SUPPLEMENT 5

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28 – 29 October 2023

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References:
1. Chung S, et al. *CNS Drugs* 2010;24:1041–1054. 2. VIMPAT Prescribing Information. Hong Kong: Updated Sept 2019. 3. Vimpat Prescribing Information (Solution for infusion) Hong Kong: Updated Sept 2019. 4. Villanueva V, et al. *Epilepsy Behav* 2013;29:349–356. 5. Stockis A, et al. *Epilepsia* 2013;54:1161–1166. 6. Halford JJ, Lapointe M. *Epilepsy Curr* 2009;9:1–9. 7. Runge U, et al. Presented at: 68th Annual Meeting of the American Epilepsy Society (AES); 5–9 December 2014; Seattle, Washington. Abstract 3.297. 8. Vecht, CJ, et al. *Oncologist* 2014;19:751–759. 9. Saria M, et al. *J Neurosurg* 2013;118:1183–1187. 10. Maschio M, et al. *J Neurol* 2011;258:2100–2104.

Abbreviated Hong Kong Prescribing Information:

Abbreviated Hong Kong Prescribing Information

NAME OF THE MEDICINAL PRODUCT
VIMPAT (Lacosamide)

PHARMACEUTICAL FORM
Film-coated tablets containing 50mg or 100mg lacosamide. Solution for infusion containing 10 mg lacosamide per ml. Syrup containing 10mg lacosamide per ml.

THERAPEUTIC INDICATIONS
Vimpat is indicated as monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 4 years of age with epilepsy.
Vimpat is indicated as adjunctive therapy
- in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 4 years of age with epilepsy
- in the treatment of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy

POSOLOGY AND METHOD OF ADMINISTRATION
Lacosamide must be taken twice a day (usually once in the morning and once in the evening). Tablets/Syrup: Lacosamide may be taken with or without food.
IV: Lacosamide therapy can be initiated with either oral or i.v. administration. The overall duration of treatment with i.v. lacosamide is at the physician's discretion; there is experience from clinical trials with twice daily infusions of lacosamide for up to 5 days in adjunctive therapy. Conversion to or from oral and intravenous administration can be done directly without titration. Monitor closely patients with known cardiac conduction problems, on concomitant medications that prolong PR interval, or with severe cardiac disease (e.g. myocardial ischemia, heart failure) when lacosamide dose is higher than 400 mg/day.

Adults, adolescents and children weighing 50kg or more
Starting dose (monotherapy for partial onset seizures and adjunctive therapy for partial onset seizures or primary generalised tonic-clonic seizures) - 50mg twice a day. Increase to initial therapeutic dose of 100mg twice a day after 1 week. For monotherapy, dose can also be initiated at 100mg twice a day.
Maintenance dose (monotherapy for partial onset seizures and adjunctive therapy for partial onset seizures or primary generalised tonic-clonic seizures) – dose can be further increased at weekly intervals by 50mg twice a day, up to a max recommended daily dose of 300mg twice a day for monotherapy or 200mg twice a day for adjunctive therapy.
Loading dose *(initial monotherapy or conversion to monotherapy in the treatment of partial-onset seizures or adjunctive therapy in the treatment of partial-onset seizures or adjunctive therapy in the treatment of PGTCS)* - May also initiate with a single loading dose of 200 mg, followed approximately 12 hours later by a 100 mg twice a day (200 mg/day) maintenance dose regimen. Administered under medical supervision with consideration of the potential for increased incidence of serious cardiac arrhythmia and central nervous system adverse reactions. Administration of a loading dose has not been studied in acute conditions such as status epilepticus.

Discontinuation - If lacosamide has to be discontinued, recommended to do it gradually (e.g. taper the daily dose by 200 mg/week). If patient develops serious cardiac arrhythmia, perform clinical benefit/risk assessment and discontinue lacosamide if needed.

Elderly (over 65 years of age) - No dose reduction is necessary in elderly patients.

Renal impairment - No dose adjustment is necessary in mildly and moderately renally impaired adult and paediatric patients (CLCR >30 ml/min). In paediatric patients weighing 50kg or more and in adult patients with mild or moderate renal impairment, a loading dose of 200 mg may be considered, but further dose titration (>200 mg daily) should be performed with caution. In paediatric patients weighing 50kg or more and in adult patients with severe renal impairment (CLCR ≤30 ml/min) or with end-stage renal disease, a maximum dose of 250 mg/day is recommended and the dose titration should be performed with caution.

Hepatic impairment - A maximum dose of 300mg/day is recommended for paediatric patients weighing 50kg or more and for adult patients with mild to moderate hepatic impairment.

Paediatric population - The physician should prescribe the most appropriate formulation and strength according to weight and dose. The dose for paediatric patients (from 4 years of age) and adolescents weighing less than 50kg is determined based on body weight. Please refer to the package insert for dosage recommendation in this population.

CONTRAINDICATIONS
Hypersensitivity to the active substance or to any of the excipients.
Known second- or third-degree atrioventricular (AV) block.

SPECIAL WARNING AND PRECAUTIONS FOR USE
Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic medicinal products in several indications. Patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.
Dose-related prolongations in PR interval with lacosamide have been observed in clinical studies. Lacosamide should be used with caution in patients with underlying proarrhythmic conditions such as patients with known cardiac conduction problems or severe cardiac disease or patients treated with medicinal products affecting cardiac conduction, including antiarrhythmics and sodium channel blocking antiepileptic medicinal products as well as in elderly patients. Consider performing ECG before dose increase to above 400mg/day and after lacosamide is titrated to steady state.
Patients should be made aware of the symptoms of cardiac arrhythmia. Patients should be counselled to seek immediate medical advice if these symptoms occur.
New onset or worsening of myoclonic seizures has been reported in both adult and paediatric patients with PGTCS, in particular during titration.
Patients should be advised to exercise caution until they are familiar with the potential effects of the medicine to prevent accidental injury or falls.
The safety and efficacy of lacosamide in paediatric patients with epilepsy syndromes in which focal and generalised seizures may coexist have not been determined.
Vimpat solution for infusion contains sodium. To be taken into consideration for patients on a controlled sodium diet.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERATION
Use with caution in patients treated with medicinal products known to be associated with PR prolongation (including sodium channel blocking antiepileptic medicinal products) and in patients treated with antiarrhythmics.
Caution when use with strong inhibitors of CYP2C9 (e.g. fluconazole) and CYP3A4 (e.g. itraconazole, ketoconazole, ritonavir, clarithromycin), and strong enzyme inducers such as rifampicin or St John's wort (Hypericum perforatum).

PREGNANCY AND BREASTFEEDING
Lacosamide should not be used during pregnancy unless clearly necessary. Breast-feeding should be discontinued during treatment with lacosamide.

UNDESIRABLE EFFECTS
Very common (≥1/10): dizziness, headache, nausea and diplopia (usually mild to moderate in intensity). Common (≥1/100 to <1/10): depression, confusional state, insomnia, myoclonic seizures, ataxia, balance disorder, memory impairment, cognitive disorder, somnolence, tremor, nystagmus, hypoesthesia, dysarthria, disturbance in attention, paresthesia, vision blurred, vertigo, tinnitus, vomiting, constipation, flatulence, dyspepsia, dry mouth, diarrhea, pruritus, rash, muscle spasms, gait disturbance, asthenia, fatigue, irritability, feeling drunk, fall, skin laceration, contusion. The use of lacosamide is associated with dose-related increase in the PR interval. Adverse reactions associated with PR interval prolongation (e.g. atrioventricular block, syncope, bradycardia) may occur.
Paediatric Population - The safety profile in paediatric population was consistent with the safety profile observed in adults although the frequency of some adverse reactions (somnolence, vomiting and convulsion) was increased and additional adverse reactions (nasopharyngitis, pyrexia, pharyngitis, decreased appetite, lethargy and abnormal behaviour) have been reported in paediatric patients.

Please refer to the *full prescribing information* before prescribing.

