with Variable Phenotypes in Three Indian Patients

Dipti Baskar[1], Kiran Polavarapu[1], Seena Vengalil[1], Saraswati Nashi[1], Veeramani Preethish Kumar[1], Akshata Huddar[1], Gopikrishnan Unnikrishnan[1], Abel Thomas Oommen[1], Mainak Bardhan[1], Atchayaram Nalini[1]

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Introduction: ADSSL-1 is a muscle-specific adenyl-succinate synthase isoform involved in adenine nucleotide synthesis. An autosomal recessive mutation in ADSSL-1 gene (chromosome 14q32.22) results in this recently described ultra-rare distal myopathy. Only a few case series are reported.

Methods: Here we present the clinical and genetic attributes of three Indian patients from two families with ADSSL1 myopathy.

Results: The brother-sister siblings of 1st family and the female patient from 2nd family were offsprings of non-consanguineous and consanguineous parents respectively. The age of onset of symptoms was 3-4years. The total duration of symptoms ranged 12-21 years. The two siblings of the same family showed significant proximo-distal weakness of limbs which was slowly progressive. Magnetic resonance imaging of muscle done in the brother showed significant fatty infiltration of Glutei and Gastrocsoleus. The patient from the second family showed distal onset limb weakness, ptosis, facial weakness, dysphagia along with seasonal fluctuation of symptoms. Nerve conduction studies were normal and repetitive nerve stimulation did not show decrement. Quadriceps biopsy showed fibre size variation, few hypertrophic fibres with central nuclei and prominent fatty vacuolation of type-1 fibres. She also showed some improvement with pyridostigmine. All the patients had normal serum creatine kinase levels. Next-generation sequencing (NGS) showed homozygous c.910C>T (p.D304N) novel mutation in the first family and homozygous c.794G>A (p.G265E) in the third patient which is reported in Japanese cohort.

Discussion: Significant phenotypic variation was noted with the siblings showing a predominant limb-girdle pattern of weakness whereas the third patient had oculo-bulbar features along with prominent seasonal fluctuation of weakness, mimicking congenital myasthenic syndrome but lacking decremental response.

Conclusion: This is the first case series from India to report this rare myopathy showing clinical heterogeneity along with a novel mutation of c.910C>T (p.D304N).

Keywords: ADSSL-1, c.910C>T mutation, distal myopathy

CPF 022

Clinico-pathological Features of Beta-sarcoglycanopathy with a Highly Prevalent Mutation in an Indian Cohort

Dipti Baskar[1], Mainak Bardhan[1], Seena Vengalil[1], Saraswati Nashi[1], Kiran Polavarapu[1], Veeramani Preethish Kumar[1], Akshata Huddar[1], Gopikrishnan Unnikrishnan[1], Abel Thomas Oommen[1], Atchayaram Nalini[1].

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Introduction: Limb-girdle muscular dystrophy recessive type 4 (LGMDR4) is a rare autosomal muscular dystrophy caused by homozygous or compound heterozygous mutation in β-Sarcoglycan (SGCB) at chromosome 14q12. We describe the clinico-pathological characteristics of patients with a rare homozygous mutation of c.544A>C (p.thr182pro) in SGCB.

Methods: This was a retrospective observational study. Targeted exome analysis was done in patients with suspected sarcoglycanopathy.

Results: Sixteen patients with c.544A>C (p. thr182pro) homozygous missense mutation in exon 4 of chromosome 14:g.52894973T>G; Depth:48x are included. In-silico predictions of the variant are probably damaging by PolyPhen-2 (HumDiv) and damaging by SIFT, LRT and MustationTaster2. M: F=1:1. Mean age at onset and evaluation are 6.3±2.8 and 9.0±2.7 years respectively. All presented with proximal lower limb weakness and three also had upper limb symptoms. Consanguinity was present in 9(56.3%). Scapular winging (n=10) and macroglossia (n=6), myalgia (n=3) was noted. Additionally, hyperextensible distal joints (n=2), low set ears (n=1) and micro-ophthalmia with corneal clouding (n=1) were seen. 14 patients were independently ambulant at presentation and subsequent loss of ambulation in 12 with mean age of 12.3±3.0. Muscle histopathological analysis in 8 patients showed absence of all sarcoglycans (SG) in 6 (75%), isolated α-SG deficiency (n=1) and combination β and γ (n=1). Additional features of mitochondrial and inflammatory changes were seen in one patient.

Discussion: This study showed salient features such as myalgia, hyperextensibility of distal joints and facial dysmorphism such as low set ears, and micro-ophthalmia with corneal clouding, which are rarely reported in sarcoglycanopathies. Most of the patients with muscle biopsy showed absence of all the sarcoglycans.

Conclusion: This is one of the first studies to describe the clinicopathological features of SGCB with this highly prevalent mutation of c.544A>C in Indian cohort.

Keywords: LGMDR4, clinicopathological features, c.544A>C mutation

CPF 023

Clinical and Genetic Study of a Spinal Muscular Atrophy Family with Variable Phenotypes

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Introduction: Spinal muscular atrophy (SMA) is a severe inherited neuromuscular disease caused by pathogenic variants in survival motor neuron 1 (SMN1; OMIM 600354) gene. According to the age of onset and achieved maximal motor function, SMA is divided into four subtypes. The phenotypic variability is mainly regulated by the copy number of *SMN2*, a homologous gene of *SMN1*.

Case Presentation: The proband, a 3 years-old boy, showed proximal limb weakness with abnormal gait at 16 months old, then was gradually unable to squat at 2 years old. Physical examination showed decreased muscle strength of proximal limbs with level 4, decreased muscle tension, muscle fasciculation in hands. The knee reflexes could not be induced, and Babinski's signs were negative. The parents are nonconsanguineous. His mother presented normal, however, very slight symptoms with difficulty in getting up from supine position beginning from childhood was queried. Her electromyography indicated neurogenic damage in the quadriceps femoris. The results of multiplex ligation-dependent probe amplification identified a homozygous deletion of exons 7-8 in *SMN1* with 3/3 copies in *SMN2* in the proband as well as his mother, and a heterozygous deletion of exons 7-8 in *SMN1* with 3/3 copies in *SMN2* in his father as well as his maternal grandparents. No abnormal copy numbers of NAIP, CFT2H2, H4F5 in 5q13 region were detected in this family.

Discussion: Copy numbers of *SMN2* is negatively correlated with the disease severity, but not the only genetic modifier for SMA. Recently, gender-specific plastin-3 as a genetic modifier for SMA was found. The variable phenotypes between the proband and his mother might due to the gender difference.

Conclusion: This report presented a SMA family of discordant intrafamilial phenotypes.

Keywords: spinal muscular atrophy; variable phenotypes; *SMN1*

CPF 024

Baseline Nutrition Investigation in a Chinese Cohort of Pediatric Patients with Spinal Muscular Atrophy

Shuang Li[1], Shan Liu[1], Ying Wu[1], Yidan Liu[1], Dandan Tan[1], Yanbin Fan[1], Cuijie Wei[1], Hui Xiong[1]*
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Introduction: Nutritional problem is frequently observed with pediatric patients with spinal muscular atrophy (SMA). In this study, we aimed to investigate the nutritional status in Chinese patients with SMA.

Methods: Clinical data including the body weight, length, body mass index (BMI) and the levels of serum 25-hydroxy Vitamin D (25-OHD) of SMA patients from January 2022 to March 2022 were collected and analyzed. We used the Z-score (standard deviation) to analyze the BMI. The levels of serum 25-OHD were graded as follows: 75-250nmol/L for normal, 50-75nmol/L for insufficiency, less than 50nmol/L for deficiency.

Results: A total of 41 pediatric patients with SMA (8 case of SMA type 1, 20 case of SMA type 2, and 13 case of SMA type 3) with ages ranging from 12 months old to 15 years old were included. Nearly 25% of SMA patients showed nutritional problems. Malnutrition was observed in 50% (4/8) of SMA 1 patients, 10% (2/20) of SMA 2 patients and15.3% (2/13) of SMA 3 patients; overweight was found in 5% (1/20) of SMA 2 patients and 15.3% (2/13) of SMA 3 patients. The 25-OHD deficiency was observed in 25% (2/8) of SMA 1 patients, 30% (6/20) of SMA 2 patients, and 38.5% (5/13) of SMA 3 patients. The 25-OHD insufficiency was found in 25% (5/20) of SMA 2 patients and 23.1% (3/13) of SMA 3 patients.

Discussion: This study showed that malnutrition was comon in SMA 1 patients, 25-OHD deficiency or insufficiency was frequent among the three types of SMA. Disease management with adjusting the diet structure and more outdoor activities would improve the nutritional problems.

Conclusion: In this study, we demonstrated the baseline nutrition situations in a Chinese cohort of pediatric patients with SMA.

Keywords: spinal muscular atrophy; obesity; undernutrition; 25-hydroxy vitamin D

CPF 025

Natural History of a Novel Mouse Model for *LAMA2*-related Congenital Muscular Dystrophy

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Introduction: We have identified *LAMA2* exons 3-4 as the high-frequency disease-causing variants region in patients with *LAMA2*-related muscular dystrophy. In this study, we generated a *Lama2* knockout mouse model, named dy^H/dy^H, aimed to investigate the early biomarker through phenotype and muscle pathology.

Methods: Mouse offspring of heterozygous *Lama2* knockout C57BL/6 mice were bred and genotyped. The differences in survival length, body weight, motor function, serum creatine kinase levels, muscle MRI, muscle biopsy and molecular pathology between wild-type and dy^H/dy^H mice were analysed.

Results: The homozygous deletion of exon 3 along with a frameshift mutation of the *Lama2* gene was identified in dy^H/dy^H mice. The median survival length of dy^H/dy^H mice was 21 days (ranging 12-35 days). The body weight of dy^H/dy^H mice was increased slowly within the postnatal day 17, then decreased, and were significantly delayed from the postnatal day 7 when compared with wild-type mice. Dy^H/dy^H mice showed poor motor function with weak gait, low limb grip and more times of electric shock during forced treadmill running compared with wild-type mice. The serum creatine kinase levels in dy^H/dy^H were 9-10 times that of wild-type mice at 2-3 weeks old. Decreased muscle volume on T1-weighted MRI and hyperintense regions on T2-weighted MRI were found in the pelvic and hindlimb muscles of dy^H/dy^H mice at 2-3 weeks old. At 2 weeks old, the most extreme muscle dystrophic changes, increased fibrosis and inflammation were observed in the biceps femoris of dy^H/dy^H mice, as well as laminin α2 deficiency.

Discussion: Dy^H/dy^H mice were generated based on clinical high-frequency disease-causing variants, and presented short survival length, low body weight, poor motor function, increased serum creatine kinase levels, muscle damages in MRI and muscle dystrophic changes with age.

Conclusion: We described the natural history of a novel mouse model of *LAMA2*-related congenital muscular dystrophy.

Keywords: mouse model; genotype-phenotype; *LAMA2*; muscular dystrophy

CPF 026

Muscle Transcriptomic Study of a Novel *LAMA2*-related Congenital Muscular Dystrophy Mouse Model

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Introduction: The pathogenesis of muscle pathology in *LAMA2*-related congenital muscular dystrophy (*LAMA2*-CMD) is not clearly understood. In this study, we analyzed the muscle transcriptome data of a novel mouse model of *LAMA2*-CMD, dy^H/dy^H, to explore the pathogenesis of muscle disorders.

Methods: The comparison of muscle changes between dy^H/dy^H and wild-type mice at 2-week-old detected by RNA sequencing, Immunofluorescence and western blot were analyzed.

Results: Compared with wild-type mice, the expressions of genes associtated with muscle cytoskeleton and contraction (*Myo5c*, *Myl3*, *Actc1*, *Myoz3*, *Myl2*, *Myh7*, etc.) were downregulated in dy^H/dy^H mice. Immunofluorescence showed the expressions of MyHC, desmin and β-tubulin were focally increased in the regeneration area, while desmin and β-tubulin were decreased in mature muscle fibers in dy^H/dy^H mice. Western blot showed that the expression of MyHC and MYH2 protein were increased, the expression of F-actin was decreased in dy^H/dy^H mice muscle, desmin and β-tubulin showed no obvious change. The expressions of muscle development-related genes (*Myog*, *Myof, Myh3*, *Myh8*, *Myo5a*, etc.) were upregulated in dy^H/dy^H mice by RNA sequencing. Immunofluorescence staining showed the expressions of MyoG, MyoD1 and Myf5 were focally increased, while the decreased expressions of MyoG and MyoD1 in dy^H/dy^H mice were detected by western blot. In addition, the expressions of many genes related to muscle cell membrane ion channels, membrane transporters and mitochondrial energy metabolism were downregulated in dy^H/dy^H mice.