Further information is available from: UCB Pharma (Hong Kong) Limited

Revised March 2023 (Ref. HK PI FCT [5 May 2022], SFI, OS [18 Jul 2022])

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36th Annual Scientific Meeting of The Hong Kong Neurological Society

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Scientific Programme

Venue: Grand Ballroom, Level 3, JW Marriott Hotel, Admiralty, Hong Kong SAR

28 October 2023, Saturday

09:15 – 09:30	Registration	Poster Room **Poster Presentation**
09:30 – 11:15	**Dissertation Highlights** Panel Judges: *Dr Herrick Lau, Dr Noble Kwan* **The Prince of Wales Hospital real-world analysis of people with drug-resistant epilepsy on perampanel (WRAPPER) study** *Charlie Chan* **Assessment of the real-world safety and effectiveness of dimethyl fumarate in a local cohort** *Joseph CH Choi* **Prevalence of impulse control disorders and apathy and associated clinical risk factors in patients with Parkinson's disease in Hong Kong** *Eva Ki* **Orthostatic hypotension in Parkinson's disease—a longitudinal study in a local specialised clinic** *Dennis Kwok* **H-SeLECT: a novel magnetic resonance imaging–based risk score for the prediction of post-stroke epilepsy** *William CY Leung, YK Wong, Shirley YY Pang, KK Lau* **Long-term outcome of patients with intracranial artery stenosis: medical therapy versus adjuvant endovascular angioplasty and stenting** *WT Lui* **Application of collateral score and clot burden score in predicting ischaemic stroke revascularisation therapy outcome—a local hospital experience** *Ian Victor Ma* **COVID-19 vaccination in patients with epilepsy** *Bingjiao Xie*	
11:15 – 11:30	Break/Air time	
11:30 – 12:05	**Eisai PD Symposium** Chairpersons: *Dr Shirley Pang, Dr Frances Lam* **Recent advances in the treatment of Parkinson's disease** *Ruey-Meei Wu*	
12:05 – 12:40	**Lundbeck Migraine Symposium** Chairpersons: *Dr June Wong, Dr Yannie Soo* **New strategies for the treatment of migraine and medication overuse headache** *Hans-Christoph Diener*	
12:40 – 12:50	Break/Air time	
12:50 – 13:00	**Opening Ceremony** Guest of Honour: *Dr Libby Lee, JP* Under Secretary for Health, Health Bureau, The Government of HKSAR	

28 October 2023, Saturday

13:00 – 13:45	**AbbVie Migraine Lunch Symposium** Chairperson: *Dr Yannie Soo* **Latest advances in the preventive treatment of episodic and chronic migraine—from clinical trial to clinical practice** *Jason Ray*	Poster Room **Poster Presentation**
13:45 – 13:55	Break/Air time	
13:55 – 14:40	**Free Paper Presentation** Free Paper Panel Judges: *Dr Noble Kwan, Dr Adrian Hui* **Klotho in the gut-cerebrovascular axis: sex-linked gut microbiome associations with stroke risk and small vessel disease** *TL Ho, PD Virwani, Crystal PL Lee, Chelsea CW Lo, Mandy YM Chan, T Lin, KK Lau* **Low low-density lipoprotein cholesterol levels and the risk of recurrent intracerebral haemorrhage** *TC Lee, C Ho, WL Chiu, CC Lam, KK Lau, KC Teo* **Characteristics and outcomes of direct oral anticoagulant–associated intracerebral haemorrhage** *CH So, Stephanie YL Ho, HH Kwan, Joshua W Fok, Edwin KK Yip, B Sheng, KH Chan, KC Teo, KK Lau* **Cross-sectional study of the association between gut microbiome and 24-hour blood pressure variability** *PD Virwani, Gordon Qian, Matthew SS Hsu, Tommy KKTS Pijarnvanit, Carman NM Cheung, YH Chow, LK Tang, YH Tse, JW Xian, Shirley SW Lam, Crystal PL Lee, Chelsea CW Lo, Roxanna KC Liu, TL Ho, BY Chow, KS Leung, HW Tsang, Emily KK Lo, Keith TS Tung, SK Chung, MF Yuen, SY Leung, Patrick Ip, Ivan FN Hung, Jimmy CY Louie, Hani El-Nezami, Joshua WK Ho, KK Lau* **Safety and efficacy of direct oral anticoagulants in the oldest old atrial fibrillation patients with recent ischaemic stroke** *X Wang, CF Sin, KC Teo, William CY Leung, YK Wong, Roxanna KC Liu, TC Lee, H Luo, KK Lau* **Impact of renal function variability on long-term prognosis in ischaemic stroke patients with atrial fibrillation prescribed with oral anticoagulants** *X Wang, CF Sin, KC Teo, William CY Leung, YK Wong, Roxanna KC Liu, Joshua W Fok, Bonaventure Y Ip, HH Kwan, TC Lee, B Sheng, Edwin KK Yip, Desmond YH Yap, H Luo, KK Lau*	
	Poster Presentation Poster Panel Judges: *Dr June Wong, Dr Germaine Chan* **A case of hereditary transthyretin amyloidosis: diagnostic complexity resolved through integrated analysis and targeted genetic investigation** *HW Cheung* **Two cases of co-existing GD1b immunoglobulin G and GM1 immunoglobulin G with severe distal weakness** *TF Cheung* **Clinical outcomes of treating migraine patients with calcitonin gene–related peptide monoclonal antibody in Hong Kong** *TF Cheung, Adrian TH Hui, Raymond CK Chan* **Inflammatory myopathy with myocarditis and orbital myositis: a case report** *William CT Ip, Colin HT Lui, Steven YW Wong*	

28 October 2023, Saturday

14:40 – 15:15	**Pfizer Migraine Symposium** Chairpersons: *Dr Yannie Soo, Dr Richard Li* **Managing migraine in women: developing patient-centred approaches to care** *Peter Goadsby*	Poster Room **Poster Presentation**
15:15 – 15:30	Break/Air time	
15:30 – 16:05	**Movement Disorder Symposium 1** (Co-organised with HKMDS) Chairpersons: *Dr Helen Yip, Dr Karen Ma* **Personalised Parkinson's disease management in the 21st century** *SY Lim*	
16:05 – 16:40	**Movement Disorder Symposium 2** (Co-organised with HKMDS) Chairpersons: *Dr Germaine Chan, Dr Michael Lee* **Deep brain stimulation in Parkinson's disease: past, present, and future** *Aparna Wagle Shukla*	

29 October 2023, Sunday

09:15 – 09:30	Break/Air time	Poster Room **Poster Presentation**
09:30 – 10:05	**Epilepsy Symposium 1** (Co-organised with HKES) Chairpersons: *Dr Noble Kwan, Dr KC Teo* **EEG and multimodal monitoring for diagnosis and prediction of neurological deterioration, coma, and neurorecovery** *Eric Rosenthal*	
10:05 – 10:40	**Epilepsy Symposium 2** (Co-organised with HKES) Chairpersons: *Dr Adrian Hui, Dr KC Teo* **Caveats in anti-seizure drug treatment in patients with physical and psychiatric co-morbidities** *Jacqueline A French*	
10:40 – 10:55	Break/Air time	
10:55 – 11:30	**Eisai MS Symposium** Chairpersons: *Dr KL Shiu, Dr LK Tsoi* **Pre-clinical multiple sclerosis: radiologically isolated syndrome** *Darin Okuda*	
11:30 – 11:40	Break/Air time	
11:40 – 12:35	**Roche SMA Lunch Symposium** Chairperson: *Dr WT Wong* **Treating adults with spinal muscular atrophy: opportunities and challenges** *Tim Hagenacker* **Sharing of Hong Kong's experience on the treatment of adult patients with spinal muscular atrophy** *Shirley YY Pang*	
12:35 – 12:45	Break/Air time	
12:45 – 13:20	**Novartis MS Symposium** (Co-organised with HKMSS) Chairpersons: *Dr WK Cheng, Dr Stephen Cheng* **Using high-efficacy treatments early in people with multiple sclerosis: practical considerations and treatment options** *Amit Bar-Or*	
13:20 – 14:05	**AstraZeneca gMG + NMOSD Symposium** Chairpersons: *Dr Winnie Wong, Dr WT Wong* **Revolutionising neuroimmunology with complement therapeutics: expanding the horizon for patients with generalised myasthenia gravis and neuromyelitis optica spectrum disorders** *Yesim Parman, Jin Nakahara*	
14:05 – 14:40	**Education Session** Chairpersons: *Dr Germaine Chan, Dr Carlin Chang* **Neurogenetics 101: who, what and how** *KY Mok*	

29 October 2023, Sunday

14:40 – 15:15	**AstraZeneca Symposium on Bleeding Management** Chairpersons: *Dr Richard Li, Dr Shirley Cheung* **Revolutionising direct oral anticoagulant–related intracranial haemorrhage management with specific reversal** *Thorsten Steiner*	Poster Room **Poster Presentation**
15:15 – 15:45	Break/Air time	
15:45 – 16:20	**Biogen Neuromuscular Disease Symposium** Chairpersons: *Dr Carlin Chang, Dr Colin Lui* **From clinical trials to the real world: antisense oligonucleotides for the treatment of neuromuscular diseases** *Maggie C Walter*	
16:20 – 16:35	Closing Ceremony	

DH 1

The Prince of Wales Hospital real-world analysis of people with drug-resistant epilepsy on perampanel (WRAPPER) study

Charlie Chan
Department of Neurology and Department of Medicine and Therapeutics, Prince of Wales Hospital, Hong Kong SAR, China

Introduction: Drug-resistant epilepsy (DRE) is a significant burden in neurology. Despite the advent and expansion of available anti-seizure medications (ASMs), the prevalence of DRE remains approximately 30% and even beyond 35% for tertiary institutions accepting referrals for presurgical evaluation of refractory epilepsy. Perampanel is the first orally active non-competitive AMPA receptor antagonist approved for adjunctive therapy in epilepsy. This study reports the real-world effectiveness and tolerability of adjunctive perampanel among patients with DRE at Prince of Wales Hospital (PWH) in Hong Kong.

Methods: The PWH real-world analysis of people with drug-resistant epilepsy on perampanel (WRAPPER) study was a prospective single-centre real world observational study which recruited people with DRE attending PWH between July 2016 to June 2021. Participants were initiated on perampanel with the dosage titrated as deemed appropriate by neurologists at clinic follow-up for a period of 16 weeks. The primary outcome was a 50% responder rate. Secondary outcomes included 25% responder rate, seizure freedom rate, change in median monthly seizure frequency, percentage change in seizure frequency, treatment adverse effect (TEAE) rate, alongside changes in the neuropsychiatric inventory (NPI) and Zarit Burden Interview (ZBI) scores. A post-hoc analysis done after the initial study period of 16 weeks assessed outcomes for an extended period up to 52 weeks.

Participants: A total of 70 people with DRE were included in the current study and 64.2% were female. The median age was 38.0 years (interquartile range [IQR], 31.8-46.0). Median age at epilepsy onset was 15.5 years (IQR, 7.8-28.5). Median duration of epilepsy in years was 20.0 (IQR, 10.0-29.0). Structural abnormalities were the most common aetiology for epilepsy in this cohort at 55.7%. Median seizure frequency at baseline was 3 per month (IQR, 2.0-7.0). The median number of concomitant ASMs was 2.0 (IQR, 2.0-3.0). Median number of previously tried ASMs before perampanel was 5.0 (IQR, 2.0-8.0). Up to 68.6% of participants were on concomitant enzyme-inducing ASMs (EIASMs).

Results: By the end of 16 weeks the median dose of perampanel was 2 mg (IQR, 2-4). The primary outcome of 50% responder rate were 40.0%, 41.5%, 48.7% at 16 weeks, 26 weeks, and 52 weeks, respectively. Secondary outcomes of seizure freedom were achieved in 12.9%, 20.7%, and 25.6% at 16 weeks, 26 weeks, and 52 weeks, respectively. The median monthly seizure frequency reduced from 3.0 (IQR, 3.0-6.6) at baseline to 2.0 (IQR, 2.0-6.0; P=0.005). Extended analysis beyond 16 weeks showed sustained reductions in monthly seizure frequencies from baseline: 2.0 (IQR, 2.0-5.0; P=0.01) at 26 weeks and 2.0 (IQR, 0.0-4.0; P=0.018) at 52 weeks. Exploratory analysis of baseline characteristics found older age to modestly predict 50% responders (odds ratio [OR]=1.08, 95% confidence interval [CI]=1.01-1.14; P=0.048). There were no other participant-, disease-, or medication-related factors affecting the 50% responder rate. Of note, autoimmune aetiology of epilepsy and concomitant EIASM use did not affect the likelihood of achieving 50% responder rate.

At 16 weeks, 51.4% (36/70) had reported TEAEs. The most common adverse effect was seizure exacerbation at 35.7% (25/70) followed by fatigue at 15.7% (11/70). Seizure exacerbation was the only adverse effect statistically significantly associated with withdrawal from perampanel in this cohort (OR=16.89, 95% CI=3.33-85.61; P=0.002). Changes in the ZBI, overall NPI and domain stratified NPI scores did not find a statistically significant increase in neuropsychiatric symptoms on perampanel; in fact, a statistically significant reduction in the NPI domain of depression/dysphoria was found instead. Subgroup analysis of changes in NPI and ZBI scores for participants on concomitant levetiracetam did not reveal any significant increase in neuropsychiatric adverse effects either. The mean retention time on perampanel was 44.5 weeks (standard deviation=1.7, 95% CI=41.2-47.8).

Discussion: These real-world findings suggest that for people with DRE in Hong Kong, adjunctive perampanel is an effective and well-tolerated treatment option. Even in such a drug-resistant cohort, up to a quarter of participants achieved seizure freedom after addition of adjunctive perampanel giving hope for better quality of life and long-term outcomes. Low-dose perampanel of 2 mg seemed to already provide improvements in seizure prophylaxis, a finding also seen in other real-world Asian cohorts. Concomitant EIASMs did not significantly affect the effectiveness of adjunctive perampanel in the WRAPPER study. Older age may be a predictor for 50% responders to adjunctive perampanel in people with DRE, a trend also observed in multiple real-world cohorts worldwide. Previously highlighted concerns of perampanel-related neuropsychiatric adverse effects in clinical trials were not observed in the real-world setting. A future area of interest may be the real-world effectiveness and tolerability of low-dose perampanel of 2 to 4 mg in elderly Asian patients for seizure prophylaxis.

Assessment of the real-world safety and effectiveness of dimethyl fumarate in a local cohort

DH 2

Joseph CH Choi
Department of Medicine and Therapeutics, Prince of Wales Hospital, Hong Kong SAR, China

Introduction: Dimethyl fumarate (DMF) is an approved disease-modifying therapy (DMT) for relapsing-remitting multiple sclerosis (RRMS). Local data of DMF therapy was lacking despite its position as a first-line oral DMT. We aimed to assess the real-world safety and effectiveness of DMF in a local cohort.
Methods: We retrospectively collected baseline parameters and data on adverse events, relapses, and magnetic resonance imaging (MRI) findings of all patients with RRMS exposed to DMF from the Hong Kong Multiple Sclerosis Registry of The Chinese University of Hong Kong from 2016 to 2022. We performed univariate logistic regressions to evaluate relationships between baseline parameters and disease activities.
Results: We analysed data of 68 patients for safety outcomes. Serious adverse events occurred in 5.9% of patients without abnormal safety signal. Sixty-four patients were included for effectiveness analysis, where 79.7% were female with mean age of 32.6 (±7.8) years at DMF initiation and median baseline Expanded Disability Status Scale (EDSS) score of 1.0 (interquartile range, 0-3.0). Dimethyl fumarate therapy significantly reduced annualised relapse rate by 68.1% (P=0.018) comparing with pre-DMF 1-year annualised relapse rate. Mean time to first relapse was 14.0 (±13.2) months and 81% of patients remained relapse free at year 1. In total, 63.3% of patients had no radiological activities on first follow-up MRI performed at 10.0 (±7.8) months. Younger age at DMF initiation and higher baseline EDSS scores were found to be associated with clinical relapse and MRI activities.
Conclusion: We confirmed that DMF has a favourable safety profile and good efficacy in treatment of RRMS in our local population.

Prevalence of impulse control disorders and apathy and associated clinical risk factors in patients with Parkinson's disease in Hong Kong

DH 3

Eva Ki
Department of Medicine and Geriatrics, Kwong Wah Hospital, Hong Kong SAR, China

Introduction: The purpose of this research is to investigate the prevalence of apathy and impulse control disorders (ICDs) in patients with Parkinson's disease (PD) in our local population, and to study their association with some important clinical variables.
Methods: A total of 103 patients with a clinical diagnosis of idiopathic PD were enrolled in this study. The Apathy Scale (AS) and the QUIP-RS (Questionnaire for Impulsive-Compulsive Disorders–Rating Scale) were applied to diagnose and quantify the severity of apathy or ICD. At the same time, the possible correlation of ICDs and the AS with some clinical characteristics were studied.
Results: The patients were classified into four groups according to documentation by the AS or ICD questionnaires: ICD-only group, apathy-only group, both ICD and apathy group, and with neither ICD nor apathy group. Among this cohort, 50 patients (48.5%) were classified as having apathy and 27 patients (26.2%) had ICDs; 37 patients (35.9%) were confirmed apathy without ICDs, while 14 patients (13.6%) were classified as having ICDs with absence of apathy; 13 patients (12.6%) were found to have ICDs coexisted with apathy, and 39 patients (37.9%) were confirmed neither apathy nor ICDs. Significant positive correlation ($P<0.05$) was established between the AS score and disease severity of PD, and between ICD scale and levodopa equivalent daily dose (LEDD) or dopaminergic agonist daily dose (DADD). Significant difference ($P<0.05$) was also found between the four groups when comparing with disease severity, LEDD or DADD.
Conclusion: This is the first study to investigate motivational disturbance of patients with PD in Hong Kong. It is found that apathy and ICDs are common psychological co-morbidities in PD patients. Severity of apathy is associated with disease severity of PD and some ICD subtypes are associated with levodopa or dopamine agonist doses. These findings may bring positive impact to the management of our local PD patients in the near future.

DH 4

Orthostatic hypotension in Parkinson's disease—a longitudinal study in a local specialised clinic

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Introduction: The natural history of Parkinson's patients with orthostatic hypotension is largely unknown. The impact of orthostatic hypotension on patients with Parkinson's disease and the pattern of progression in these patients were not studied thoroughly in previous studies. This study aimed to describe the natural course of Parkinson's patients with orthostatic hypotension by assessing the prevalence, clinical associations, and disease outcomes.
Methods: In this longitudinal retrospective study, 160 patients who were newly diagnosed to have Parkinson's disease from 2010 to 2017 were recruited and retrospectively reviewed. The prevalence of orthostatic hypotension was 46.9% with median onset time of 5.8 years; 11.3% of patients were diagnosed to have orthostatic hypotension within 3 years of disease onset.
Results: Patients with orthostatic hypotension were associated with longer duration of disease and required higher dose of levodopa. They had poor disease outcome when compared to those without orthostatic hypotension in terms of earlier fall and earlier onset of dementia; they also tend to reach Hoehn and Yahr stage 5 earlier.
Conclusion: Orthostatic hypotension was not an uncommon non-motor manifestation of Parkinson's disease even in early stages of disease and is associated with poor disease outcome. Hence, the occurrence of orthostatic hypotension can provide a prognostic implication to patients. Repeated testing with high index suspicion should be considered in patients with Parkinson's disease at any stage of the disease for early treatment and complication prevention.