Discussion: Muscle cytoskeleton, contraction, and development related genes and proteins were changed, which might result in the dysfunction of myofibers, and impaired regeneration and development of muscle fibers in dy^H/dy^H mice. A series of upregulated genes related to inflammation and pathological fibrosis would aggravate the muscle pathology of dy^H/dy^H mice.

Conclusion: We provided important information about pathogenesis of *LAMA2*-CMD based on muscle transcriptomic data of a novel mouse model.

Keywords: transcriptome; mouse model; *LAMA2*; muscular dystrophy; RNA sequencing

CPF 027

A Novel Spinocerebellar Ataxia Characterized by Exonic CAG Repeat Expansion in The THAP11 Gene

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Introduction: Spinocerebellar ataxias (SCAs) are a group of inherited, heterogeneous neurodegenerative disorders that mainly affect the cerebellum. To date, over 40 distinct pathogenic genes have been identified to be associated with SCAs. Here, we diagnosed a Chinese SCA pedigree and identified CAG repeat expansions in exon 1 of *THAP11*.

Methods: CAG repeat expansions in THAP11 gene were identified in this SCA family by using a comprehensive strategy combining long-read whole-genome sequencing, capillary electrophoresis fragment analysis, and direct DNA sequencing. The pathogenesis of SCA caused by CAG repeat expansions in THAP11 gene was studied in skin fibroblasts of patients, and mutant HEK293 and neuro-2a.

Results: Normal *THAP11* contained 28/29 CAG repeats while affected patients had $(CAG)_{45}$ to $(CAG)_{100}$ repeat expansions. Intracellular aggregates caused by mutant THAP11-polyglutamine proteins with CAG repeat expansions were observed in cultured skin fibroblasts from affected patients, as well as mutant HEK293 and neuro-2a. RNA sequencing indicated that the dysregulations of cell differentiation and DNA-binding might involve in the pathogenic mechanisms. Furthermore, SQSTM1/p62, phospho-ubiquitin and c-Myc were co-localized with intracellular aggregates in skin fibroblasts of SCA patients. Meanwhile, the protein levels of THAP11, SQSTM1/p62 and c-Myc were increased.

Discussion: These results demonstrated that CAG repeat expansion in *THAP11* was associated with SCA, and strongly suggested that the toxic THAP11-polyglutamine gain-of-function mechanism might contribute to the pathogenesis.

Conclusion: This study confirmed a novel SCA characterized by exonic CAG repeat expansion in the THAP11 gene, and provided information for possible pathogenesis of SCA due to mutant THAP11.

Keywords: spinocerebellar ataxia; THAP11; polyglutamine disease; intracellular aggregate; long-read whole-genome sequencing

CPF 028

Clinical and Genetic Study of Rare Cases with Coexistence of Dual Genetic Diagnoses

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Introduction: In this study, we aimed to analyse the clinical and genetic characteristics of patients with dual genetic diagnoses.

Methods: Clinical and genetical data of patients with dual genetic diagnoses from January 2021 to February 2022 in Peking University First Hospital were collected and analyzed.

Results: Among these 10 children, 7 were boys and 3 were girls, with last follow-up ages ranging from 2.0 to 7.9 years old. Cases 1-5, all boys, showed myopathic gait, poor running and jumping, and significantly increased serum creatine kinase level, as well as pathogenic variations in DMD gene, and were diagnosed as DMD/BMD. However, they all had other symptoms and signs that inconsistent with DMD/BMD. The 5 patients also had a second genetic disease, including hypertrophic osteoarthropathy, spinal muscular atrophy, fragile X syndrome, Phelmn-McDerimid syndrome and intracranial cavernous hemangioma. The remaining five cases had complicated clinical manifestations, or disease development could not explained by one diagnosed disease. Type IX collagen gene related disease, and neurofibromatosis type 1 were identified in case 6. Collagen VI-related myopathy with and osteogenesis imperfecta type XV were identified in case 7. Turner syndrome with chromosome karyotype of 45,X, and Segawa syndrome were identified in case 8. Chromosome 22q11.2 microduplication syndrome and autosomal dominant lower extremity-predominant spinal muscular atrophy-1 were confirmed in case 9. KBG syndrome and neurodevelopmental disorder with regression, abnormal movement, language loss and epilepsy were identified in case 10. We found between the two pathogenic genes, either or both of them were de novo mutation.

Discussion: The clinical manifestations of patients with dual genetic diagnoses were complex and diverse. Whole exome sequencing of the core pedigree combining with a variety of molecular genetic tests would be helpful for accurate diagnosis and individualized management.

Conclusion: This study provides important information for patients with coexistence of dual genetic diagnoses.

Keywords: genetic disease; coexistence; phenotype; next-generation sequencing

CPF 029

Clinical and Genetic Study of *LAMA2*-related Muscular Dystrophy Patients with Seizures

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Introduction: *LAMA2*-related muscular dystrophy (*LAMA2*-MD) included *LAMA2*-related congenital muscular dystrophy (*LAMA2*-CMD) and autosomal recessive limb-girdle muscular dystrophy-23 (LGMD R23). Seizures frequently occurred in *LAMA2*-MD, however, the relationship between seizures and genotype in *LAMA2*-MD is not fully known.

Methods: The clinical information of seizures and genetic data of *LAMA2*-MD patients between January 2003 and March 2022 were collected and analyzed.

Results: Among 141 *LAMA2*-MD patients, seizures were observed in 10.5% (13/124) of *LAMA2*-CMD patients and 29.4% (5/17) of LGMD R23 patients, including 14 patients with epilepsy and 4 patients with febrile seizures. The median (range) age of first seizure episode was 5 (0.1-20) years in LAMA2-CMD and 14 (1-24) years in LGMD R23. Eight patients with epilepsy showed focal seizures. Abnormal results of electroencephalography were found in 8/10 patients, manifesting as temporal, occipital or temporo-occipital epileptiform abnormalities. Brain magnetic resonance imaging (MRI) was performed in 16 patients with seizures, showing occipital pachygyria in 4 patients, cerebellum and brain stem dysplasia in 2 patients. Brain MRI of 41 *LAMA2*-MD patients without seizures were reassessed, showing occipital lobe pachygyria in 6 patients. Therefore, there was no significant association between seizures and occipital pachygyria in our cohort (P=0.18). Nine patients received antiepileptic drugs, while patients with occipital lobe pachygyria showed poor seizure control. The pathogenic variants included splice mutation (n = 8), nonsense mutation (n = 6) and frameshift mutation (n = 6) in *LAMA2*-CMD patients, while missense mutation (n = 5), frameshift mutation (n = 4) in LGMD R23 patients.

Discussion: Compared with *LAMA2*-CMD, seizures were more frequently occurred in LGMD R23 patients and mainly manifested as focal seizures. No correlation between genotype and seizures was observed.

Conclusion: In this study, we found that seizures occurred in 10.5% of *LAMA2*-CMD and 29.4% of LGMD R23 patients, and described the features of seizures in *LAMA2*-MD patients.

Keywords: seizures; *LAMA2*; muscular dystrophy; occipital pachygyria; genotype

CPF 030

PARS2 Related Developmental and Epileptic Encephalopathy: a Case Report

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Introduction: The PARS2 gene encodes prolyl-tRNA synthetase 2, which is necessary for protein translation, biosynthesis and oxidative phosphorylation. Here, we report a rare case of developmental and epileptic encephalopathy caused by pathogenic variants in the PARS2 gene.

Clinical Presentation: This patient is a 1-year-3 months old boy, who was born at 38 weeks of gestation without asphyxia from non-consanguineous parents. He presented normal development until 6 months of age when he showed epileptic spasms. Electroencephalography (EEG) revealed hypsarrhythmia, and topiramate and vitamin B6 were received to control seizures. However, poor curative effect was found. He could sit without support at 8 months old. Brain magnetic resonance imaging (MRI) revealed frontal atrophy, delayed myelination and abnormal hyperintensities in the bilateral cerebellar white matter around the dentate nuclei. Magnetic resonance spectrum showed elevated Cho, decreased NAA and inverted lactate peak. The visual evoked potential examination and brainstem auditory evoked potential test were normal. Echocardiography showed interventricular septum hypertrophy. After treatment with adrenocorticotropic hormone and vigabatrin, his spasms and hypsarrhythmia on EEG were significant improved. Whole-exome sequencing identified compound heterozygous variants in PARS2 gene: c.337G>A(p.Gly113Arg) (a novel variant of uncertain significance) and c.283G>A(p.Val95Ile) (a reported pathogenic variant), inherited from the heterozygous healthy parents.

Discussion: To date, a total of 13 patients with PARS2 mutations have been reported with similar phenotype, presenting seizures, global developmental delay, hypotonia, microcephaly, structural brain abnormalities and lactic acidemia.

Conclusion: We described the clinical and genetic features of a Chinese patient with developmental and epileptic encephalopathy due to the pathogenic variants in PARS2 gene.

Keywords: PARS2; developmental and epileptic encephalopathy; infantile spasm

CPF 031

Uniparental Disomy Unmasks a Homozygous Mutation of *POMGNT1* in a Case of Muscle-Eye-Brain Disease

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Introduction: *POMGNT1*, encoding protein O-mannose beta-1,2-N-acetylglucosaminyltransferase, is one of the genes responsible for dystroglycanopathy (DGP) including multiple phenotypes: muscle-eye-brain disease (MEB), congenital muscular dystrophy with mental retardation (CMD-MR), limb-girdle muscular dystrophy (LGMD), and so on. Here, we report a case of MEB due to a homozygous mutation in *POMGNT1* unmasked by uniparental disomy (UPD).

Case Presentation: The patient, an 8-month-old boy, was admitted for "mental and motor retardation". He raised his head unsteadily at 4-month-old. He could not roll over or sit without support at 8 months. Physical examination found a head circumference of 43 centimeters, esotropia, hypotonia, muscle weakness with the muscle strength of limbs between level 3 to level 3+, predominantly proximal. Tendon reflex could not be induced and Babinski's signs were negative. Serum creatine kinase (CK) was 1799 IU/L. Brain magnetic resonance imaging (MRI) showed white matter abnormal signal, a flat brainstem, and cerebellar hypoplasia. Trio-based whole-exome sequencing identified a homozygous variant c.636C>T (p.Phe212Phe) in exon7 of *POMGNT1* in the patient, a heterozygous variant c.636C>T in the father, and wild type in the mother. Quantitative polymerase chain reaction found no abnormal copy number in exon 7. Chromosomal microarray analysis revealed a 99319 kb loss of heterozygosity (LOH) on 1q21.2-q44 and a 120451 kb LOH on 1p36.33-p11.2 encompassing *POMGNT1*, which indicated UPD. RNAseq verified that the variant c.636C>T was a splice-site mutation.

Discussion: UPD is defined as two copies of a whole or partial chromosome derived from one parent. The two copies can be maternal (UPDmat) or paternal (UPDpat). LOH is one mechanism that leads to UPD. Somatic cell recombination between chromatids results in two populations of cells with reciprocal segments with LOH. The case in the present study is the first case of DGP caused by UPDpat.

Conclusion: In this study, our findings indicated that UPDpat could lead to MEB.

Keywords: uniparental disomy; muscle-eye-brain disease; *POMGNT1*; dystroglycanopathy

CPF 032

A Rare Case of Epileptic Encephalopathy Due to a de novo Heterozygous Variation of c.1213C>T in *KCNA1*

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Introduction: Epileptic ataxia type 1 and epileptic encephalopathy could be caused by pathogenic variants in *KCNA1*. Here we report a rare case due to a de novo heterozygous variation c.1213C>T(p.P405S) in *KCNA1*.

Case Presentation: The patient showed first convulsion with focal seizures at 15-day-old and there are twice status epilepticus. Four antiepileptic drugs including levetiracetam, valproate, zonisamide and lamotrigine were used, but were less effective. Then, symptoms of paroxysmal ataxia including gait instability, unstable fetching and intentional tremor were observed, which were triggered by fever, seizures and mood changes, and could disappear in less than 3 days. The patient also presented motor, language and mental retardation, otherwise with gradual improvements. At the disease onset, the electroencephalography (EEG) showed normal; however with the development of ataxia, the EEG showed diffuse slow waves and spikes, which were dominant in the left hemisphere firstly, then were turned to the right. No abnormalities were found in the neuroimaging. A de novo heterozygous variation c.1213C>T (p.P405S) in *KCNA1* was identified by trio-based whole-exome sequencing. The *KCNA1* c.1213C>T was previously reported as a pathogenic variation.

Discussion: *KCNA1* encodes the α subunit of fast potassium channel Kv1.1, which maintains hyperpolarization of cell membrane and inhibits the neuronal hyperexcitability. Patients with epileptic encephalopathy due to *KCNA1* c.1213C>T (p.P405S) as well as c.1213C>G (p.P405A) were reported. Our patient with *KCNA1* c.1213C>T also showed epileptic encephalopathy and developmental delay.

Conclusion: We report a rare case caused by a de novo heterozygous variation c.1213C>T(p.P405S) in the KCNA1 gene.

Keywords: *KCNA1*; epileptic encephalopathy; de novo variation

CPF 057

Clinical and Genotypic Characterization of Glycosylation Defects in Congenital Myasthenic Syndrome in Indian Patients

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Introduction: Mutations in UDP-N-acetylglucosamine—dolichyl-phosphate N-acetylglucosamine-phosphotransferase (DPAGT1), Glutamine-fructose-6-phosphate transaminase 1 (GFPT1) and GDP-mannose-pyrophosphorylase B (GMPPB) cause Congenital Myasthenic Syndrome (CMS) due to glycosylation defects.

Methods: Clinical features and Whole exome sequencing data of patients with glycosylation defects were analysed from a cohort of genetically confirmed CMS.

Results: Among 141 genetically confirmed cases of CMS, we identified mutations in DPAGT1 (13), GMPPB (12) and GFPT1(10) in 35 patients (24.8%). Mean age at onset and presentation were 12.46 ±11.72 (0-35 years), 23.4±15.5 years (4-56) respectively. All patients had fatigable limb weakness. 12 (34%) ptosis, 14 (40%) facial weakness, 2 (5.7%) bulbar involvement, seizures 3(8.6%), mental retardation 5 (14.3%) and myalgia in 14(40%) were seen. Mean Creatine Kinase was 1056±1469 IU/L. 14. All patients had decremental response to 3 Hz Repetitive Nerve Stimulation in limb girdle muscles. In 13 unrelated patients biallelic missense mutations in DPAGT1 were identified (compound heterozygous -10, homozygous). All except one mutation affected transmembrane helical domains. Among the transmembrane mutations, a novel recurrent T380I missense mutation in compound heterozygous state was seen in 9. 7/9 patients had I29F in the second allele. Homozygous missense mutations were seen in 8/10 unrelated patients with GFPT1. Missense mutations affected the proximal glutamine amidotransferase type-2 domain and three novel mutations in distal SIS-1domain were seen. A recurrent missense mutation D334N with a likely founder effect in the C-terminal region of GMPPB (c.1000G > A (p.Asp334Asn) was causative in 12 patients. Good response to treatment with Pyridostigmine and Salbutamol was seen in nearly all patients.

Conclusion: Glycosylation defects account for a significant proportion of CMS in Indian cohort with limb girdle fatigue. Creatine kinase is elevated nearly 10-fold. Genetic heterogeneity exists. We found a possible founder mutation in GMPPB associated CMS in patients of South Indian descent.

Keywords: congenital myasthenic syndrome, glycosylation defects, genotype

CPF 063

Charcot-Marie-Tooth Disease (CMT)

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Introduction: Charcot-Marie-Tooth disease (CMT) is a genetically heterogeneous group of conditions that affect the peripheral nervous system. Mutations in this gene cause a polyneuropathy collectively termed as CMT.

Case Presentation: A 34-years old woman had weakness in both of her lower and upper extremities gradually since 12 years old. The Weakness begins in both legs that occurs simultaneously then in both hands ± 1 year later. Weakness was initially felt in the ends of the feet and hands so the patient had difficulty walking and often fell and also writing ability during school period. Numbness and tingling are found in the fingers and toes intermittently. Both lower extremities showed deformities and become smaller. There was no history of urinary or defecation disturbances. Blood tests found no abnormalities. A history of similar complaints in the family was denied. She denied a history of diabetes, thyroid dysfunction, alcohol consumption, infectious diseases, tumors and trauma. Growth and development history before weakness compliant showed no abnormalities. In physical examination found her muscle strength in upper extremities 44433/44433 and lower extremities 33333/33333, hyporeflex, hypotonic, flaccid, atrophy, pes cavus and also hammer toes. Electrophysiology studies showed mixed sensoric and motoric polyneuropathy with axonal degeneration. Management were B complex vitamin and physiotherapy.

Discussion: Charcot-Marie-Tooth disease (CMT) is hereditary polyneuropathy that occurs and develops over decades with clinical symptoms distal muscle weakness with prominent atrophy and deformity of the foot. CMT is the most common hereditary polyneuropathy.

Conclusion: Electrophysiological examination was first step to diagnose CMT and to rule out other differential diagnoses and to determine the pathology.

Keywords: Charcot-Marie-Tooth disease, hereditary polyneuropathy, atrophy, foot deformity

CPF 067

Magnetic Resonance Imaging of Muscles in Different Subtypes of Inflammatory Myositis

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Background and Aims: We sought to determine Magnetic resonance imaging (MRI) characteristics of different muscles in sub types of inflammatory myositis.

Methods: A retrospective, observational study of 48 patients of inflammatory myositis, who underwent lower limb MRI-axial STIR, T1 sequences (1.5 T Aera; SIEMENS healthcare MR scanner) from 2017-2020. Muscle power grading was used for clinical severity, modified Stramare scoring to grade muscle edema and modified Mercuri scale for muscle atrophy on MRI.

Results: In this cohort, among 48 patients, 15 had Anti-SRP, 16 had Anti-Mi2b, 11 had Anti-Ro antibodies, 4 had Anti-PM/scl, 1 had Anti-OJ and 1 had both Ro and PM/scl antibodies. F:M ratio is 1.28:1. Median age at diagnosis for SRP group is 38 years (Q1=26, Q3=53), Mi2b group is 46.5 years (Q1=36.5, Q3=53.5) and anti-synthetase group is 45 years (Q1=28, Q3=53.5). Median duration of illness is 12 months (Q1=4, Q3=27). In our study, 45 (93.75%) patients presented with proximal muscle weakness, 14 (29.1%) had bulbar weakness, 22 (45.8%) had wasting and 29 (60.4%) had skin manifestations. Wasting was predominantly seen in SRP group and skin changes were more common in Mi2b group.

Based on muscle edema on MRI, most common and severely affected muscles in SRP group were iliopsoas followed by gluteus muscles in thigh and in leg mild diffuse involvement was seen. In Mi2b group, it was vastus muscles followed by hamstrings in thigh and in legs deep posterior compartment muscles and peroneus group were significantly affected. In anti-synthetase group, vastus muscles were more affected in thigh and both anterior and posterior muscles were equally affected in leg. None of the muscles showed atrophy of grade > 3.

Conclusions: This study showed preferential affection of muscles in different subtypes of inflammatory myositis with varying severity. We are planning to do larger study to conclude these findings.

CPF 068

Debilitating Osteo-chondral Manifestations in Patients with Congenital Insensitivity to Pain with Anhidrosis (CIPA) due to NTRK1 Mutations

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Introduction: Congenital Insensitivity to Pain with Anhidrosis (CIPA) is a rare autosomal recessive disorder caused by mutations in the *NTRK1* gene, which encodes the tropomyosin receptor kinase A (TrkA) protein. CIPA, also known as Hereditary Sensory and Autonomic Neuropathy (HSAN) Type IV, is characterised by unexplained fever, decreased or absent sweating; and their inability to feel pain and temperature.

Methods: We report a 20-year-old CIPA patient, on top of the cardinal clinical features, she also suffers from a history of bone fractures from a young age, and subsequently with recurrent large joint effusions as charcot osteoarthropathy with severe bone and joint destructions since adolescence despite no major injury. She has CIPA due to compound heterozygous mutations of the *NTRK1* gene: c.2089 G>A (p.Gly697Lys) and c.744 del (p.Leu249*). We therefore performed a literature review on PubMed searching for published case reports and series of NTRK1-related CIPA between 1999 and 2020.

Results: Amongst the reported 208 *mut-TRK1*-related CIPA patients, 51% (105 patients) had bone problems, 23% (47 patients) had joint disorders, and 17% (35 patients) had both bone and joint problems.

Discussion and Conclusion: As evident from our search, severe debilitating osteo-arthropathic complications are highly prevalent amongst CIPA patients, yet its pathophysiology and corresponding treatments remain to be elucidated.

Keywords: CIPA, Charcot Joints, Fractures, *NTRK1*

CPF 084

Clinico-Genetic Profile of Congenital Myasthenic Syndromes: Study of Mutations in Neuromuscular Junction Development And Maintenance Genes

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Background: Mutations in DOK7, MUSK, AGRN, RAPSN and MACF1 genes associated with end plate development and AChR aggregation cause Congential Myasthenic Syndromes (CMS).

Methods: A descriptive study of clinico-genetic profile of CMS caused by mutations in neuromuscular junction development and maintenance genes.

Results: Disease causing mutations were identified in 32 patients from 31 families. Among these DOK7 was most common (19/31; 61%). The common frameshift mutation c.1124_1127dupTGCC(A378Sfs*30) was identified in 13 families either in homozygous(7) or compound heterozygous(5) form. However, in one patient A378Sfs*30 was present in heterozygous with no significant variant in second allele. Another seven frameshift mutations affected the same SH2 domain as A378Sfs*30. Only three DOK7 missense variants were reported among which P146L and R158W occurring in PTB domain were previously reported. A novel homozygous DOK7 missensec.652G>A(D218N) was identified in the same SH2 domain as other frameshift variants and is likely to cause splicing defect. Recessive MUSK mutations in probands of eight familie of which five had recurrent homozygous missense mutation(I581N). All MUSK mutations except R166* (IgL2 domain) were located in topological distal cytoplasmic domain having tyrosine kinase region and juxta-membrane DOK7 binding region. Two had novel recessive AGRN mutations in homozygous (L1138P) and compound heterozygous form (A1768T, V2022del). While L1138Pis located in the highly conserved SEA domain, A1768T and V2022del affect LG2 and LG3 domains. A previously reported 5'UTR mutation c.-210A>G affecting E-box promoter site of RAPSN was identified along with novel missenseC382R in ring domain. One case had a homozygous missense mutation V1563M in Plakin domain of MACF1, a novel CMS gene.

Conclusion: The study highlights the diverse genetic mutation patterns in Indian patients. Majority had DOK7 gene mutations. The study features the significance of NGS in diagnosis, identifying novel variants and expands the genotype-phenotype correlation of CMS.

CPF 091

Guillain-Barre Syndrome Post Sinovac Vaccination: A Case Report

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Introduction: The COVID-19 vaccination in Indonesia is an ongoing mass immunization in response to the COVID-19 pandemic in Indonesia. Several Guillain–Barré syndrome (GBS) cases associated with coronavirus disease 2019 (COVID-19) infection after vaccination for COVID-19 were reported internationally. Herein, we report a case who developed GBS following Sinovac vaccination within one week after the first dose vaccination. Verbal consent was obtained from the patient to publish the report.

Case Presentation: The case of a 22-year-old woman complaining her four extremities numbness and weakness visited our hospital on November 4, 2021, after her a first dose Sinovac Vaccine on 30 September, 2021. A week later she developed tingling and weakness on both hands followed by her feet. There was no recent history of respiratory, gastrointestinal, and urinary tract infection. On the initial examination, she showed symmetrical tetraparesis (G2 in upper, G2 in lower limbs symmetrically) and all of vital signs within normal. CSF protein was increased to 140 mg/dL and normal cell (white blood cells 1/µL and 50 red blood cells/µL). The EMG showed motoric and sensory polyradiculoneuropathy neuropathy compatible with AIDP.

Discussion: The relation between vaccination and GBS (both AIDP and AMSAN) was causal or coincidental remains speculative. That SARS-CoV-2 vaccinations are usually well tolerated. However, there are a few reports about class 1–4 adverse events after COVID-19 vaccination. According to the current literature, the risk for GBS after COVID-19 is higher than the risk after vaccination. Overall, there is a need to further improve the diagnosis and therapy of GBS regardless of the causative trigger.

Conclusion: GBS is one of the possible side effects that might be encountered after the COVID-19 Sinovac vaccine. To establish an eventual causal relation, it needed more extensive studies between Sinovac vaccine and GBS.

Keywords: COVID-19; Guillain-Barre syndrome; vaccine; Sinovac; AIDP

CPF 092

Diagnostic Approach of Polymyositis and Dermatomyositis: A Case Report

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Introduction: The inflammatory myopathies such as polymyositis (PM) and dermatomyositis (DM) are autoimmune inflammatory muscle disorders characterized by the development of proximal and symmetrical muscle weakness. Levels of serum muscle enzymes such as creatine kinase (CK), lactate dehydrogenase (LDH), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are usually elevated.

Case Presentation: First case, a 42 years old female patient complaining of symmetrical proximal muscle weakness of the four limbs during 4 months, which markedly increased when she stood up after squatting. Physical examination showed symmetrical tetraparesis (G3 in upper and lower extremities). Level of serum CK, CKMB, LDH, AST and ALT were increasing (6137, 528, 997, 177, 371). EMG findings suggestive of myopathy. Second case, a 34 years old female patient complaining of symmetrical proximal muscle weakness of lower limbs during 3 months, myalgia and a macular hyperpigmentation. Physical examination showed symmetrical paraparesis (G4). Level of serum CK, CKMB, LDH, AST and ALT were increasing (6868, 207, 638, 140, 241)

Discussion: Polymyositis can be a complex and difficult diagnosis due to its overlapping features with other Idiopathic Inflammatory Myopathies and other autoimmune diseases. The Bohan and Peter criteria for DM and PM following: (1) Symmetrical muscle weakness (2) Muscle biopsy evidence of myositis (3) Elevation of CK and other muscle enzymes (4) EMG findings suggestive of myopathy (5) Characteristic rashes of dermatomyositis. The pathophysiology is not fully understood, genetic susceptibility, external insults, and dysregulation of both innate and adaptive immunity are thought to underly its pathogenesis.