DH 5

H-SeLECT: a novel magnetic resonance imaging–based risk score for the prediction of post-stroke epilepsy

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Introduction: Clinical tools for prediction of post-stroke epilepsy (PSE) [eg, SeLECT (Severity, Large-artery atherosclerosis, Early seizures (≤7 days post-stroke), Cortical, Middle cerebral artery [MCA] Territory) score] are largely derived from clinical parameters and computed tomography (CT) findings. With the increasing use of magnetic resonance imaging (MRI), we aimed to identify new clinical and MRI characteristics to develop a novel risk score for PSE.
Methods: This was a single-centre retrospective study, consisting of 852 consecutive patients admitted to Queen Mary Hospital for acute ischaemic stroke from August 2018 to December 2020. All patients received a CT brain scan during admission, whilst 70.1% had an MRI of the brain. We determined the risk associations of individual components of SeLECT with PSE, and further included new parameters including infarct size and haemorrhagic transformation (HT). Predictive values were illustrated by calculating the area under curve (AUC) of receiver operating characteristic (ROC) curves.
Results: At median follow-up of 893 days, PSE occurred in 5.3% of patients (mean time to first seizure: 311.2 ± 367.0 days). Severe stroke (NIHSS [National Institutes of Health Stroke Scale] score of ≥11), MCA territory involvement, cortical involvement, and large infarct size (≥5 cm or ≥1/3 of MCA territory) were associated with PSE. Multivariate regression further showed that HT of any severity was independently associated with PSE (sub-distribution hazard ratio=4.72, 95% confidence interval=2.36-9.41; P<0.001). H-SeLECT score was obtained by adding 2 marks to SeLECT score for presence of any HT, which was calculated by dividing its sub-distribution hazard ratio (6.99) with the median of the lowest three values (3.43) in univariate analysis and rounding to the nearest integer. The AUC of ROC curve of H-SeLECT was significantly increased when compared with SeLECT using Z test (0.813 vs 0.774, Z=2.67; P=0.008).
Conclusion: The newly proposed H-SeLECT score significantly increases the predictive value in detecting PSE compared to existing risk scores. Further studies are required to externally validate the utility of H-SeLECT beyond the Hong Kong Chinese population.

DH 6

Long-term outcome of patients with intracranial artery stenosis: medical therapy versus adjuvant endovascular angioplasty and stenting

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Introduction: Intracranial atherosclerotic disease (ICAD) was a major ischaemic stroke subtype that portended a high rate of recurrence. Landmark randomised controlled trials showed a higher ischaemic stroke risk after angioplasty and stenting compared to medical therapy. Current guideline recommended against stenting as first-line treatment. Yet, post-marketing surveillance studies demonstrated short-term safety of intracranial stenting with experienced neuro-interventionists in carefully selected patients. While the clinical outcome and durability of endovascular treatment remained uncertain, we aimed to elucidate the long-term safety and efficacy of intracranial angioplasty and stenting in this cohort study.

Methods: In this multi-centre referral registry–based study, we recruited consecutive patients with high-grade ICAD confirmed by cerebral digital subtraction angiogram from 22 April 2004 to 11 August 2022 in Prince of Wales Hospital. We analysed the clinical outcome based on the treatment received: medical group vs adjunctive endovascular treatment group (ie, submaximal balloon angioplasty followed by immediate deployment of a self-expandable Wingspan stent). We retrieved and studied the demographics, medical co-morbidities, laboratory parameters, follow-up imaging tests, and clinical events.

Results: Primary outcome was recurrent ischaemic stroke or transient ischaemic attack in the same vascular territory of the symptomatic ICAD or any vascular territory. Secondary outcome was stroke-related mortality. Safety outcomes were periprocedural complication within 30 days. We adopted time-to-event analysis for evaluating cumulative incidence of stroke and death using the Fine-Gray model. Among 239 ICAD patients, there were 122 patients in the medical group and 117 patients in the endovascular treatment group. Risk of all strokes (recurrent ischaemic stroke/transient ischaemic attack regardless of vascular territory) did not differ significantly between the two groups (hazard ratio=1.11; 95% confidence interval=0.68-1.83; P=0.7). There was also no difference between these two groups in recurrent ischaemic stroke/transient ischaemic attack in the same territory (hazard ratio=1.01; 95% confidence interval=0.59-1.72; P>0.9). The endovascular treatment group had five stroke-related deaths while the medical group had no stroke-related death during the 120-month follow-up period. The number of stroke-related deaths was small for statistical analysis. We observed a stroke relapse rate of 7.7% and a mortality rate of 1.7% within 30 days in the endovascular treatment group.

Conclusion: In patients with high-grade symptomatic ICAD, the risks of stroke relapse and stroke-related mortality did not differ between the medical and the endovascular treatment groups. First-line treatment of ICAD remained dual anti-platelet agents and aggressive risk factor control. Further study was needed to determine the role of endovascular treatment in subgroup of ICAD prone to recurrence.

DH 7

Application of collateral score and clot burden score in predicting ischaemic stroke revascularisation therapy outcome—a local hospital experience

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Introduction: Stroke often results in severe neurological deficit or mortality. Computed tomography perfusion imaging provides important information on eligibility for revascularisation therapy, but is not widely available. Computed tomography angiography (CTA) is a more accessible tool to look for large vessel occlusion and provides other useful parameters. Collateral score (CS) and clot burden score (CBS) can be derived by CTA to grade collateral supply and degree of clot burden. Some studies have established the importance of collateral supply and clot burden in the prediction of stroke outcome. Evidence from our local hospitals in recent years is sparse. This study aimed to find an association between CS and CBS with stroke outcome in patients admitted for acute ischaemic stroke between 1 January 2019 and 30 June 2022 who underwent CTA.
Methods: Patients with a baseline modified Rankin Scale (mRS) score of 0 to 2 presented with acute ischaemic stroke who underwent CTA for clinical suspicion of large vessel occlusion and received revascularisation therapy in the form of recombinant tissue plasminogen activator, mechanical thrombectomy or both were retrospectively identified from the Pamela Youde Nethersole Eastern Hospital stroke registry. Patients were divided into two groups based on their stroke outcome at 90 days. Those with a change in mRS score of ≤2 from baseline were classified as having good outcome; those with a change of 3 to 6 from baseline were classified as having poor outcome. The CS and CBS were then correlated with stroke outcome using logistic regression models. Pearson's correlation was first done to look for a linear correlation. A receiver operator characteristic (ROC) curve was then used to show the diagnostic ability of CS and CBS in predicting stroke outcome.
Results: A total of 109 subjects were identified. Higher CS and CBS were both correlated with greater likelihood of good stroke outcome (Pearson's correlation coefficient: CS=-0.404, P<0.01; CBS=-0.382, P<0.01), and were associated with lower chances of mortality (Pearson's correlation coefficient: CS=-0.326, P<0.001; CBS=-0.324, P<0.001). The two scores achieved acceptable threshold on the ROC curve to predict stroke outcome (area under curve: CS=0.696, P=0.001; CBS=0.713, P<0.001), with cutoff points being 1 for CS and 7 for CBS.
Conclusion: Collateral score and CBS are positively correlated with good outcomes in patients having acute anterior circulation ischaemic stroke.

DH 8

COVID-19 vaccination in patients with epilepsy

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Introduction: A vaccination gap between patients with epilepsy and the general population has been reported in the literature. However, knowledge of whether coronavirus disease 2019 (COVID-19) vaccination could lead to epilepsy-related problems is still limited. The present study aimed to investigate the potential risk of breakthrough seizures and other epilepsy-related complications associated with COVID-19 vaccination.
Methods: This was a hospital-based retrospective cross-sectional study. Patients with epilepsy who were hospitalised in the Department of Medicine of Alice Ho Miu Ling Nethersole Hospital between June 2021 and May 2022 were recruited. Demographic data, clinical characteristics, and COVID-19 vaccination records were obtained from electronic patient records. Pattern of vaccination was examined. Factors associated with vaccination uptake, epilepsy-related events after vaccination, as well as mortality rates were analysed.
Results: A total of 502 electronic patient records were screened and 194 patients with epilepsy were recruited in the study. By the time of 31 December 2022, 143 study subjects (73.7%) were vaccinated, compared to 93.3% in the general population at the same time point. Most of the patients (69.2%) had received at least 2 doses of COVID-19 vaccines. Among vaccinated patients, 83 (42.8%) selected Sinovac vaccine, 56 (28.9%) selected BioNTech vaccine, and 4 (2.1%) received mixed vaccines. Elderly (age ≥65 years) was less likely to get vaccinated than young patients (34.3% vs 65.7%; P<0.05). Eleven cases (5.7%) were hospitalised within 2 weeks of COVID-19 vaccination; five patients (2.6%) had new onset seizure within 2 weeks after vaccination. No status epilepticus was found in patients who were vaccinated. Demographics and clinical characteristics were not significantly different between patients hospitalised for post-vaccination seizures and the control group (P<0.05). A high mortality rate (24.2%) and COVID-19 infection rate (32.2%) were found in this study. Age, COVID-19 infection, and doses of vaccination were independently associated with mortality in logistic regression analyses (P<0.05).
Conclusion: There was a significant discrepancy in vaccination rates between epilepsy patients and the general population. Receiving COVID-19 vaccination was not associated with increased risk of epilepsy-related adverse events. In contrast, unvaccinated patients had a considerably higher rates of COVID-19 infection and mortality than vaccinated patients. These findings together suggest the safety and necessity of COVID-19 vaccination for patients with epilepsy.