Conclusion: Awareness of polymyositis criteria diagnosis lead to proper treatment and improved clinical outcomes as disease progression can be rapid and severe.

Keywords: polymyositis, dermatomyositis, autoimmune disease, diagnosis

CPF 094

Spinal Muscular Atrophy-Type 3: Early Diagnostic and Management in Yogyakarta, Indonesia, A Case Report

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Introduction: Spinal Muscular Atrophy (SMA) is a genetic disorder characterized by weakness and muscle atrophy. SMA type-3 has mild and slow progressivity. Right diagnosis and management are very important. RSUP dr. Sardjito, Yogyakarta as pediatric neurological center since 2018 can diagnose and give multidiscipline management.

Case Presentation: A 6-years old girl, came with difficulty in stand up from squat. She had motoric development delayed since 10 months old. The parents had sought for medical treatment, but the doctor said it was only delayed. She was late for prone, skipped the crawl stage, couldn't sit by herself, had walking difficulty, and had to creep on the wall. When she went to bed, she must climb the bed and lift the legs, then she was referred to RSUP Dr. Sardjito. She had normal cognitive (MMSE child: 35). Her father had mild delayed motor function but her sister was normal. The pedigree showed 3 female babies' miscarriage from the father's family and 1 boy baby died at age 4 days from the mother's family. Creatinine Kinase and CKMB level was normal and gastrocnemius biopsy showed atrophic fibers and adipocyte infiltration. The genetical testing showed SMN-2 gene. The patient gets valproic acid and salbutamol and intensive physiotherapy to reduce progressivity and improve the quality of life (QOL).

Discussion: The diagnosis of SMA is based on clinical, electromyography, biopsy and genetical finding. SMA type-3 symptoms appears in childhood or adolescence. When the medication for SMA (nusineran, onasemnogne abeparvovec-xioi, or ridiplam) is not available, the alternatives are salbutamol and valproic acid. Correct diagnosis, timely management, and good interdisciplinary approach will bring positive outcome and improve the patient's QOL.

Conclusion: Prompt diagnosis and management have important role to prevent progressivity, disability and improve the QOL.

Keywords: spinal muscular atrophy, Type-3, early diagnostic, management

CPF 095

Guillain-Barré Syndrome Following COVID-19 Vaccination: A Case Report

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Introduction: Coronavirus Disease 2019 is an infectious condition that can present some of neurological symptoms. For the prevention, there are vaccines which available one of them is AstraZeneca. Some report has indicated that some COVID-19-vaccinated individuals can develop as a Guillain-Barré syndrome (GBS), a severe neurological autoimmune condition in which the immune response against the peripheral nerve system.

Case Presentation: A 35-years old man came the weakness of the four limbs that preceded tingling in the tips of the fingers and toes. Symptoms appear 3 days after the He got the third AstraZeneca vaccine. ENMG showed the results of axonal type polyradiculoneuropathy and demyelination according to AIDP type GBS. After 7 days of hospitalization, He experienced dyspnea and desaturation with the results of moderate ARDS. X-rays of thorax show the presence of bilateral pneumonia. He received a plasma exchange therapy, antibiotics, and maintenance in intensive care room.

Discussion: The latency between first AstraZeneca vaccine and onset of GBS ranged from 8 day to 39 day, where in this case the symptoms appear faster 3 days post the third vaccine. The molecular mimicry and immune mediated inflammatory response are plausible concept in pathophysiological mechanism of GBS post-SARS-CoV-2 vaccination. The patient's condition was aggravated by the presence of lung infections obtained during hospital treatment. The absence of serious symptoms in the first vaccine is not a reason not to observe the side effect of the post vaccine booster.

Conclusion: This case illustrates that GBS may develop time-linked to the third dose of a AstraZeneca vaccination. Observation of side effects on the administration of booster vaccines is still needed to be done even if the patient does not show serious symptoms in the first vaccine administration. Although there is a causal relationship between vaccination and GBS remains speculative, early diagnose and treatment of GBS may improve the outcome

Keywords: AstraZeneca, vaccine, covid-19, Guillain-Barré

CPF 099

Myasthenic Crisis in Covid-19: A Challenging Case in Dr. Sardjito General Hospital Yogyakarta, Indonesia

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Introduction: Myasthenia gravis (MG) is an autoimmune disease that affects neuromuscular junction. This disease is a treatable disease but can develop into exacerbation in which patient may experience restrictive respiratory failure known as myasthenic crisis. Patients with MG are high risk of COVID-19 due to routine consumption of immunosuppressant. This case report describes how challenging to treat myasthenic crisis who was infected with COVID-19.

Case Presentation: A 44-year-old male was brought to the emergency room with progressive dysphagia and dysphonia since 2 weeks. He had difficulty in breathing and expectorating. There is no history of fever, cough, odynophagia, or hyposmia. The patient has not been SARS-CoV-2 vaccinated. The patient was diagnosed with myasthenia gravis since a year prior. He was tested positive for COVID-19 by Real Time Polymerase Chain Reaction (RT-PCR) test, his chest X-ray showed bilateral pneumonia and his blood examination showed respiratory acidosis. The patient has been treated for more than a month in intensive care isolation unit on ventilator. His routine medication consists of Pyridostigmine 120 mg 4 times a day, methylprednisolone 8 mg 2 times a day, azathioprine 100 mg 2 times a day was continued during hospitalization. Patient was given intravenous immunoglobulin (IVIg) treatment once. Recovery of the dysphagia was observed after the IVIg treatment.

Discussion: Infections are the most common cause of MG exacerbation and crisis. Myasthenic patients are more vulnerable when infected by COVID-19 due to chronic immunosuppression and high probability of respiratory muscle weakness. Recommended treatment options are IVIg and plasmapheresis. Altering immunomodulatory therapy abruptly may worsen the disease.

Conclusion: Patients with MG need to be treated with caution regarding high risk of crisis when infected by COVID-19. Immunosuppressant therapy and treatment escalation need to be adjusted according to individual condition and severity of MG and COVID-19.

Keywords: myasthenic crisis, COVID-19, IVIg

CPF 114

Genetic Diagnosis of Facioscapulohumeral Muscular Dystrophy in Hong Kong Chinese Patients Using Molecular Combing

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Introduction: Facioscapulohumeral Muscular Dystrophy type 1 (FSHD1) is the third most common types of hereditary muscular dystrophy caused by toxic expression of DUX4 in skeletal muscles. It is often underdiagnosed owing to underlying complex molecular genetic mechanism and heterogeneous clinical presentations. Next generation sequencing cannot provide the genetic diagnosis. Traditional method included Southern blotting has technical limitation and the recent molecular combing methodology allows direct visualization of D4Z4 arrays and qA/qB haplotype to yield robust genomic data for FSHD1. In this study, we aim to confirm the diagnosis of a cohort of Chinese patients suspected to have FSHD1 using molecular combing and to study their phenotypes.

Methods: Blood samples from 56 clinically suspected FSHD patients from 35 families were collected and DNA was extracted. Molecular combing has been used to examine the D4Z4 array length and qA/qB haplotype at the 4q35 and 10q26 loci by the hybridization of multi-colour DNA probes onto uniformly stretched DNA fibres.

Results: Overall, 71.4% (40/56) FSHD patients were genetically confirmed to have FSHD1 with pathogenic contraction of 4q D4Z4 presented with less than 10 repeats on haplotype A. The 40 patients with FSHD1 are from 26 families involving either 1st, 2^{nd,} or 3rd generations. The age of the patients ranged from 13 to 83 years (mean=52.8 years; median=58.5 years). The repeat units of D4Z4 ranged from 2 to 9 (mean=4.9; median=4) with no intrafamily difference.

Discussion: Most genetically confirmed FSHD1 patients have classical FSHD phenotypes with progressive disease courses but atypical manifestations such as facial sparing and distal-onset weakness could also be found.

Conclusion: Molecular combing provides a precise tool for the diagnostic confirmation of FSHD1 and shortened the diagnostic odyssey. A confirmed FSHD1 diagnosis allows better clinical care, management, prevention of recurrence in future pregnancy and clinical trials participation.

Keywords: facioscapulohumeral muscular dystrophy, FSHD, molecular combing, D4Z4, DUX4, genetic

CPF 115

Rare Forms of Genetically Mediated Familial and Sporadic Amyotrophic Lateral Sclerosis from India

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Introduction: Amyotrophic lateral sclerosis (ALS) is a clinically and genetically heterogenous neurodegenerative condition. Various genetic mutations have been identified that cause familial ALS (FALS) or sporadic ALS (SALS). Here we describe genotype and clinical features of series of ALS cases.

Methods: A retrospective analysis of 22 genetically confirmed ALS cases evaluated between 2016 to 2021, and their family members who underwent Next Generation Sequencing (NGS) to identify the pathogenic mutations.

Results: Out of 22 cases (17 males and 5 females), 15 were familial and 7 were sporadic cases. C9orf72 (6/22) was the most common genetic variant found in our cohort, followed by SOD1 (4/22), FUS (3/22), CHCHD10 (2/22), and SPG11 (2/22), while mutations in TARDBP, VCP, TBK1, OPTN, ERBB4, FIG4, and SETX genes were found in one case for each gene. Mutations in both OPTN and ERBB4 genes were found in one patient and another patient showed mutation in SPG and SETX genes. Consanguinity was reported in 2/22 cases and both had positive family history. The familial group reported an earlier onset of disease (39.9 ± 12.8 years) as compared to sporadic cases (54.7 ± 5.8 years). However, the mean duration of illness was longer among familial cases (54.7 ± 46.7 months) as compared to sporadic cases (12.3 ± 5.7 months).

Discussion: Interfamilial and intrafamilial phenotypic variations owing to reduced penetrance, genetic pleiotropy, oligogenic and polygenic inheritance are known in ALS. C9orf72 was the most common genetic mutation among sporadic cases and overall and SOD1 in familial cases.

Conclusion: The genetic aetiology of ALS is complex due to the significant sharing of major causative genes with FTD and other neurogenerative disorders.

Keywords: Amyotrophic lateral sclerosis, frontotemporal dementia, familial amyotrophic lateral sclerosis, genetically mediated ALS

CPF 117

Hirayama Disease: Surgical Outcome in a Large Cohort of Indian Patients

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Introduction: Hirayama disease (HD), is a cervical compressive myelopathy. Anterior cervical discectomy and fusion (ACDF) is the best treatment option.

Methods: Between 2015 and 2019, 135 HD patients underwent ACDF. Contrast MRI of cervical spine with full flexion was done. Clinical examination and pre / post operative assessment of hand function using Fugl-Meyer, Jebsen-Taylor hand function test and handheld dynamometry were done at 3 monthly intervals for one year. Telephonic follow-ups were done in December 2021.

Results: Age at onset and duration of illness=12 to 31 years(mean:18+2.7) and 1-96 months (32.7+24.4) respectively. Right upper limb (UL)=[66(48.9%)], left UL=[51(37.8%)], both UL's=[18(13.3%)]. All had weakness and wasting. Cord signal changes occurred in 86.7%, cord atrophy (89.6%), posterior epidural space prominence (35%). Contrast study showed prominent epidural detachment and enhancement in all except 2 patients. 126(93.3%) underwent ACDF, 9 had posterior approach. The disc levels of fusion: Single disc [C5,C6] in 109(80.7%), two [17(12.6%)], three [5 (3.7%)], 4 [4(3%)]. Bone fusion levels: single [2(1.5%)], two [109(80.7)], three [16(11.5)], 4[5(3.7)], 5[3(2.2)]. 18 followed-up at 1 year and 15 had significant subjective improvement and in Fugl-Meyer and dynamometry scores. During December 2021, telephonic contact in 83(61.5%) patients and Michigan hand outcomes questionnaire was administered. Total follow-up=18-77 months (44.9±16.5).Very good hand functions and improvement of 60-90% from baseline=12(14.5%), good(31-60%)=16(19.3%), and fair improvement (10-30%)= 23(27.7%) and stabilization=32(38.6%). Improvement at last follow- up had a negative correlation with duration of illness, age at onset and a positive correlation with good pre-operative Fugl-Meyer score.

Discussion: First large series from India and reiterates the benefits of surgery in Hirayama Disease.

Conclusion: Anterior cervical discectomy and fusion resulted in prominent improvement or stabilization in the neurological deficits occurred in a significant proportion of HD patients. Significant motor disability ensues over time and early surgical intervention during the progressive phase is advocated.

Keywords: Hirayama Disease; cervical decompression; India; follow-up

CPF 121

Effectiveness of 5% Dextrose Subcutaneous Injection in Painful Diabetic Neuropathy Patients in Mohammad Hoesin General Hospital Palembang

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Introduction: Treatment of Painful Diabetic Neuropathy (PDN) is challenging as treatment responses are often varied. Despite the therapeutic advances, there remains a lack of treatment options that are able to effectively control PDN. Injection of 5% dextrose (D5%) has been progressively used to treat many peripheral neuropathies and proven to have promising effects in a few high-quality studies. Hence, this study aims to investigate the effectiveness of D5% injection in PDN.

Methods: In a double blind study, a total of 24 patients diagnosed with PDN were enrolled and randomized to two groups: study group (0,5-1 ml of D5% injection at medial and lateral sides of cutaneous sural nerve), or control group (0,5-1 ml of Normal Saline injection through the same method). Numeric Pain Rating Scale (NPRS) and Toronto Clinical Neuropathy Score (TCNS) were evaluated before, after intervention and at two, four, six and eight weeks after intervention.

Results: In total, 20 patients (57.7 ± 9.3 years old; 55% female) completed the study, 10 patients in each group respectively. There were no baseline differences between groups. After interventions, NPRS decreased significantly in study group compared to control group ($p = 0.005$ and $p < 0.063$, respectively). TCNS decreased significantly in study group compared to control group ($p = 0.000$ and $p < 0.025$, respectively)

Discussion: Decrease of NPRS and TCNS after D5% injection in study group could due to dextrose indirectly downregulate capsaicin-sensitive receptors (transient receptor potential vanilloid receptor1, TRPV1) which in turn impedes the discharge of substance P and calcitonin gene-related peptides, which are pro-nociceptive substances that contribute to neurogenic inflammation and neuropathic pain.

Conclusion: Subcutaneous injection of D5% is effective in decreasing pain intensity and staging of diabetic sensorimotor polyneuropathy in patients with PDN.

Keywords: painful diabetic neuropathy, dextrose, subcutaneous injection

CPF 123

Myofibrillar Myopathy: Clinico-Genetic Spectrum from an Indian Neuromuscular Centre

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Introduction: Myofibrillar myopathies (MFM) occur secondary to mutations in DES, CRYAB, MYOT, LDB3, FLNC, BAG3, FHL1, TTN and PYROXD1 genes. The study aims to characterize the clinico-genetic spectrum in the Indian population.

Methods: A description of the clinical, radiological and mutation spectrum of 15 genetically confirmed MFM patients.

Results: Male:female ratio=11:4. Mean age of onset, presentation and illness duration were 16.6, 27.6 and 11 years, respectively. Consanguinity (26.7%), motor developmental delay (26.7%). Almost one-third had ptosis and bulbar symptoms at childhood. Ptosis and ophthalmoparesis (40%), bifacial weakness and flaccid dysarthria (20%), neck weakness (46.7%), proximal weakness of upper and lower limbs (26.7%), proximodistal lower limb weakness (53.3%), foot drop (26.7%) and exertional dyspnoea (26.7%). Ankle contractures (60%), cardiac involvement (33.3%). Mean CK=1544U/L. Muscle MRI-fatty infiltration in glutei muscles, thigh adductors and pancompartmental leg muscles. Muscle biopsy-reduced/absent desmin expression. NGS-DES gene mutation in one-third patients. DES mutations with intron 5, c.1023+5G>A, had ptosis or easy fatigability in childhood and subsequently quadriparesis and oculofacialbulbar weakness. Other DES mutations include [Exon1, c.20C>A, p.Ser7Tyr; Exon 1, c.448C>T, p.Arg150Ter; Exon 5, C958delG, p. E320fs*2; Exon 6, c.1030T>C, p.Ser344Pro; Exon 6, c.1216C>T, pArg406Trp; Exon 7, c.1280A>T, p.Asn427Ile]. TTN [Exon343, c.95134T>C, p.Cys31712Arg], HSPB8 [Exon 3, c.566_567del, p.Asp189GlufsTer26], FLNC [Exon 39, c.6398G>T,p.Arg2133Leu], CRYAB [Exon 3, c.238G>A, p.Asp80Asn], LDB3 [Exon 12, c.1909A>G,p.Thr637Ala] gene mutations in each of the patients. Intronic and exonic DES mutations and exonic TTN and CRYAB mutations represent novel variants.

Discussion: The study highlights the diverse clinical manifestations and genetic mutation patterns in Indian MFM patients. Majority had DES gene mutations. Few patients with congenital oculobulbar weakness resembling congenital myasthenic syndrome had intronic DES mutations.

Conclusion: The study features the significance of NGS in diagnosis, identifying novel variants and expanding the genotype-phenotype correlation associated with MFM in Indian population.

Keywords: myofibrillar myopathy, DES

CPF 126

Asymmetrical Triangular Shoulder in Fascioscapulohumeral Muscular Dystropy (FSHD)

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Introduction: Facioscapulohumeral Dystrophy (FSHD) is an autosomal dominant result of the 4q35 genetic mutation that produces the DUX4 product which causes dystrophy abnormalities in muscle. Diagnosis depends on a combination of genetic and clinical features, the clinical heterogeneity of FSHD makes it difficult to predict the course of the disease, The classic clinical presentation of FSHD is asymmetry weakness of the face and shoulders, followed by weakness of the extensor legs, abdomen, and pelvic muscle due to atrophy and fat infiltration.

Case Presentation: Male patient, aged 15 years, complained of limited movement of the left arm. Limited movement is said to be unable to lift maximally on the left arm, compared to the right arm. The patient also complained of a more prominent deformity of the left shoulder blade. The patient's clinical and ENMG examination led to the diagnosis of Facioscapulohumeral dystrophy

Discussion: The patient is diagnosed based on the main complaints that often arise, namely the presence of complaints on the back and changes in shape (Triangular Shoulder) and limited movement of the left arm. The diagnosis is supported by ENMG examination with the results of the diagnosis leading to myopathy.

Conclusion: A 15 years old male patient has been reported with dominant symptom in the form of left triangular shoulder asymmetry which leads to a diagnosis of Facioscapulohumeral Muscular Dystrophy (FSHD). As for definitive diagnostics (gold standard) in patients, a muscle biopsy and a chromosome examination or examination of the toxic DUX4 protein can be performed

Keywords: facioscapulohumeral dystrophy (FSHD), asymmetrical triangular shoulder, ROM disorders.

CPF 132

Guillain Barré Syndrome with Vitamin D Deficiency in Pregnancy Woman, A Case Report

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Introduction: Guillain-Barré syndrome (GBS) is an acute monophonic type of inflammatory demyelinating polyradiculoneuropathy associated with symmetrical progressive muscle, weakness, areflexia. Vitamin D deficiency is known to be related to the development of autoimmune diseases and may worsen clinical course of polyneuropathy. Vitamin D deficiency during pregnancy has been linked with strong independent risk factor for preeclampsia.

Case Presentation: A 29-years-old female patient, G4P3A0 20 weeks pregnant, complained of weakness in all limbs since 2 weeks before admission, starting with numbness tingling sensations in the legs, followed by weakness started in the distal part and progressed proximally. From motor examination, we found mild weakness in distal of four limb with hyporeflexes, and absent Babinski sign. In Sensory examination, there was hypoesthesia of gloves and stockings. The GBS disability score 3, Egos score 0, Egris score 0, it means prediction the chance of respiratory insufficiency dan being able to walk independently was good. The Electrophysiology revealed impression of Axonal Polyneuropathy, Vitamin D levels of 4.51 ng/mL and positive ANA IF.

Discussion: The patient presented with signs and symptoms of polyneuropathy in pregnancy with positive ANA IF which confirmed the diagnosis of GBS. The condition was complicated with low vitamin D level which may worsen the clinical course of the disease. Clinical management of GBS in pregnancy in general is similar to that in non-pregnant patient. Studies found vitamin D supplementation to be beneficial in deficient patients with autoimmune disease.

Conclusion: Patients with immune-mediated polyneuropathy including GBS often have low level of vitamin D which may worsen disease severity. Vitamin D monitoring and supplementation is recommended in all patients with immune-mediated disorders and pregnancy.

Keywords: Guillain-Barré syndrome, pregnancy, vitamin-D, prognosis

CF 134

Recurrent Hypokalemic Periodic Paralysis In COVID-19 and Hyperthyroid: A Case Report

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Introduction: Hypokalemic periodic paralysis (HPP) is a rare neuromuscular disorder characterized by transient episodes of flaccid paralysis due to a defect in muscle ion channels and can be caused by hyperthyroid. COVID-19 is associated with a higher risk of thyrotoxicosis and a slight temporary reduction in the circulating TSH concentration, which might also be interpreted as hyperthyroidism.

Case Presentation: A 42-year-old-man was admitted after two days of muscular weakness in the lower limbs with an ascending evolution and without a defined sensory level. The patient was diagnosed with COVID-19 and HPP three month earlier with a laboratory result of potassium level was 1.75 mmol/L. The patient received standard covid therapy and potassium infusion until being discarded of COVID-19 and HPP improved (potassium level 3.58 mmol/L). The patient was hospitalized again with the same complaint without COVID-19. From the laboratory result, potassium level was 1.59, FT4 3.75 ng/dL, TSH <0.005 uIU/mL. He received potassium infusion and thiamazole 5mg until clinical and potassium level improved (3.48 mmol/L).

Discussion: HPP is the most common associated with metabolic and electrolyte abnormalities. Typical attack is characterised by transient episode of muscular weakness usually involving lower limb and sensory functions, however bowel and bladder were not affected. In Hyperthyroidism, the increasing response of adrenergic and high circulating levels of thyroid hormone can cause of hypokalemia and subsequent periodic paralysis. COVID19 may correlate with a higher risk of thyrotoxicosis due to the systemic immune activation by SARS-CoV-2 viral infection.

Conclusion: The incidence of recurrent HPP in this patient could be associated with hyperthyroidism and is accompanied by risk factor of previous COVID1-19 infection which could contribute to increase the recurrence of HPP.

Keywords: hypokalemic periodic paralysis, COVID-19, hyperthyroidism.

CPF 143

The Profile Quality of Life Myasthenia Gravis Patients in General Hospital Haji Adam Malik Medan

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Introduction: Quality of life is a broad concept influenced by various factors such as a person's physical health, psychological state, level of independence, social relations and their relationship with their environment. Those factors could affect the quality of life of myasthenia gravis patients. In patients with myasthenia gravis there is a decrease in quality of life compared to previous time prior to suffering from myasthenia gravis. The objective of this study was to assess the profile of quality of life in myasthenia gravis patients in Haji Adam Malik General Hospital

Methods: We performed a descriptive cross-sectional study in myasthenia gravis patients who visited Haji Adam Malik General Hospital. Data obtained from primary data through interviews with 43 patients with myasthenia gravis. Descriptive analysis was conducted using SPSS version 22

Discussion: Myasthenia Gravis is an autoimmune neuromuscular disease characterized by varying and fluctuating degrees of skeletal muscle weakness. The weakness directly affects the patient's daily activities and ability to work. Despite the advances in treatment have changed the prognosis of MG, but spontaneous remission is not frequent and affect the quality of life of the patients.

Results: The sample in this study were 43 subjects and 76.7% were women with the largest age group between the range of 18-49 years. The most common type of MG found was the generalized type around 55.8% and 4.7% of patients with thymoma. Approximately 72.1% of patients having early onset myasthenia. The mean of MG Composite Score was 7.47. Approximately 83.7% of patients were successfully treated with pyridostigmine alone. The mean quality of life assessment of patients using MG-QOL15 INA was 29.28 and using MG-ADL was 5.63.

Conclusion: The majority of patients at Haji Adam Malik Hospital Medan have a good quality of life

Keywords: myasthenia gravis, quality of life

CPF 151

A Rare Case of Juvenile Amyotrophic Lateral Sclerosis

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Introduction: Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disorder that affects the upper and lower motor neurons. The term juvenile ALS (JALS) is used for patients whose symptoms start before 25 years of age. This report was written to discuss the clinical presentation of JALS, a very rare form of motor neuron disease.

Case Presentation: We reported a male patient, 25 years old, with JALS who came to the neurology clinic with complaints of weakness in the upper and lower limbs which occurred progressively since the age of 21. The patient also had slurred speech. No family history was found. Neurological examination found mixed upper and lower motor neuron weakness and muscle wasting of the upper and lower limbs, as well as dysarthria with tongue muscles atrophy. Magnetic resonance imaging of the cervical spinal cord showed no significant finding. Nerve conduction study found axonal lesions in the compound muscle action potential and normal sensory nerve action potential. Electromyography found signs of active and chronic denervation of the masseter muscle, thoracic paravertebral muscle, and muscles of the superior and inferior extremities. This patient met clinical definite ALS according to the revised El Escorial criteria.