S 1

Eisai PD Symposium
Recent advances in the treatment of Parkinson's disease

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For a long time, levodopa/carbidopa has been considered the gold standard therapy for Parkinson's disease. However, its use comes with dose-dependent motor complications, such as wearing off and dyskinesias. These complications can be managed with the use of a monoamine oxidase B (MAO-B) inhibitor, a catechol-*O*-methyltransferase inhibitor or a dopamine agonist, although each of these classes has its own tolerability or safety consideration. In recent years, safinamide has gained significant attention as third-generation MAO-B inhibitor which stands out as a reversible and selective inhibitor of voltage-sensitive sodium channel and excessive glutamate release. In this presentation, an overview and comparison of MAO-B inhibitors will be provided. How safinamide works as an add-on therapy to levodopa/carbidopa and results from landmark studies of safinamide will also be discussed. Finally, practical experience, advice, and guidance regarding the use of safinamide in patients with Parkinson's disease will be shared.

S 2

Lundbeck Migraine Symposium
New strategies for the treatment of migraine and medication overuse headache

Hans-Christoph Diener
Department of Neuroepidemiology, Institute for Medical Informatics, Biometry and Epidemiology, University of Duisburg-Essen, Essen, Germany

The breakthrough discovery of calcitonin gene–related peptide (CGRP) is an important new target for developing new treatments for migraine and medication overuse headache (MOH). Both CGRP antagonists and anti-CGRP antibodies are now available in Hong Kong. Among all anti-CGRP antibodies, eptinezumab is a humanised monoclonal antibody selectively and readily binding to both α- and β-CGRP ligands blocking them from binding to CGRP receptors. It is specifically designed to be administered through intravenous infusion to provide efficacious, fast and sustained preventive migraine treatment. In this lecture, the speaker will attempt to differentiate eptinezumab from the other CGRP-targeted treatment for working out the right treatment strategies to manage migraine.

S 3

AbbVie Migraine Lunch Symposium

Latest advances in the preventative treatment of episodic and chronic migraine—from clinical trial to clinical practice

Jason Ray
Alfred Health, Melbourne, Australia

Calcitonin gene–related peptide (CGRP)—targeting therapies represent the culmination of 40 years of translational neuroscience. This session will discuss the development of these therapies and consider them in the context of the existing treatment landscape. The health-economic burden of migraine and existing treatment gaps will be discussed. A summary will be provided on the pivotal clinical trials of CGRP-targeting therapies and key real-world studies that have summarised the efficacy, tolerability and safety of these therapies, and informed the current international treatment guidelines and consensus statements. From this evidence, the position of these therapies in the preventative treatment of migraine and medication overuse headache will be considered. Finally, the safety of the therapies and patient selection will be discussed, and unanswered clinical questions with regard to their use will be explored.

S 4

Pfizer Migraine Symposium

Managing migraine in women: developing patient-centred approaches to care

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[2] King's College Hospital and the Hospital for Sick Children, London, United Kingdom

Migraine is a complex neurological disorder and is estimated to affect over 1 billion people globally.[1] It is characterised by recurrent attacks of headache accompanied by symptoms such as nausea, photophobia, and phonophobia. The severity and frequency of attacks often change over time and can lead to varying degrees of disability. Epidemiological studies consistently demonstrate a higher prevalence of migraine in women compared to men, suggesting a crucial role of sex hormones.

Hormonal fluctuations, particularly those associated with the menstrual cycle, such as oestrogen, are believed to play a role in migraine pathophysiology in women. The treatment of migraine ideally considers each patient's unique characteristics, including migraine frequency, severity, co-morbidities, and hormonal influences.

Calcitonin gene–related peptide receptor antagonists, such as rimegepant, have emerged as promising therapeutic options for acute treatment and prevention of migraine. Clinical trials have demonstrated the efficacy and safety of rimegepant in providing rapid relief from migraine symptoms. Medications offering individualised treatment plans that take into consideration the unique needs of each patient are crucial for optimal management of migraine.

Reference

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S 5

Movement Disorder Symposium
Personalised Parkinson's disease management in the 21st century

SY Lim
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In this talk, the speaker will outline the state-of-art in terms of current management for Parkinson's disease (PD), from diagnosis to treatment. This will include the recent move towards a more biology-centred approach to the diagnosis and classification of PD (incorporating genetics, alpha-synuclein seeding assays, and other biomarkers), pharmacological agents as well as non-pharmacological treatments, including functional neurosurgery.

Because "It is difficult to make predictions, especially about the future", the speaker will only make some tentative speculations about how PD management is likely to evolve in the coming years but with the obvious caveat that totally disruptive technologies cannot really be anticipated.

S 6

Movement Disorder Symposium
Deep brain stimulation in Parkinson's disease: past, present, and future

Aparna Wagle Shukla
Department of Neurology, University of Florida, Gainesville, United States

Deep brain stimulation is a standard of care for managing symptoms of Parkinson's disease. It delivers adjustable electrical stimuli to specific brain targets to modulate functions of pathological circuitry. In the past, deep brain stimulation was utilised for treating symptoms of advanced disease; however, there is compelling data to support its use early in the course, and breakthroughs in lead and battery designs such as directional stimulation and rechargeable systems, development of novel stimulation paradigms such as closed-loop and on-demand stimulation, and availability of sensing and remote programming technologies have led to improved efficacy and tolerability. Specialised imaging sequences, imaging tractography, and connectomics facilitate more accurate targeting and lead positioning. There is a better understanding of Parkinson's disease symptoms more likely to improve and disease subtypes with better outcomes. With these advances, the future of Parkinson's disease therapeutics involving precision and personalised medicine has undoubtedly become highly promising.

S 7

Epilepsy Symposium

EEG and multimodal monitoring for diagnosis and prediction of neurological deterioration, coma, and neurorecovery

Eric Rosenthal
Harvard Medical School, Harvard University, Boston, United States

This talk demonstrates the value of EEG biomarkers in characterising acute neurological illness, detecting seizures, and predicting neurological deterioration and recovery. The talk also clarifies contextual factors including practice pattern and institutional variation necessary for integrating patient-specific knowledge.

S 8

Epilepsy Symposium

Caveats in anti-seizure drug treatment in patients with physical and psychiatric co-morbidities

Jacqueline A French
NYU Comprehensive Epilepsy Center, New York University, New York, United States

In 2023 there are many anti-seizure medicine (ASM) options from which to select for treatment of patients with newly diagnosed and treatment-resistant epilepsy. Each drug has unique characteristics that must be matched with the characteristics of patients to optimise therapy. Therefore, there is no "drug of first choice". Selection must be individualised. The first important aspect of selecting appropriate ASM therapy is choosing a drug that is appropriate for the patients' epilepsy syndrome. However, specific impact of different ASMs on patient's co-morbidities must also be considered.

The most important co-morbidities are mood and psychiatric in nature, including depression, anxiety and suicidality, which can all be worsened by certain ASMs.[1] Some ASMs actually improve mood. Weight is also important to consider, as many ASMs are associated with weight gain, while others can decrease appetite, which can be problematic in children with feeding difficulties. The choice of ASM may be complicated by organ disease, including hepatic and renal dysfunction, and history of renal calculi. Some ASMs may also impact on the heart, either in the near term due to risk for cardiac arrhythmias, or over time as a result of changes in cholesterol metabolism and other factors. It is important to understand the specific adverse reactions associated with specific ASMs, to select the ideal drug for a specific patient.[1-3]

In summary, there is no one-size-fits-all in epilepsy therapy. One needs to assess the needs of individual patients.

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S 9

Eisai MS Symposium
Pre-clinical multiple sclerosis: radiologically isolated syndrome

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The radiologically isolated syndrome (RIS) is characterised by the incidental observation of high-signal anomalies within the brain and/or spinal cord that appear highly suggestive of autoimmune inflammatory demyelination in people without typical symptoms of multiple sclerosis (MS). Retrospective data from large multi-national registries have highlighted risk factors for a first acute demyelinating event or the development of an insidious neurological symptom with progression, fulfilling the criteria for primary progressive MS. The proper identification of subjects with brain lesions typical for MS, at times, remains a challenge due to the high sensitivity of magnetic resonance imaging (MRI) technology. However, applied novel techniques have improved lesion specificity, better differentiating non-specific or microvascular white matter features from those related to MS. In addition, non-neurological symptoms may be present in those without known MRI data prior to the formal diagnosis of MS. The promise of treatment in this pre-clinical phase of MS, known as RIS, is highly appealing, having the capability of preventing or delaying the onset of a first clinical symptom associated with MS. Recently, the results from seminal randomised clinical trials in RIS studying the effects of dimethyl fumarate and teriflunomide on the time to a first clinical event related to MS were released. The results from these studies provide evidence of the benefit of early treatment using two distinct disease-modifying therapies, having different mechanisms of action. Immediately following these two clinical trials, the original 2009 RIS Criteria were updated to better encompass individuals vulnerable to disease that may have been originally excluded. This presentation aims to provide recent scientific advances involving RIS. The 5- and 10-year risk estimates for a first clinical event will be discussed along with identified risk factors for initial symptom onset. The findings from the two recent therapeutic trials aimed at symptom development prevention, namely ARISE (Assessment of Tecfidera® in Radiologically Isolated Syndrome) and TERIS (Randomized, Double-blinded Study of Treatment: Teriflunomide in Radiologically Isolated Syndrome), will be detailed along with the significance of these results to the field of neuroimmunology. Additionally, the revised diagnostic criteria for RIS as well as a discussion involving future research efforts focused on disease prevention will be provided.