Discussion: About 5% of ALS is estimated to occur in people under 30 years of age. Most of JALS are familial, but some cases occur sporadically with negative family history. Disease prognosis varies from rapidly progressive to an indolent course. Diagnosis of JALS should be based on the development of a clinical syndrome that meets ALS diagnostic criteria with an age of onset less than 25 years.

Conclusion: JALS is a diagnosis to consider in young adult with combined clinical manifestations of upper and lower motor neuron dysfunction with bulbar palsy, although it is a rare disease.

Keywords: clinical manifestation, juvenile amyotrophic lateral sclerosis, young onset

CPF 164

Exomiser Accelerates The Identification of Second Pathogenic Variants by Prioritizing The Variants by Pathogenicity

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Introduction: Next-generation sequencing is now widely accepted for the diagnostic purpose of rare neuromuscular diseases. However, substantial number of patients are still undiagnosed. In some patients, one heterozygous pathogenic variant was identified in a known recessive causal gene, but another pathogenic variant is not found. After routine filtration considering population frequency and inheritance model, many variants left in the gene. it is difficult to distinguish the causal one from those of benign nature. However, Exomiser can help prioritize the variants by pathogenicity.

Here, we described three patients from three families suggested to have Congenital myopathy with no disease-causing variant(s) identified during the first-round whole-exome sequencing analysis. After routine filtration, only one heterozygous pathogenic variant was identified in the recessive causal gene. Using Exomiser and Human phenotype ontology, we discover the second pathogenic missense variant for these three patients.

Method: WES/WGS sequencing was done for the patients**.** GATK best practice pipeline was used to call the SNVs/Indels. The Human phenotype ontology project was used to convert the clinical features into HPO terms. Exomiser was used to prioritize the genes and variants.

Results: Using Exomiser, the missense pathogenic variants were identified. Combined with the pathogenic variants found using the traditional filtration-based method. The identification of compound heterozygous variants for recessive causal variants in TBCK and TTN genes is completed.

Discussion: Traditional routine filtration methods usually leave hundreds of variants of unknown significance to be inspected. It is laborious to investigate all these variants. Exomiser prioritizes the variants based on *in silico* prediction and population frequency. It accelerates the identification of causal variants, especially for missense variants, which are difficult to interpret and common in the genome.

Conclusion: Exomiser can prioritize the pathogenicity of variants and improve the genetic diagnosis of patients with neuromuscular diseases of diagnostic challenges.

Keywords: exomiser, human phenotype ontology, missense variant, prioritization

CPF 167

Pain and Motor Disorders Accompanied of Chronic Carpal Tunnel Syndrome Showed Improvement After Ultrasound-guided of 10% Dextrose Perineural Dissection Injection: A Case Report

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Introduction: Carpal tunnel syndrome presented by pain, sensory and motor problems affecting three or half fourth radial digits. Its prevalence was 4% to 5% and more common among females aged 40-60 years old than males (9.2%: 6%). Perineural and endoneurial edema leads to vascular thickening, and fibrosis, then followed by demyelination or degenerative lesions.

Case Presentation: A 35-year-old female nurse diagnosed with bilateral carpal tunnel syndrome in 2016, suffered from moderate pain, and handgrip weakness (manual motor test 3-4). Motorcycle riding and job occupancy might cause repetitive injury. Mecobalamin 500 mcg/ 12 hours, gabapentin 300mg/ 12 hours also night splint and stimulation with partial improvement. In 2019 the pain and burning sensation appear accompanied by arms atrophy. C5 to Th1 degenerated and posterocentral bulged discs observe, while neurophysiology examination showed axonal degeneration. Serial ultrasound-guided insertion by 25-G of a needle into median perineural tissue (July 2021, October 2021, and January 2022), for administrating 10 mL of 10% dextrose. It was gently flushed so the perineural seemed to expand. The motor weakness improvement seemed better than the sensory function 3 months afterward, as the demyelination would need more time to repair. Gabapentin with reduced doses (50 to 100mg daily) or when needed, so medication focus on neurotrophic drugs.

Discussions: Clinical improvement is caused by the separation of median perineural tissues that is supported by 10mL volume administration. Meanwhile, the 10% dextrose might maintain the cells, promote angiogenesis factors, and keep the growth cells working. Cervical disc disorders associate with radiculopathies.

Conclusions: Perineural dissection might improve nerves entrapment, while prolotherapy facilitates the repair process.

Keywords: carpal tunnel syndrome, perineural fibrosis, pain, motor weakness, axonal degeneration, 10% dextrose, prolotherapy

CPF 173

Utilisation of Whole-Exome Sequencing for Muscular Disorders in Thai Paediatric Patients: Diagnostic Yield and Mutational Spectrum

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Introduction: Muscular dystrophy (MD) and congenital myopathy (CM) are heterogeneous groups of inherited muscular disorders. Their accurate diagnosis is challenging due to their complex clinical presentations and genetic heterogeneity. We aim to determine the utility of whole-exome sequencing (WES) for Thai paediatric patients with muscular disorders.

Methods: Blood samples from patients with diagnoses of MD and CM were investigated by WES. Cases were identified with pathogenic or likely pathogenic variants in genes consistent with the phenotype and with zygosity test results matching the inheritance pattern.

Results: Of 176 paediatric patients suspected of genetic/inherited myopathies, 133 received a molecular diagnosis after performing conventional investigations, single-gene testing, and gene panels. The remaining 43 patients from 42 families were classified into 3 groups. They were Group 1, MLPA-negative Duchenne MD (DMD; 9/43; 21%); Group 2, other types of MD (18/43; 42%); and Group 3, CM (16/43; 37%). All patients underwent WES, which identified pathogenic variants in 8/9 (89%), 14/18 (78%) and 8/16 (50%) patients in each group, respectively. Overall, the diagnostic yield of the WES was 70% (30/43), and 36 pathogenic/likely pathogenic variants were identified in 14 genes. Fourteen variants had never been reported. The molecular diagnoses provided by the WES changed the management of 22/30 (73%) patients.

Discussion: The confirmation of DMD point mutations allowed for steroid treatment, while identifying the nonsense mutation made one patient a candidate for premature stop codon read-through treatment. The other patient in which WES unravelled the diagnosis and allowed for choice of medication was the patient with COLQ-congenital myasthenic syndrome.

Conclusion: Our study demonstrates the clinical utility and implications of WES in inherited myopathies.

Keywords: congenital myopathy; muscular dystrophy; next generation sequencing; novel variants; whole-exome sequencing

CPF 177

Very Long-chain Acyl-CoA Dehydrogenase Deficiency due to Compound Heterozygote Variants of ACADYL Gene

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Introduction: Very-long-chain acyl-CoA dehydrogenase (VLCAD) deficiency (OMIM#201475) is a mitochondrial long-chain fatty acid oxidation metabolic disorder inherited in an autosomal recessive manner. According to the severity of the clinical symptoms of VLCAD insufficiency, there are three clinical types. We present a patient diagnosed with a later-onset episodic myopathic type of VLCAD deficiency carrying compound heterozygous variants, verified by plasma acylcarnitine analysis and multigene panel sequencing.

Case Presentation: A 44-year-old female patient visited a neurology clinic with a history of recurrent weakness on both lower extremities and occasional rhabdomyolysis. Her little sister also presented similar symptoms. Among undergoing diagnostic process, plasma acylcarnitine analysis revealed elevated levels of C14:1 (1.293 µmol/L; reference, <0.24), C14:2 (0.451 µmol/L; <0.18), C14 (0.341 µmol/L; <0.12), C16:1 (0.140 µmol/L; <0.10), and C16 (0.260 µmol/L; <0.23). The patient's ACADVL gene presented two heterozygote variants (NM_000018.3:c.1096C>T; p.R366C, c.1276G>A; p.A426T), which were not present in general population databases (gnomAD and Korean Reference Genome Database).

Discussion: This is the newly discovered combination of compound heterozygotes which have been introduced separately.

Conclusion: Rare lipid storage disease causing mild symptoms in adults confirmed by acylcarnitine analysis also should undergo genetic sequencing to evaluate genetic variants.

Keywords: Very-long-chain acyl-coenzyme A Dehydrogenase Deficiency, ACADVL gene, compound heterozygote

CPF 180

A Female Carrier of Spinal and Bulbar Muscular Atrophy Diagnosed with DNAJB6-related Distal Myopathy

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Introduction: The *DNAJB6* gene, which encodes a member of the HSP40 family of co-chaperones, has been related to limb girdle muscular dystrophy D1 (LGMD D1) and distal myopathy, characterized by rimmed vacuoles and myofibrillar aggregates on muscle pathology. With the discovery of new mutations, the phenotypic spectrum of DNAJB6-related myopathy has been extended, making the diagnosis more complicated.

Case Presentation: In this study, we describe a female carrier of spinal and bulbar muscular atrophy (SBMA) diagnosed with DNAJB6-related distal myopathy. The c.292_294delGAT (p. Asp98del) mutation in the *DNAJB6* gene and a 49 CAG repeat expansion in the *androgen receptor* (*AR*) gene were identified. According to the clinical manifestations of distal-dominant lower limb involvement, a myogenic pattern in the electrophysiological study, and rimmed vacuoles on muscle pathology, the patient was ultimately diagnosed with DNAJB6-related distal myopathy. A functional study in a zebrafish model indicated that the c.292_294delGAT (p. Asp98del) mutation contributed to muscle structure defects.

Discussion: Currently, with the development of next-generation sequencing technologies, many variants harbored by patients are easily identified. The correct interpretation of the results is crucial for identifying therapeutic options and providing genetic counselling. Furthermore, in families where a pathogenic variant is identified, when the clinical phenotype of the patients is inconsistent with that of other family members, de novo mutational events should be taken into consideration.

Conclusion: This study offers useful insights for the differential diagnosis of a condition in which patients carry pathogenic variants in different genes.

Keywords: DNAJB6; myopathy; human genetics; zebrafish

CPF 181

Steroid-Induced Myopathy in Nephrotic Syndrome: A Case Report

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Introduction: Corticosteroid-induced myopathy is a common toxic non-inflammatory myopathy that occurs as an adverse reaction to long-term oral or intravenous glucocorticoids and characterized by proximal muscle weakness in the arms and legs with incidence rate 50-60%. It can be caused by excess endogenous or exogenous steroids and can be acute or chronic.

Case Presentation: A 21-year-old man came to the ED with weakness in the lower limbs characterized by a progressive proximal weakness. The patient had previously been diagnosed with Nephrotic syndrome and was regularly taking corticosteroids at 64mg/day. Physical examination revealed proximal dominant flaccid paraparesis was also found. The laboratory examination of creatine kinase (CK), aspartate aminotransferase (AST), and aldolase are normal, elevated lactate dehydrogenase (LDH), Muscle biopsy and ENMG were not performed. Complaints improve after stopping steroids and physical exercise.

Discussion: The diagnosis of glucocorticoid-induced myopathy is most often based mostly on facts and physical examination, as there may be no definitive check for this condition. Serum CK or aldolase ranges are usually inner normal limits and aren't frequently elevated. However, serum lactate dehydrogenase (LDH) ranges may be elevated. Electromyography studies regularly show no abnormalities in conduction rates. Muscle biopsy of the affected muscle businesses may show prolonged numbers of sarcolemmal nuclei, loss of fiber cross-striations of type IIb fibers, without necrosis or inflammation. Symptoms of weak point usually show improvement after three to four weeks following discontinuation of steroid therapy.

Conclusion: The patient has been treated with a diagnosis of steroid induced myopathy. Weakness appears in the lower limbs after taking high doses of steroids. After treatment with cessation of steroid use and physical exercise, after 2 weeks the patient experienced a significant improvement in strength. Steroid induced myopathy is reversible, accurate and prompt diagnosis can reduce morbidity and improve clinical outcome

Keywords: corticosteroid, myopathy, nephrotic syndrome

CPF 191

Clinical and Pathological Analysis of Four Chinese Patients with LGMD2G

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Introduction: LGMD2G is a very rare disease. Patients diagnosed with LGMD2G mainly have nonsense or frameshift variants of the TCAP gene. In contrast, pathogenic dominant missense variants have only been found in patients with selective cardiac involvement or intestinal pseudo-obstruction.

Methods: In this article, we retrospectively analysed the clinical features, findings of muscle imaging, muscle pathology, immunohistochemistry, and ultrastructural characteristics of four patients diagnosed with LGMD2G at a single center in China.

Results: The clinical symptoms of our patients were similar to those previously reported in LGMD2G patients. Three different pathogenic TCAP variants were identified in these patients, including two frameshift variants and one intronic variant. Autophagolysosomes have been observed in one patient by electron microscopy. Our research expands the genetic spectrum of TCAP mutations in China, indicating c.165-166insG is likely the common pathogenic variant.

Discussion: Our cases showed that variants in the TCAP can cause distal myopathy with rimmed vacuoles. Misdiagnosis or delayed diagnosis often occurs in muscular dystrophies. This article also suggests that c.165-166insG is likely the common mutation of TCAP gene in Chinese populations. The intron variant in patient 3 indicates that studies of hereditary diseases should consider not only variants in exons but also those in introns.

Conclusion: This study expands the clinical and pathological spectrum of LGMD2G. The absence of labelling for telethonin in a muscle biopsy is highly predictive of a defect in TCAP and thus confirmation by variant testing is required.

Keywords: limb-girdle muscular dystrophy; LGMD2G; distal myopathy; TCAP

CPF 196

Myofibrillar Myopathy Presenting with Muscle Biopsy Findings of Mitochondrial Myopathy

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Introduction: Myofibrillar myopathies (MFMs) refer to a group of genetically heterogeneous disorders with a similar morphological phenotype, characterized by progressive muscle weakness. On the other hand, Mitochondrial Disorders are a genetically and phenotypically heteregoneous group of disorders that result from functional and structural deformities of the mitochondria.

Recently, a patient whose clinical presentations and the muscle biopsy resembled mitochondrial myopathy was later diagnosed with Myofibrillar myopathy. The patient's genetic study demonstrated one variant of FLNC gene (c.[8101A>T]-p.Lys2701*) and one variant of NDUFB gene (c.[77 C>T]-p.Ser26Phe).

Case Presentation: A 63-years old Korean male patient presented with slowly progressive both leg weakness and muscle wasting after 3 years from the onset, and he had a few relatives who shared the symptoms. His older sister and her son and the patient's younger brother shared the symptoms though the relative seriousness varied for every individual. The patient complained of difficulty walking up or down the stairs due to his weakness in both thighs. The muscle biopsy was performed from the patient's Rt. Vatus lateralis and was sent to two Pathology lab. One lab discovered abnormal subsarcolemmal accumulation and 'ragged-red fibers' which refers to a disrupted, red-staining fibers on the Gomori trichrome stain, suggesting possibility of mitochondrial myopathy. On the contrary, the other lab suggested the possibility of inflammatory myopathy, describing perivascular and endomysial

lymphocytic infiltration. We performed whole exome sequencing (WES) to the patient, and two variants were identified: one variant of FLNC gene (c.[8101A>T]-p.Lys2701*) and one variant of NDUFB gene (c.[77 C>T]-p.Ser26Phe).

Discussion: The patient's clinical presentations and pathologic report suggested the possibility of mitochondrial myopathy, even though the patient did not complain other systematic symptoms. Moreover, the patient's pedigree is capable of explaining both Autosomal dominant and maternal inheritance. Because the patient had 'ragged red fiber' histopathology and also had family history that resembled maternal inheritance, the initial assessment was mitochondrial myopathy. However, the WES genetic study found FLN-C pathogenic variant as reported.

Conclusion: It is challenging to distinguish myofibrillar myopathy from mitochondrial myopathy just from clinical presentations. It is needless to say the importance of muscle biopsy and genetic study in the diagnosis of many different myopathies.

Keywords: myofibrillar myopathy, filamin C, mitochondrial myopathy

CPF 197

Clinical, Pathological, and Molecular Genetic Analysis of 7 Chinese Patients with Hereditary Myopathy with Early Respiratory Failure

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Introduction: Hereditary myopathy with early respiratory failure (HMERF) typically presents in adulthood. Respiratory failure is a consistent feature in the early stages of the disease; the severity of respiratory failure may vary and is not associated with the severity of muscle weakness. Mutations located on exon 344 of the titin-A band, the 119th fibronectin-3 domain (FN3 119), are responsible for HMERF.

Methods: In this article, we retrospectively analysed the clinical features, findings of muscle imaging, muscle pathology, immunohistochemistry, and ultrastructural characteristics of seven patients diagnosed with HMERF at a single center in China.

Results: Muscle MRI showed involvement of semitendinosus in four patients. The common pathological features were variability in fiber diameter, increased internal nuclei, endomysial fibrosis, and cytoplasmic bodies. On immunohistochemical examination, the cytoplasmic bodies stained positive for calpain-3, p53, and programmed death ligand 1. Electron microscopy showed cytoplasmic bodies, distorted sarcomere architecture, glycogen pool, and subsarcolemmal accumulation of mitochondria and lysosomes. We retrospectively reviewed four reported HMERF patients in China. Among the 11 patients, the median age at onset was 34 years (range 14–54). Allelic frequency of mutation c.95195C>T was 36.36%.

Discussion: This study characterizes the phenotype and genotype spectrum of HMERF in China.

Conclusion: In this study, we characterized the clinicopathological features of seven Chinese patients with HMERF, which helps expand the phenotype and genotype spectrum of HMERF in China. In addition, stress may act as a trigger for disease onset. Pathological findings suggest that autophagy may be a secondary change induced by CBs. However, further studies are required to elucidate the precise cause of HMERF.

Keywords: hereditary myopathy with early respiratory failure, TTN, necklace-like cytoplasmic bodies, titin

CPF 199

Hypokalemic Periodic Paralysis with Myokymic Movements Due to Secondary Distal Renal Tubular Acidosis: Initial Manifestation in Sjogren Syndrome Without Any Sicca Symptom

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Introduction: Sjögren's syndrome is a autoimmune disease characterized by exocrine gland involvement and marked lymphocytic infiltration. Distal renal tubular acidosis (dRTA) is a known cause of hypokalemia, which may rarely be severe enough to present as hypokalemic paralysis.

Case Presentation: We report a 28-year-old female case who presented with episodes of hypokalemic periodic paralysis, which was diagnosed as hypokalemic periodic paralysis due to distal renal tubular acidosis with bilateral renal stones and proteinuria. After correction of hypokalemia, weakness was fully recovered but diffuse myokymic movements in hands were persisted few days. In electromyography, myokymic discharge in ADM and neuromyotonic discharge in soleus were seen. The myokymic movement in hands were well controlled after using carbamazepine. At that time, dRTA were considered idiopathic because paraneoplastic antibodies and autoantibodies shown in channelopathies, and whole exome sequencing for inherited dRTA and periodic paralysis were normal. However, secondary dRTA may be the presenting manifestation of autoimmune diseases such as Sjögren's syndrome. Despite of absent sicca symptom, severely decreased uptake in bilateral parotid and submandibular glands in salivary gland scan with positive shirmer test and anti-Ro/La antibody are suggesting Sjogren's syndrome in this case.

Discussion: Presentation of this case highlights the necessity of notice to rare myokymic movements and hypokalemic periodic paralysis, which could be one of the rare clinical manifestations of dRTA. Secondary dRTA may be the presenting manifestation of autoimmune diseases such as Sjögren's syndrome. Thus, adults with seemingly idiopathic distal RTA should be evaluated for Sjögren's syndrome.

Conclusion: Throughout the case, periodic paralysis with distal RTA must be evaluated for Sjogren syndrome.

Keywords: periodic paralysis, distal RTA, myokymia, Sjogren syndrome

CF 200

Tcap Deficiency in Zebrafish Leads to ROS Production and Mitophagy, and Idebenone Improves Its Phenotypes

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Introduction: Limb-girdle muscular dystrophy 2G (LGMD2G) is a subtype of limb-girdle muscular dystrophy caused by nonsense or frameshift mutations in TCAP. However, the disease's mechanisms are still not fully understood, and no established therapeutic targets have been found. TCAP encodes telethonin, a 19 kD protein located in the periphery of Z-discs.

Methods: Using a morpholino-based knockdown approach, we established an LGMD2G zebrafish model. We analyzed the ROS level, mitophagy related proteins, citrate synthase expression, and OCR of LGMD2G zebrafish. Then, we administered vitamin C, coenzyme Q10, idebenone, metformin, or dexamethasone to rescue LGMD2G in zebrafish.

Results: In this study, we found that the ROS level increased in LGMD2G zebrafish. The expression of the mitophagy-related protein BNIP3L, LC3A-II/LC3A-I, and LAMP1 were increased in LGMD2G zebrafish. The oxygen consumption rate and citrate synthase expression was significantly decreased. Thus, mitophagy was presumed to be involved in the LGMD2G to reduce ROS levels. Idebenone reduced the curly tail phenotype and ROS level. Also, it reduced BNIP3L expression in LGMD2G zebrafish models and improved their motor function.

Discussion: As shown in the present study, after tcap knockdown, ROS increased. Dysfunctional mitochondria might produce ROS. Then the expression of LC3A-II/LC3A-I and BNIP3L increased to eliminate dysfunctional mitochondria to reduce ROS. Damaged mitochondria are recognized by phagophores to form autophagosomes. Then, the autophagosome fuses with the lysosome to induce mitophagy.

Conclusion: In conclusion, mitophagy might be involved in the LGMD2G, and idebenone ameliorated LGMD2G by downregulating ROS level.

Keywords: LGMD2G, TCAP, mitophagy, idebenone, zebrafish, ROS

CPF 203

Elongation and Truncation Variants in The TTN Gene Causing Limb-Girdle Muscular Dystrophy Type 2J in a Han Chinese Family

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Introduction: Limb-girdle muscular dystrophy (LGMD) is a group of clinically heterogeneous muscle disorders commonly manifesting proximal limb girdle muscle weakness. There have been more than 30 subtypes of LGMD associated with causative genes and Limb-girdle muscular dystrophy type 2J (LGMD2J) is caused by mutations in the *TTN* gene.

Case Presentation: We report a Han Chinese family with LGMD2J. The proband and his sister both presented with weakness in the proximal lower limbs bilaterally. A muscle sample was taken from the left quadriceps femoris of the proband. HE staining showed dystrophic changes. Immunohistochemical analysis for CD3 and CD8 indicated T cells infiltration. The MGT staining revealed rimmed vacuoles. Lobed muscle fibers were present on NADH staining. Whole-exome sequencing identified novel compound heterozygous mutations in the *TTN* gene, including elongation (c.107962_107963delAT, p.I35988Sfs*26) and truncation (c.99125_99128dupACAG, p.S33043Rfs*9) variants in the proband and his sister (according to the transcript NM_001267550).

Discussion: According to the HGMD database, the two variants have never been reported, and we are the first to identify an elongation mutation in the *TTN* gene. The structure of titin can be divided into four regions. The c.99125_99128dupACAG (p.S33043Rfs*9) mutation lies in exon 355 and the A-band region of titin. The c.107962_107963delAT (p.I35988Sfs*26) mutation lies in the last exon (exon 364) and M-band region (C-terminal fragment) of titin. Some variants in the last exon of the TTN gene have been reported, one of which was associated with LGMD2J.

Conclusion: LGMD2J should be distinguished by other myopathies caused by mutations in the *TTN* gene. The pathogenesis and specific curative methods for LGMD2J remains to be further elucidated.

Keywords: LGMD2J, TTN gene, elongation mutation, truncation mutation, titin

CPF 212

A Case Report of Miyoshi Myopathy with a Novel Variant of DYSF

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Introduction: Miyoshi myopathy is an allelic disorder to autosomal recessive limb girdle muscular dystrophy (LGMD) type 2 which is the second most prevalent LGMD. It is associated with >450 *DYSF* variants that encoding important membrane repair protein. However, the Indonesian pathogenic variant of *DYSF* is unknown.

Case Presentation: A 26-year-old Indonesian male, born from non-consanguineous parents, had progressive all extremities muscle weakness for six years, starting as myalgia and muscle weakness in both legs, displaying difficulty in tiptoeing followed by loss of stairs climbing and independent walking abilities in two years. Two years later, the upper extremities were affected. On presentation, we identified generalized hypotonia and atrophy predominating distal legs. Additional examination revealed remarkably elevated serum CK level (5796 U/L) and myogenic MUAP with spontaneous activities. The muscle biopsy displayed advanced dystrophic features with loss of dysferlin detected on immunohistochemistry and western blot (0.4%) in concordance with two Sanger sequencing-confirmed heterozygous variants of the *DYSF*, which were c463G>T(P.G155*) and c.1053+4A>G. The latter variant produced more aberrant splicing patterns comprising exon 9 to 11 and exon 11 skipping.

Discussion: The phenotype of our patient was similar to previous reports. However, distal muscle onset and myalgia should be carefully differentiated from peripheral nerve disease that usually displays distal muscle weakness. Therefore, CK and EMG evaluation are needed. c463G>T(P.G155*) variant was convincingly pathogenic as it introduces premature stop codon. Meanwhile, c.1053+4A>G was reported causing aberrant splicing including exon 11 and exon 9-11 skipping. Those splicing abnormalities produced frameshift affecting domain FerI, and subsequent domains, and in-frame deletion affecting C2B and FerI domain, respectively. C2B-FerI-C2C domain plays a role in regulation of dysferlin normal plasma membrane expression.

Conclusion: We identified a Miyoshi myopathy from Indonesia with a novel variant and a previously reported variant that causes more than one aberrant splicing pattern.