S 10

Roche SMA Lunch Symposium
Treating adults with spinal muscular atrophy: opportunities and challenges

Tim Hagenacker
Department of Neurology, Essen University Hospital, Essen, Germany

Prof Hagenacker will be speaking on the new treatment landscape of spinal muscular atrophy, with a focus on the management of adult patients, which is historically a population that has gone untreated due to limitation of treatment options. Prof Hagenacker will be sharing his personal experience and practical considerations.

S 11

Roche SMA Lunch Symposium

Sharing of Hong Kong's experience on the treatment of adult patients with spinal muscular atrophy

Shirley YY Pang
Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong SAR, China

With the recent availability of disease-modifying treatment for spinal muscular atrophy, Dr Pang will share her experiences on the treatment of adult patients with this condition in Hong Kong. Preliminary data on treatment outcome will be presented.

S 12

Novartis MS Symposium

Using high-efficacy treatments early in people with multiple sclerosis: practical considerations and treatment options

Amit Bar-Or
Perelman School of Medicine, University of Pennsylvania, Philadelphia, United States

With increase in treatment options for people with multiple sclerosis, different treatment paradigms are being discussed in the management of the disease. Recent research has highlighted the importance of early intervention with high-efficacy treatments (HETs) to potentially alter the disease course and improve long-term outcomes. In this presentation, Prof Bar-Or will be providing an overview of the rationale behind early HETs, showcasing data on reduction in disease activity and disability progression, as well as discussing the potential benefits and risks of such treatment approach. He will also be addressing the practical considerations for implementing HETs, the rationale behind different treatment options, and the selection of patients. Through this presentation, Prof Bar-Or hopes to share his valuable insights on early HET approach, aiding physicians in deciding the right therapy for the right patient.

S 13

AstraZeneca gMG + NMOSD Symposium

Revolutionising neuroimmunology with complement therapeutics: expanding the horizon for patients with generalised myasthenia gravis and neuromyelitis optica spectrum disorders

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[2] Department of Internal Medicine (Neurology), Keio University School of Medicine, Keio University, Tokyo, Japan

This session explores the advancements in neuroimmunology, focusing on generalised myasthenia gravis (gMG) and neuromyelitis optica spectrum disorders (NMOSDs). Prof Yesim Parman discusses evolving treatment approaches for gMG and her real-world experience of using complement inhibitors. Prof Jin Nakahara presents the latest therapies and research in NMOSDs, with a specific focus on complement therapeutics in Asian patients. The lecture aims to provide healthcare professionals with valuable insights and practical knowledge in managing these conditions. A brief question and answer session allows for participant engagement. Attendees will gain a comprehensive understanding of the potential of complement therapeutics in revolutionising patient care for gMG and NMOSDs.

S 14

AstraZeneca Symposium on Bleeding Management

Revolutionising direct oral anticoagulant–related intracranial haemorrhage management with specific reversal

Thorsten Steiner
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The consumption of direct oral anticoagulants (DOACs), especially in more developed countries, has been increasing over the past decade, accompanied by a recent decrease in warfarin consumption. As a complication of DOAC therapy, major bleeds occur in about 2% to 4% of OAC-treated patients per year. Major DOAC-related bleeding is associated with substantial morbidity and mortality. Intracranial haemorrhage (ICH), although uncommon, is associated with a risk of 30-day mortality that approaches 50%. Concerns about bleeding also likely influence decisions to withhold OACs in eligible patients and to use inappropriately low doses of DOACs for which net clinical benefit is not established. Over the next 50 years, the number of patients with indications for OACs is expected to increase by ≥2.5-fold, making OAC-related bleeding complications a growing major health issue.

Prof Steiner will deliver a keynote lecture to cover the epidemiology, management and unmet need of DOAC-related ICH. With the data support from the ANNEXA (Andexanet Alfa, a Novel Antidote to the Anticoagulation Effects of Factor Xa Inhibitors) trial programme and other real-world evidence, Prof Steiner will also share his experience with the factor Xa inhibitor–specific reversal agent in Germany.

S 15

Biogen Neuromuscular Disease Symposium

From clinical trials to the real world: antisense oligonucleotides for the treatment of neuromuscular diseases

Maggie C Walter
Department of Neurology, Ludwig Maximilians University of Munich, Munich, Germany

Neuromuscular disorders (NMDs), such as Duchenne muscular dystrophy, spinal muscular atrophy and amyotrophic lateral sclerosis, are neurodegenerative diseases characterised primarily by motor neuron loss, muscle weakness and wasting. These diseases are associated with mutations in one or multiple genes, which cause disease by toxic loss-of-function or gain-of-function mechanisms. Antisense oligonucleotides (ASOs), which are short, single-stranded nucleic acids or their analogues complementary to specific sequences in RNA targets, have demonstrated promising experimental results and are at different stages of regulatory approval as treatment for NMDs. In this presentation, key development milestones and mechanism of action of ASOs as therapeutics for NMDs will be described. Potential of ASOs as a therapy will be illustrated by clinical trial results and real-world evidence of nusinersen, a treatment indicated for spinal muscular atrophy. Some ASO therapies in clinical development pipeline will also be discussed.

ES 1

Education Session

Neurogenetics 101: who, what, and how

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The field of genetics has seen a continuing episode of knowledge explosion in the past two decades rooting in the technology development. The huge expansion, even just within the realm of neurology, is becoming difficult to be mastered by single person. On top of explosion, such knowledge now starts to translate into clinical practice, again due to technology advancement.

The amount of information generated in the past two decades should not and cannot be delivered in 30 minutes. Hence the Neurogenetics 101 talk will not be a rundown of introduction to genetics in each and every subspecialty in neurology. Rather, it reflects how the speaker would approach a clinical scenario, perhaps with some personal bias. The discussion will mainly be in the footing of clinicians and will not concentrate much on the societal aspect of genetics.

FP 1

Klotho in the gut-cerebrovascular axis: sex-linked gut microbiome associations with stroke risk and small vessel disease

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Introduction: Causal analysis remains lacking between gut microbiota and cerebrovascular health. Klotho, an antioxidative protein, and vitamin D, implicated in cerebrovascular disease pathogenesis when deficient, may mediate these associations.

Methods: We measured 24-hour ambulatory blood pressure, serum Klotho level, and vitamin D from healthy Chinese aged 39 to 65. Stool shotgun sequencing was performed. Small vessel disease (SVD) scores were calculated from cerebral magnetic resonance imaging, assessing for lacunes, microbleeds, white matter hyperintensities, and enlarged perivascular spaces (EPVS). Linear regression with covariate adjustment (age, sex, body mass index, and smoking status) was conducted using R (version 4.3) with lavaan. A P value of <0.05 (two-sided) was considered significant.

Results: A total of 235 subjects (mean age, 54 ± 7 years; 54.9% women) were included. With covariate adjustment, Klotho was negatively associated with 10-year Framingham Stroke Risk score and hypertension. Klotho was not associated with SVD across sexes but was associated with lacunes and basal ganglia EPVS in females. Vitamin D deficiency (<50 nmol/L) was associated with Klotho, 24-hour systolic blood pressure (SBP), and SVD in females.

Shotgun sequencing revealed enrichment of *Ruminococcus gnavus* in hypertensives, and *Bacteroides fragilis* with white matter hyperintensities and EPVS burden only detected in females. Klotho was negatively associated with *R gnavus* (both sexes) and *B fragilis* (females only).

Covariate-adjusted multiple linear regression of *R gnavus*, Klotho, and vitamin D significantly predicted 24-hour SBP across sexes (R^2=0.12, $\beta 1$=0.13, $\beta 2$=-0.26, and $\beta 3$=-0.16; P=0.02), while *B fragilis*, Klotho, and vitamin D predicted SVD score in females (R^2=0.07, $\beta 1$=0.08, $\beta 2$=-0.12, and $\beta 3$=-0.06; P=0.04).

Only in females did Klotho and vitamin D demonstrate competitive mediation between *R gnavus* and 24-hour SBP (average causal mediation effect [ACME]=0.07; P<0.01) and between *B fragilis* and SVD score (ACME=0.05; P=0.04). Interaction analysis indicated a possible synergistic effect between Klotho and vitamin D.

Conclusion: Species-specific effects in cerebrovascular health are sex-linked and partially mediated by Klotho and vitamin D. Expanded investigations may support downstream causal dynamics from microbiota dysbiosis involving Klotho/vitamin D interactions, allowing sex-specific stroke prevention and prognosis.

FP 2

Low low-density lipoprotein cholesterol levels and the risk of recurrent intracerebral haemorrhage

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Introduction: Recent studies have demonstrated that aggressive low-density lipoprotein cholesterol (LDL-C) lowering did not significantly increase the risk of intracerebral haemorrhage (ICH). However, these results were mainly based on patients without prior ICH. As ICH survivors are prone to recurrence, the safety of aggressive LDL-C lowering post-ICH remains uncertain. We therefore aimed to study the association between LDL-C levels and risk of ICH recurrence.