Keywords: miyoshi myopathy, muscular dystrophy, novel variant, DYSF

CPF 214

SOD1 Variants in Korean Patients with Motor Neuron Disease

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Introduction: Motor neuron disease (MND) is a neurodegenerative disorder characterized by progressive weakness with loss of motor neurons. The pathophysiological mechanisms of MND remain less understood. The expansion of a C9orf72 gene has been identified as the most common cause of familial and sporadic amyotrophic lateral sclerosis (ALS) in Caucasian populations. However, C9orf72 repeat expansion is uncommon in Korean ALS patients. In subsequent studies, SOD1 gene mutation in Korean fALS patients was the most common causing gene. In this study, we analyzed SOD1 variants and clinical features in a large cohort of Korean patients with ALS and pure LMND.

Method: We enrolled 1338 Korean patients with ALS and pure LMND including 33 unrelated patients with a familial MND. Clinical characteristics of patients include the age of onset, sex, site of onset, family history of neuromuscular disease, ALSFRS-R, and delta FS at initial. Sequence analysis was performed for the detection of SOD1 variants.

Result: SOD1 variants were detected in 13 (39.3%) familial MND and 12 (0.7%) sporadic MND. SOD1 variant were identified in 40% (12 of 30) of fALS and 0.5% (6 of 1124) of sALS. The frequency of the SOD1 variant was 33.3% (1 of 3) in fLMND and 2.8%(5 of 181) in sLMND. We identified 16 nonsynonymous heterozygous variants including 1 splice site variant (p.Ala5Phe, p.Gly11Val, p.Gly17Ala, p.Phe21Cys, p.Gly38Arg, p.His44Arg, p.Phe46Cys, p.His49Arg, p. Glu50Val, p.Pro67Ser, p.Gly86Ser, p.Asn87Ser, p.Ile105Thr, p.His121Arg, p.Gly142Ala, p.Gly142Glu and c.239+3_239+5delinsGGT). The mean age onset of patients with SOD1 variants was 47.9 (SD 11.0). In large families with p.Phe21Cys mutations, prognosis and onset of age were different in family members.

Conclusion: Through this study, the spectrum of the SOD1 variant was revealed in Korean MND patients.

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Mitochondrial Myopathy in a 50-Year-Old Woman Mimicking Ocular Myasthenia

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Introduction: Mitochondria are intracellular organelles that play important roles in energy-producing and organismal survival via oxidative phosphorylation. The defection of this system leads to mitochondrial dysfunction and mitochondrial myopathies. The usual ocular motor presentation is a chronic, symmetrical, and diffuse weakness of extraocular muscle.

Case presentation: A 50-year-old woman presenting with chronic progressive bilateral ptosis and ophthalmoparesis or chronic progressive external ophthalmoplegia (CPEO) and bilateral generalized muscle weakness with fluctuation since 15 years. Physical examination revealed bilateral ptosis, limited extraocular movements in all directions, weakness of orbicularis oculi of both eyes, facial diplegia, symmetrical uvula and palatal elevation, nasal voice, muscle power grade IV+/V on all extremities and areflexia. There was no evidence of cardiac conduction block, cerebellar ataxia or pigmentary retinopathy. Initially, even though the serologic investigation for acetylcholine receptor antibody was negative, the patient partially responded to symptomatic treatment for myasthenia gravis (pyridostigmine). Twenty-two years later, her clinical symptoms worsened. The muscle biopsy was performed due to differential diagnoses of oculopharyngeal muscular dystrophy (OPMD) and mitochondrial myopathy.

Discussion: The muscle biopsy showed a large amount of cox-deficient/negative fibers on oxidative enzymatic stains under the light microscope. The ultrastructural study showed subsarcolemmal accumulations of abnormal mitochondria, paracrystalline inclusions (PCIs) and cristae linearization with angular features. These findings were compatible with mitochondrial myopathy.

Conclusion: We present a mitochondrial myopathy in a 50-year-old woman mimicking ocular myasthenia. Echocardiogram and genetic testing are pending for definite diagnosis, which is crucial for prognosis, genetic counseling and proper management.

Keywords: mitochondrial myopathies, chronic progressive external ophthalmoplegia (CPEO), ocular myasthenia

CPF 227

Performance of Diagnostic Studies of Muscle Diseases in Department of Neurology Dr. Cipto Mangunkusumo Hospital: Results of the Myopathy Registry

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Introduction: Myopathy is a group of diseases affecting ion channels, structures, or metabolism of skeletal muscle whose diagnostic approach has been challenging as it requires muscle radiology to full battery-staining muscle biopsy and genetic analysis. This study aims to describe our current ability in diagnosing myopathy in Indonesia.

Methods: This study was a cross-sectional descriptive study conducted in Dr. Cipto Mangunkusumo Hospital. Data were extracted from the Myopathy Registry from 2018 to April 2022 with incomplete data excluded. Final diagnosis was considered if meeting the diagnostic criteria, pathologically, or genetically confirmed.

Results: Fifty-two patients were enrolled in this study with female predominance (50%). The median of age was 29 (9 – 71) years old. NCV and EMG were performed in 96.2% patients, while creatinine kinase was performed in 98.1% patients. None of them had serum aldolase and lactate from cerebrospinal fluid data. Muscle imaging was performed in 40.4% patients. Myositis-specific antibody (MSA) test was performed in 55.6% of 27 required patients. Muscle specimen was obtained in 36.53% patients in which 68.4% of them underwent full battery staining in health facilities abroad and 31.6% had limited (H&E) staining in Indonesia. Overseas genetic examinations were performed in 25.8% of 31 required patients. Final diagnosis was reached in 48.1% of total patients, with interval time 3 to 300 days. The most common diagnosis was immune-mediated necrotizing myopathy (13.3%) and dermatomyositis (13.3%), followed by dysferlinopathy (5.7%).

Discussion: More than half of myopathy patients in our facilities have not reached final diagnosis due to limited diagnostic resources. Among those who reached final diagnosis, most diagnostic studies (e.g. biopsy staining, genetic examinations) were done abroad.

Conclusion: Accessibility to full battery staining muscle biopsy, serum MSA, and genetic analysis in Indonesia needs to be improved to increase diagnostic accuracy, thus leading to better care of myopathy patients.

Keywords: characteristics, myopathy, registry

CPF 229

A Case of Seronegative Immune Mediated Necrotizing Myopathy with Nonspecific Interstitial Lung Disease

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Introduction: Immune-mediated necrotizing myopathy (IMNM) is a subtype of idiopathic inflammatory myopathy manifesting muscle weakness, remarkable elevated serum creatinine kinase, associated with anti-3-hydroxy-3-methylglutaryl-CoA (anti-HMGCR) and anti-signal recognition particle (anti-SRP) autoantibodies. Compared to antisynthetase syndrome and MDA5-associated dermatomyositis, IMNM rarely associates with severe interstitial lung disease (ILD).

Case Presentation: A 21-year-old Indonesian female presented with progressive proximal predominant weakness for 6 months before presentation to our hospital, accompanied by dysphagia, dyspnea, and fever. She had a history of hypothyroid and was on levothyroxine. The serum CK level was 10,972U/L but anti SRP and HMGCR were negative. Electromyography displayed myogenic lesions with spontaneous activities. Muscle pathology reflected myofiber necrosis with sarcolemmal MAC deposition. The muscle strength was then partially improved with methylprednisolone and mycophenolate mofetil but methylprednisolone reduction caused muscle strength deterioration and recurrent elevated CK level. After four years of immunosuppressants, pelvis muscle MRI showed muscle atrophy and adipose tissue infiltration without edema sign. On follow up, she developed worsening dyspnea with high resolution thorax CT displayed ground glass opacity, thickening interlobular septum, bronchiectasis, paraseptal emphysema, multiple bullae, and pneumatocele, representing nonspecific interstitial pneumonia (NSIP). The PCR of SARS CoV-2 and pulmonary tuberculosis exploration were negative. Spirometry was not performed due to COVID-19 pandemic.

Discussion: Recent evidence shows ILD is uncommon among IMNM, especially with SRP followed by HMGCR antibodies, but more common in dysphagia and older SRP-associated IMNM patients. In contrast to previous studies, although having dysphagia, our patient was young. Similar to the previous study showing NSIP as the most common pattern ILD in IMNM, NSIP was identified in our patient.

Conclusion: We reported a young patient of typical IMNM without detectable autoantibodies who developed ILD. Although ILD is uncommon among IMNM, physicians should carefully identify early clinical signs of ILD and exclude the possibility of infection.

Keywords: immune-mediated necrotizing myopathy, seronegative, interstitial lung disease

CPF 230

Clinical, Pathological and Genetic Diagnosis of Multiminicore Myopathy in Three Taiwanese Patients: SEPN1 Myopathy and MEGF10 Myopathy

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Introduction: Multiminicore disease (MmD) is a rare recessive congenital myopathy. It is named by the characteristic pathological features of muscles, showing 'multiple cores.' Although the causative genes are diverse, there are also some hallmarks of clinical phenotype in MmD including rigid spine, early scoliosis and early respiratory failure.

Case Presentation: We performed comprehensive clinical, pathological, and genetic analysis of three Taiwanese patients diagnosed as multiminicore disease based on muscle pathology. All of our three patients exhibited hypotonia in infancy, motor developmental delay, predominant truncal/axial muscle weakness, early onset scoliosis and respiratory impairment when being ambulant status. Molecular findings revealed three reported mutations in SEPN1 such as c.802C>T (p.Arg268Cys), c.1574T>G (p.Met525Arg) and c.1209dup (p.Lys404Glnfs*32) and one other reported mutation, c.1096G>T (p.Glu366*) in our SEPN1 myopathy patient. The novel mutation, c.2065C>T (p.Gln689*) and the other reported mutation, c.2450G>C (p.Cys817Ser) were identified in our MEGF10 myopathy patient.

Discussion: The early onset scoliosis often need surgical intervention while the progressive scoliosis deteriorate patient's respiratory function, influence ambulation, and cause muscle pain. Two of our patients had received corrective osteotomy and posterior spinal fusion surgery when their 11 and 13 years old. The respiratory involvement of MmD patient is disproportionate to limb weakness; most patients suffer from early respiratory failure and required noninvasive ventilation while they were still ambulant. All of our three patients were using BiPAP (Bi-level positive airway pressure) ventilation since their 14, 10 and 9 years old.

Conclusion: Our patients all presented the typical clinical manifestations of MmD despite the heterogenicity of causative genes. The novel mutations of MEGF10 widened the genetic spectrum of MEGF10-related myopathy. Although there is still no cure for patients with MmD, the accurate diagnosis could guide appropriate multidisciplinary cares.

Keywords: congenital myopathy, multiminicore disease, SEPN1 myopathy, MEGF10 myopathy

CLINICO-PATHOLOGICAL CONFERENCE ABSTRACT

CPF 213

Late Onset Distal Myopathy Masquerading as Right Common Peroneal Nerve Palsy

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Introduction: Adult-onset distal myopathies are rare and often challenging to diagnose. We are presenting a case of late onset distal myopathy for discussion.

Case Presentation: A 62-year-old Chinese male presented with progressive right lower limb distal weakness for 2-3 years duration. He is an active recreational sailor who would also jog in the past. He had no family history of progressive weakness. Examination mimicked a right common peroneal nerve palsy with wasting in right tibialis anterior (TA).

Nerve conduction study showed bilateral peroneal motor responses at extensor digitorum brevis robustly normal with markedly reduced response at TA (right worse than left), and normal superficial peroneal and sural sensory potentials. Needle electromyography showed ongoing abnormal spontaneous activity in bilateral TA (right worse than left) with myopathic recruitment on the right. Right gastrocnemius and Gluteus Medius muscles were spared. These findings were suggestive of probable distal myopathy affecting the anterior leg compartment bilaterally.

Further evaluation was as follows: Creatine kinase was 351 U/L. Aldolase normal. Inflammatory myositis autoantibody panel was unremarkable**.** Magnetic resonance imaging myography of pelvis and bilateral lower limbs revealed bilateral symmetrical diffuse edematous changes and fatty atrophy affecting semimembranosus, biceps femoris and quadratus femoris muscles in addition to anterior compartment muscles of bilateral legs.

Left TA muscle biopsy showed fibre size variability, endomysial fibrosis, necrotic fibres, regenerating fibres and mild perivascular inflammation consistent with chronic myopathy such as muscular dystrophy. Furthermore, there were few rimmed vacuoles and many lobulated and moth-eaten fibres. Comprehensive Neuromuscular Disorders Genetic Panel revealed MYH7 c.3551A>T (p.Gln1184Leu) heterozygous genotype seen in the phenotype of Laing Distal Myopathy.

Conclusion/Discussion: In view of unexpected findings in the genetic testing panel, we would like to discuss clinicopathologic and genetic correlation in this case of late onset distal myopathy and solicit views from AOMC panelists.

Keywords: distal myopathy

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