Methods: We analysed follow-up data of consecutive ICH survivors from The University of Hong Kong's prospective stroke registry who were admitted during January 2011 to March 2019. The mean follow-up LDL-C values was categorised as <1.8 and ≥1.8 mmol/L. The association between LDL-C levels and recurrent ICH was determined and adjusted for confounders including ICH aetiologies and blood pressure control using multivariate Cox regression.

Results: In 508 ICH survivors (mean age, 64 ± 14 years; mean follow-up LDL-C level: 2.7 ± 0.7 mmol/L, 28% with LDL-C level <1.8 mmol/L), 45 had ICH recurrence during a mean follow-up of 6.0 ± 2.9 years. A mean follow-up LDL-C level of <1.8 mmol/L was associated with increased risk of recurrent ICH (adjusted hazard ratio [aHR]=1.91, 95% confidence interval [CI]=1.02-3.56). The effect was more pronounced in individuals aged ≤75 (aHR=2.32, 95% CI=1.06-5.09), male (aHR=3.12, 95% CI=1.35-7.23), post-stroke non-statin users (aHR=2.62, 95% CI=1.00-6.84), and patients with ICH attributable to cerebral amyloid angiopathy [CAA] (aHR=2.58, 95% CI=1.09-6.11). However, post-ICH statin use was not associated with recurrent ICH (aHR=1.02, 95% CI=0.55-1.88).

Conclusion: A LDL-C level of <1.8 mmol/L during follow-up was independently associated with increased risk of ICH recurrence. The association was predominantly observed in subgroups of CAA patients and non-statin users. Statin use and intensive LDL-C targets can still be considered in ICH survivors with established atherosclerotic diseases. However, caution should be exercised in patients with CAA.

FP 3

Characteristics and outcomes of direct oral anticoagulant–associated intracerebral haemorrhage

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Introduction: Direct oral anticoagulants (DOACs) are currently the preferred anticoagulant over warfarin. With its increasing use, DOAC-associated intracerebral haemorrhage (DOAC-ICH) is a common clinical encounter. Whether DOAC-ICH is less severe and associated with better outcomes than warfarin-associated ICH (warfarin-ICH) remains debatable. We therefore aimed to compare the clinical and radiological characteristics as well as outcomes between DOAC-ICH, warfarin-ICH, and non–anticoagulant-associated ICH (non-AC ICH).

Methods: We retrospectively analysed data from The University of Hong Kong stroke registry. Consecutive anticoagulant-associated ICH (AC-ICH) retrieved from the registry included patients admitted to Queen Mary Hospital from 2011 to 2022 and with the addition of three other hospitals (Ruttonjee Hospital, Yan Chai Hospital, and Princess Margaret Hospital) from 2020 to 2022. For controls, we included non-AC ICH patients from Queen Mary Hospital from 2011 to 2018. Outcomes of interest include hematoma expansion (absolute hematoma increase of >6 mL or relative increase of >33%), 1-month and 6-month mortality, and 6-month poor outcome (modified Rankin Scale score of 4 to 6). We performed multivariate logistic regression to investigate the association between DOAC and ICH outcomes.

Results: There were 167 AC-ICH patients. Compared to non-AC ICH, AC-ICH patients were older, with the mean age of DOAC-ICH, warfarin-ICH, and non-AC ICH patients being 80, 71, and 69 years, respectively (P<0.001), and occurred less at deep-seated hypertensive ICH sites (55.1% vs 68.5%; P=0.001). The 1-month mortality, 6-month mortality and 6-month poor outcome rates were comparable between DOAC-ICH and warfarin-ICH patients (45.6% vs 37.7%, 54.4% vs 42.2%, and 78.6% vs 69.7%, respectively; all P>0.05), but were significantly higher than non-AC ICH. Warfarin was associated with a higher risk of hematoma expansion (adjusted odds ratio [aOR]=2.69, 95% confidence interval [CI]=1.18-6.17), 6-month mortality (aOR=2.17, 95% CI=1.01-4.68), and poor outcome (aOR=2.74, 95% CI=1.21-6.20), but not DOACs (all P>0.2).

Conclusion: DOAC-ICH is attributed to both hypertensive arteriopathy and cerebral amyloid angiopathy, and its high mortality and morbidity was likely driven by age.

FP 4

Cross-sectional study of the association between gut microbiome and 24-hour blood pressure variability

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Introduction: Blood pressure (BP) variability is a potential risk factor for several neurological diseases, including Alzheimer's disease, dementia, depression and cerebral small vessel disease. Whilst gut microbiota (GM) dysbiosis may contribute to the pathology of BP dysregulation, the association between GM and BP variability is poorly understood.

Methods: We recruited 241 asymptomatic Hong Kong Chinese (113 males and 128 females; mean age, 54 ± 6 years) who were not on anti-hypertensive agents. Shotgun metagenomic sequencing, 24-hour ambulatory BP monitoring, and short-chain fatty acid (SCFA) measurements in the stool and plasma were performed. Blood pressure variability was assessed using standard deviation (SD) and coefficient of variation (CoV). Statistical analysis was conducted under covariate-adjusted models.

Results: Men had a higher mean 24-hour BP than women (127 ± 13/81 ± 9 mm Hg vs 117 ± 12/71 ± 8 mm Hg; P<0.0001). Despite lower ambulatory BP levels, women had a significantly higher 24-hour systolic BP (SBP) [P=0.0005] and diastolic BP (DBP) [P=0.002] CoV than men. Consistently, we detected a significant negative association between GM α-diversity and 24-hour SBP and DBP CoV and SD in women, but not men, upon covariate adjustments (all P<0.05). No significant correlations between plasma SCFAs and 24-hour SBP/ DBP and CoV or SD were detected. However, several bacterial species were found to be significantly associated with BP variability measures in our cohort. Of note, *Parabacteroides merdae*, which has recently been reported to protect against cardiovascular damage in animal models, had a significant negative association with 24-hour SBP and DBP CoV and SD under different models of covariate adjustments in our cohort. Importantly, *P merdae* had a significant negative association with 24-hour SBP CoV and SD in both women and men upon stratification by sex.

Conclusion: Our shotgun sequencing data unravelled novel sex-linked associations between GM and BP variability measures. Future studies to determine whether oral administration of *P merdae* may reduce BP variability in humans are warranted.

FP 5

Safety and efficacy of direct oral anticoagulants in the oldest old atrial fibrillation patients with recent ischaemic stroke

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Introduction: Evidence on the efficacy and safety of direct oral anticoagulants (DOACs) among atrial fibrillation (AF) patients with recent ischaemic stroke especially among the oldest old is limited, and which DOAC is the optimal choice is unclear.

Methods: Using the electronic health database in Hong Kong, we identified AF patients who were hospitalised for acute ischaemic stroke/transient ischaemic attack with a history of AF or newly diagnosed AF from 2016 to 2020. Clinical endpoints included ischaemic stroke/systemic embolism (SE), intracerebral haemorrhage (ICH), total bleeding, major adverse cardiovascular events (MACE), and all-cause mortality. Competing risk regression and Cox proportional hazards models were used to assess the associations of different antithrombotic strategies at discharge with clinical adverse outcomes.

Results: A total of 1725 patients aged ≥85 were included. Direct oral anticoagulants decreased the risk of all-cause mortality (adjusted hazard ratio [aHR]=0.49, 95% confidence interval [CI]=0.41-0.59) compared to no antithrombotic agent and the risks of ischaemic stroke/SE (aHR=0.61, 95% CI=0.40-0.91) and all-cause mortality (aHR=0.54, 95% CI=0.45-0.64) compared to antiplatelet agent. Direct oral anticoagulants decreased the risks of ischaemic stroke/SE (aHR=0.53, 95% CI=0.30-0.92), MACE (aHR=0.65, 95% CI=0.48-0.88) and all-cause mortality (aHR=0.62, 95% CI=0.47-0.81) compared to warfarin. For individual DOAC, apixaban decreased the risks of ischaemic stroke/SE (aHR=0.49, 95% CI=0.31-0.77) and MACE (aHR=0.68, 95% CI=0.52-0.89) compared to rivaroxaban. Dabigatran decreased the risks of ischaemic stroke/SE (aHR=0.56, 95% CI=0.35-0.90), ICH (aHR=0.32, 95% CI=0.11-0.92), MACE (aHR=0.56, 95% CI=0.42-0.76) and all-cause mortality (aHR=0.72, 95% CI=0.53-0.99) compared to rivaroxaban.

Conclusion: In this population-wide study, DOACs are safe and effective in AF patients with a recent ischaemic stroke aged ≥85. Either apixaban or dabigatran may be a preferable choice when compared to rivaroxaban.

FP 6

Impact of renal function variability on long-term prognosis in ischaemic stroke patients with atrial fibrillation prescribed with oral anticoagulants

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Introduction: Although renal dysfunction is associated with adverse outcomes in patients with atrial fibrillation (AF) following stroke, the impact of renal function variability is unclear. We evaluated the association of renal function variability with various adverse outcomes in patients with AF following transient ischaemic attack (TIA)/ischaemic stroke who were prescribed anticoagulant therapy.

Methods: This was a retrospective, population-based study with data retrieved from electronic health records. Patients hospitalised with a diagnosis of TIA/ischaemic stroke and AF from January 2016 to December 2020 were included. Renal function variability was calculated by the coefficient of variation of estimated glomerular filtration rates (eGFR) during follow-up. Clinical endpoints included ischaemic stroke/systemic embolism, intracerebral haemorrhage (ICH) and extracranial bleeding, major adverse cardiovascular events (MACE), and all-cause mortality. Competing risk regression and Cox proportional hazards regression models were used to assess the association of renal function variability with the outcomes of interest. Patients were also prospectively recruited from hospital-based registries to validate such associations.

Results: A total of 4,014 patients were recruited with a mean follow-up of 2.5 ± 1.5 years. The mean age was 80 ± 11 years and 44% of patients were men. A greater eGFR variability was associated with increased risk of recurrent ischaemic stroke/systemic embolism (adjusted hazard ratio [aHR]=1.10, 95% confidence interval [CI]=1.02-1.19), total bleeding (aHR=1.09, 95% CI=1.02-1.16), MACE (aHR=1.24, 95% CI=1.17-1.32), and all-cause mortality (aHR=1.47, 95% CI=1.42-1.52). In patients prescribed a direct oral anticoagulant, greater eGFR variability was also significantly associated with ICH (aHR=1.33, 95% CI=1.06-1.66).

Conclusion: Visit-to-visit renal function variability was associated with adverse clinical outcomes in patients with AF following TIA/ischaemic stroke.

A case of hereditary transthyretin amyloidosis: diagnostic complexity resolved through integrated analysis and targeted genetic investigation

P 1

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Introduction: Hereditary transthyretin amyloidosis, a genetic condition typically manifesting as late-onset polyneuropathy, has been frequently misdiagnosed as chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). This underlies the importance of a thorough diagnostic process in accurately identifying and managing the condition.

Case report: A 73-year-old gentleman of East-Asian descent with pre-existing hypertension and hyperlipidaemia initially presented with difficulty in ascending stairs. His clinical course showed gradual worsening of length-dependent polyneuropathy, evidenced by muscle wasting, numbness and diffuse hyporeflexia. Besides, he also complained of some autonomic symptoms such as frequent diarrhoea. An extensive evaluation that covered metabolic, endocrine, paraneoplastic, autoimmune, and infectious causes, including lumbar puncture, magnetic resonance imaging of the brain and spine, positron emission tomography–computed tomography, myeloma screening, and ganglioside antibody testing, yielded either negative or non-significant results. His nerve conduction studies displayed axonal neuropathy, yet sural nerve biopsy hinted at early CIDP, a contradiction between electrophysiological and histological results. He was initially managed as CIDP with intravenous immunoglobulin, corticosteroids, and rituximab, but showed no response to any of these interventions. A significant turn in the diagnostic process occurred when he was found to have an elevated serum free kappa light chain level (29.36 mg/L) and revealed a family history of his father having similar neuropathic manifestations at the age of 70s. Nuclear scintigraphy was performed and revealed myocardial amyloidosis. Eventually, a transthyretin full gene analysis identified a pathogenic single nucleotide polymorphism of the DNA change (c.148G>A) and the subsequent amino acid change (*p. V50M*). In light of this, the patient was initiated on tafamidis therapy to manage transthyretin amyloidosis.

Conclusion: This case highlights the complexity involved in distinguishing hereditary transthyretin amyloidosis from CIDP. It emphasises the importance of a positive family history and elevated serum free kappa light chain level, along with genetic analysis, to initiate timely and appropriate targeted treatment for patients with this condition.

Two cases of co-existing GD1b immunoglobulin G and GM1 immunoglobulin G with severe distal weakness

P 2

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Introduction: Gangliosides are glycosphingolipids enriched on neuronal cell surface, and antibodies against such gangliosides are associated with various forms of neuropathies. Two cases with co-positive GD1b immunoglobulin G (IgG) and GM1 IgG presented with severe distal weakness are reported.

Case reports: A 23-year-old man had a 2-day history of distal four limb weakness. Wrist extension and ankle dorsiflexion were weak (grade 2 on the Medical Research Council [MRC] scale) bilaterally with generalised hyporeflexia. Light touch sensation was impaired in a glove-and-stocking distribution. No albuminocytological dissociation was detected in cerebral spinal fluid and the patient defaulted nerve conduction study. However, blood test showed strongly positive for GD1b IgG and GM1 IgG. He was treated as Guillain-Barré syndrome with a course of intravenous Ig but improvement was mild.

A 66-year-old lady had a 1-day history of bilateral lower limb weakness preceded with diarrhoea. Hip flexion, knee extension and flexion, plantarflexion, and dorsiflexion were of MRC scale grade 5, 4, 3, and 1, respectively, with areflexic knee and ankle jerk. Sensation was intact. Nerve conduction study showed severe sensory and motor polyneuropathy of axonal type with secondary demyelination. Again, no albuminocytological dissociation was detected in cerebral spinal fluid, while blood tests showed strongly positive for GD1b IgG and GM1 IgG. She was then given a course of intravenous Ig followed by five exchanges of plasmapheresis. However, recovery was slow with being a frame walker after 1 month of rehabilitation.

Conclusion: Anti-GD1b antibody predominantly attacks sensory neurons in dorsal root ganglia, while anti-GM1 antibody targets the motor endplates of axon. Therefore, the co-existence of both sensory and motor neuropathies resulted in poor outcome seen in these two patients. The lack of albuminocytological dissociation should not deter us from ordering anti-gangliosides antibody to reach the diagnosis of Guillain-Barré syndrome.

Clinical outcomes of treating migraine patients with calcitonin gene–related peptide monoclonal antibody in Hong Kong

P 3

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Introduction: With the approval of calcitonin gene–related peptide (CGRP) monoclonal antibody (mAb), the symptom control of frequent episodic migraine (EM) and chronic migraine (CM) has improved significantly. The data of its use in local Hong Kong migraineurs has been lacking.

Methods: We performed a retrospective review of the clinical outcomes in patients using subcutaneous CGRP mAb for the treatment of frequent EM and CM from Headache and Facial Pain Clinic of United Christian Hospital.

Results: After excluding patients with poor drug compliance or default of follow-up, 35 patients were prescribed with erenumab, 29 were prescribed with galcanezumab, and one was prescribed with fremanezumab. As the number of fremanezumab users was very limited, treatment outcome was not compared with the other two CGRP mAbs in this study.

Among erenumab users, 10 (29%) patients showed <50% response in the reduction of monthly migraine days, 13 (37%) patients were 50% to 75% responders, and 12 (34%) were ≥75% responders. Among galcanezumab users, 10 (34%) patients showed <50% response, 11 (38%) patients were 50% to 75% responders, and 8 (28%) were ≥75% responders.

For adverse effects, injection site reaction (including rash, itchiness and pain) was common but was very mild in both groups. Constipation was more common in erenumab users (6 cases of mild constipation, 3 moderate and 1 severe). One galcanezumab user reported mild constipation. Other uncommon side-effects included dizziness, nausea, malaise, hoarseness, and exacerbation of headache. Eleven patients had switched between CGRP mAb therapies because of the adverse events or suboptimal efficacy. Most patients showed good drug adherence and found it convenient for self-injection at home.

Conclusion: A significant number of erenumab and galcanezumab users can achieve >50% reduction in monthly migraine days (71% and 66%, respectively). Constipation is more common after erenumab injection, and most cases are mild to moderate. Switching between CGRP mAbs can be considered when the side-effect profile or efficacy are of concern. A larger sized study is warranted in the future to draw a more conclusive result.

Inflammatory myopathy with myocarditis and orbital myositis: a case report

P 4

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Idiopathic inflammatory myopathies (IIMs) are autoimmune-mediated diseases with high heterogeneity and multisystem involvement. Distinct subtypes of IIMs include dermatomyositis, polymyositis, inclusion body myositis, immune-mediated necrotising myopathy, anti-synthetase syndrome, and overlap myositis. Limited reports have described patients with concurrent inflammatory myositis, orbital myositis and myocarditis. We hereby present a rare case of inflammatory myopathy in a 54-year-old woman who experienced subacute onset of progressive external ophthalmoplegia and dysphagia, further complicated by cardiomyopathy and decompensated type II respiratory failure requiring mechanical ventilation. Skeletal muscle involvement was not profound and her limbs' power was only mildly reduced to grade 4+/5 on the Medical Research Council Scale for Muscle Strength. Serum creatinine kinase and troponin I levels were elevated at 8290 U/L and 8030 ng/L at presentation, respectively. Electrocardiogram showed dynamic changes over precordial leads. Mildly reduced left ventricular ejection fraction of 40% without any regional wall movement abnormality was detected on echocardiogram. Myositis-specific and myositis-associated autoantibodies were tested negative. Muscle biopsy sampled at vastus lateralis revealed endomysial and perimysial inflammatory infiltrates consistent with inflammatory myopathy. Treatment was initiated with systemic corticosteroid, intravenous immunoglobulin and azathioprine, which showed good response. Mechanical ventilation was successfully weaned off. Improvement was seen in extraocular movement. Serum muscle and cardiac enzymes had gone down to within normal limits. Our case highlights a distinct presentation of seronegative IIMs with prominent extra skeletal muscle involvement.

AUTHOR INDEX

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